

Amivantamab Plus Pembrolizumab in Previously Untreated Recurrent/Metastatic Head & Neck Squamous Cell Cancer: Results From the Phase 1b/2 OrigAMI-4 Study

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Disclosures

- Raneeh Mehra received consulting fees from Johnson & Johnson, Merck KGaA, Merus, and Summit; and received support for travel from Bicara. Spouse has stock options with GSK; and is an employee of AstraZeneca

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Background

- In first-line R/M HNSCC, pembrolizumab and pembrolizumab plus chemotherapy demonstrated an ORR of 19% and 36%, with a median PFS of 3.2 months and 5.0 months, respectively^{1,a}
- Amivantamab (anti-EGFR/MET bispecific) monotherapy has shown an ORR of 45% in HPV-unrelated R/M HNSCC after disease progression on checkpoint inhibitor and platinum-based chemotherapy²
 - FDA has granted breakthrough therapy designation for this setting
- Combining EGFR & MET inhibition with PD-1 blockage may be beneficial
 - We evaluated **subcutaneous amivantamab Q3W** in combination with **pembrolizumab** in first-line HPV-unrelated R/M HNSCC

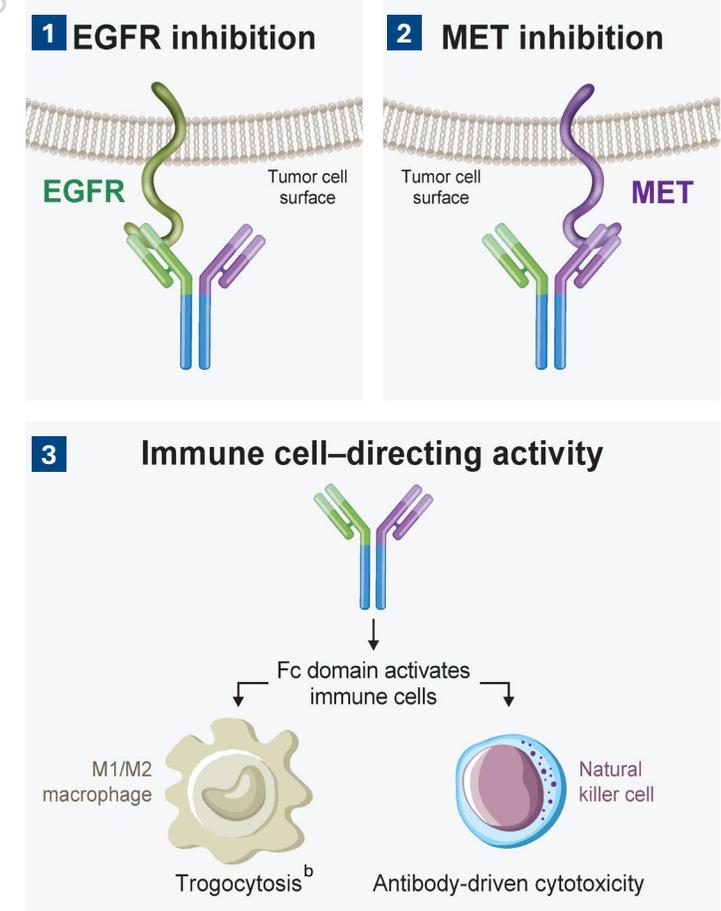
Approved uses of amivantamab

- *Amivantamab-based combinations have been approved in 4 NSCLC indications³*
- *In first-line common EGFR-mutated advanced NSCLC, amivantamab plus lazertinib (3rd-gen EGFR TKI) improved OS and reduced EGFR- and MET-related resistance vs osimertinib^{4,5}*

^aIn participants with CPS ≥1. ^bTrogocytosis is defined as tumor-targeted antibody-mediated transfer of membrane fragments/ligands from tumor cells to effector cells.⁷

1. Burtneß B, et al. *Lancet*. 2019;394(10212):1915–1928. 2. Harrington KJ, et al. *Oral Oncol*. 2025;171:107791. 3. RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) injection, for subcutaneous use [package insert]. Janssen Biotech, Inc., 2025. 4. Hayashi H, et al. Presented at: World Conference on Lung Cancer (WCLC); September 6–9, 2025; Barcelona, Spain. Poster PT1.03.06. 5. Yang JCH, et al. *N Engl J Med*. 2025;393(17):1681–1693. 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.

Amivantamab's triple-action mechanism^{6,7}



Study Design

Eligibility criteria for Cohort 2

- R/M HNSCC
- PD-L1 CPS ≥1
- Negative p16 status for oropharyngeal tumors
- No prior anti-EGFR or anti-PD-(L)1 therapy^a
- ECOG PS score: 0 or 1

Subcutaneous amivantamab was administered at 2400 mg (or 3360 mg if ≥80 kg) Q3W^b

IV pembrolizumab was administered at 200 mg Q3W

Cohort 1: Amivantamab monotherapy in HPV-unrelated
Post-PD-(L)1 inhibitor and platinum-based chemotherapy

Preliminary results of Coh 1 was presented at ESMO 2025 and published in Oral Oncology (Harrington KJ, et al. 2025)

Cohort 2: Amivantamab plus pembrolizumab in HPV-unrelated
Treatment naïve in the R/M setting

Focus of this presentation

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

End points for Cohort 2^c

- ORR (primary)
- Duration of response
- Clinical benefit rate^d
- Progression-free survival
- Overall survival
- Safety

Responses were assessed by the investigator per RECIST v1.1

Coh 6 TiP to be presented by Dr. Adkins on Feb 19, 4:30–5:30 pm

ClinicalTrials.gov Identifier: NCT06385080.

Note: All cohorts in OrigAMI-4 utilized the subcutaneous formulation of amivantamab (coformulated with recombinant human hyaluronidase PH20) and manually injected in the abdomen. ^aOther systemic therapies were permitted if they were given as part of treatment for locally advanced disease with curative intent, completed ≥6 months prior to first study treatment administration, and did not result in disease progression within 6 months of completion. ^bEach cycle was 21 days (3 weeks); Cycle 1: 1600 mg (or 2240 mg if ≥80 kg) on Day 1, 2400 mg (or 3360 mg if ≥80 kg) on Day 8 and Day 15; Cycle 2 (and thereafter): 2400 mg (or 3360 mg if ≥80 kg) on Day 1. ^cDisease assessment began at Week 9, with subsequent assessments conducted every 6 weeks for Cohort 2. ^dClinical benefit rate was defined as percentage of confirmed complete or partial responders or durable stable disease (at the second disease assessment).

For more information on OrigAMI-4, please scan this QR code.



Demographic and Baseline Disease Characteristics

- Cohort 2 is fully enrolled, with 39 participants having received subcutaneous amivantamab plus pembrolizumab
- As of December 16, 2025, the median follow-up was 10.4 months (range, 1.6–12.5)
- As of the data cutoff, first-line study treatment was ongoing in 18 of 39 (46%) participants
- 19 participants received prior platinum-based systemic therapy for locally advanced disease
 - Platinum-refractory disease progression ≤6 months was exclusionary

Characteristic, n (%)	All participants (N=39)
Age, median (range), years	63 (39–77)
Male / female	33 (85) / 6 (15)
Race	
Asian	18 (46)
White	20 (51)
Not reported	1 (3)
ECOG PS score 0 / 1	17 (44) / 22 (56)
Primary tumor location	
Oropharynx ^a	6 (15)
Oral cavity	18 (46)
Hypopharynx	8 (21)
Larynx	7 (18)
PD-L1 CPS^b	
1–19	19 (49)
≥20	20 (51)

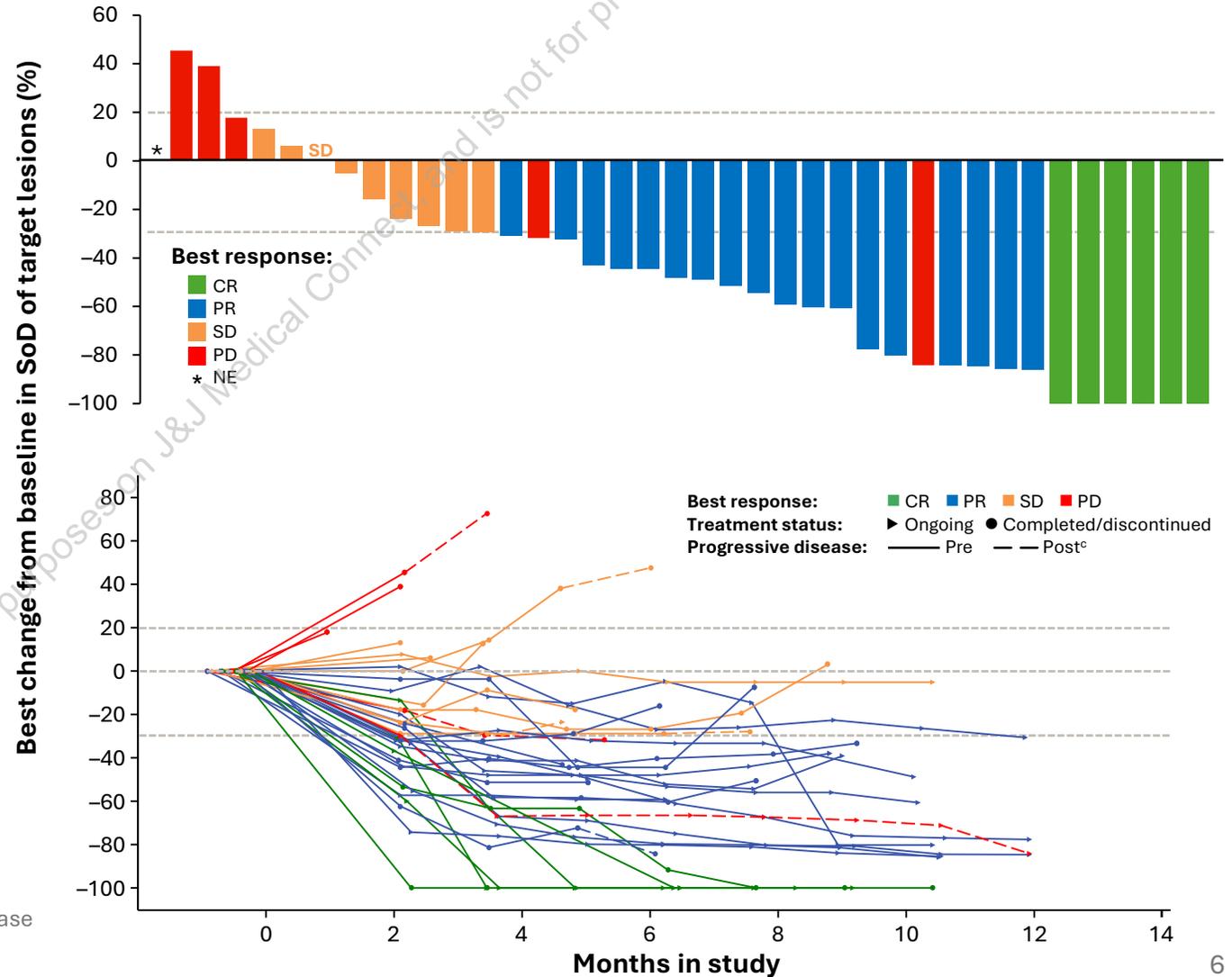
^aPer inclusion criteria, all 6 participants with oropharynx as primary tumor location were HPV-negative. ^bPD-L1 CPS was documented by local testing using a 22C3 antibody test.

ORR and Best Response

INV-assessed	N=39
Confirmed ORR	56% (95% CI, 40–72)
Best confirmed response	
CR	4 (10%)
PR	18 (46%)
SD	11 (28%)
PD	5 (13%)
Not evaluable	1 (3%)
Time to first response^a	9.7 weeks
Clinical benefit rate^b	74% (95% CI, 58–87)

- A majority of participants (82%) experienced tumor shrinkage of their target lesions
- ORR was 47% (95% CI, 24–71) for CPS 1–19 and 65% (95% CI, 41–85) for CPS ≥20

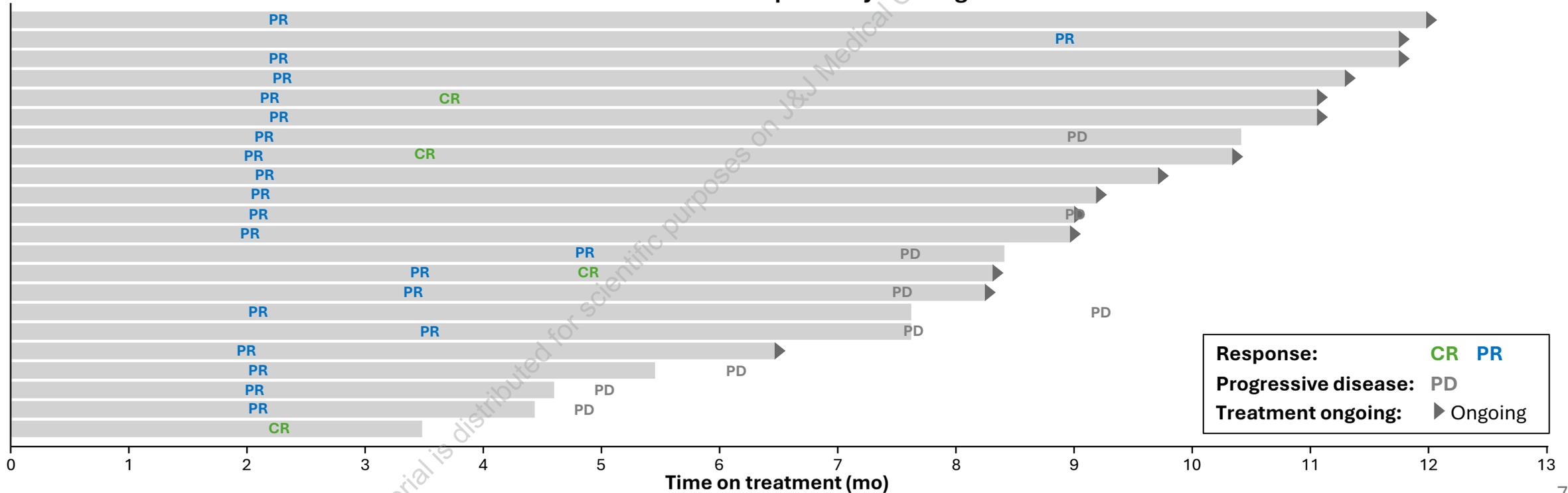
^aAmong all responders; first scan occurred at Week 9. ^bClinical benefit rate was defined as percentage of confirmed complete or partial responders or durable SD (at the second disease assessment). ^cTreatment beyond disease progression was allowed if there was continued clinical benefit.



Durability

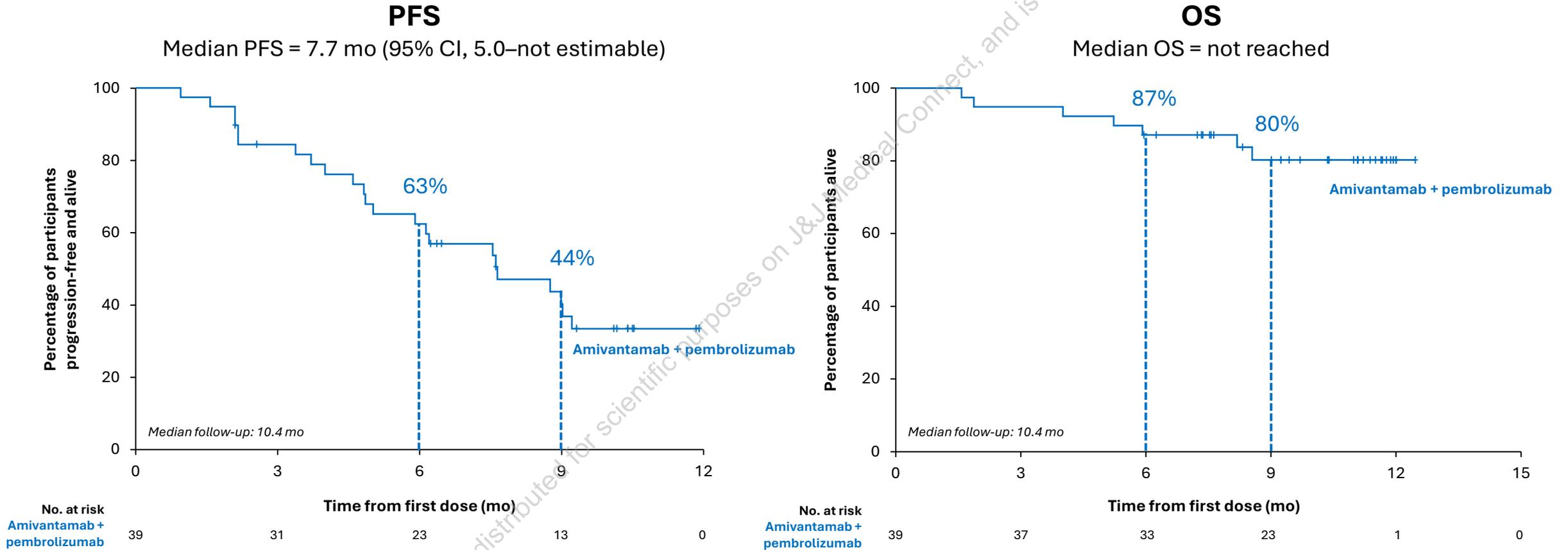
- Among the 22 participants with a confirmed response, 64% are ongoing treatment:
 - Five had a late first response (after 3 months of treatment)
 - Of the remaining 17 with sufficient follow-up, median duration of response was not reached
 - 59% had a DoR \geq 6 months

Confirmed duration of response by investigator review



PFS and OS

- A durable PFS and OS benefit was observed, with 44% of participants remaining progression-free and 80% alive at 9 months^a

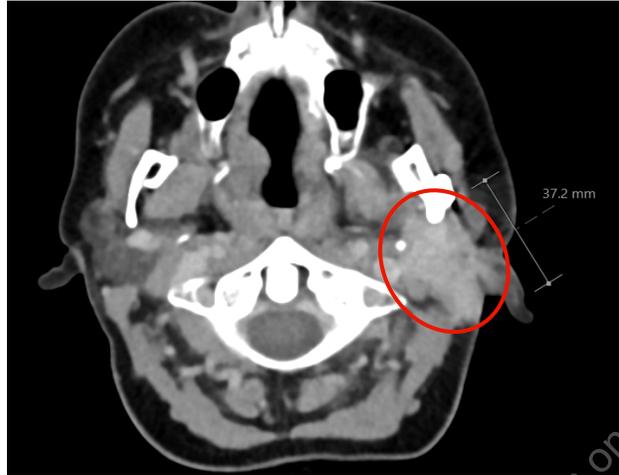


^aIn KEYNOTE-048, median PFS and median OS with pembrolizumab monotherapy in the total population was 2.3 months (95% CI, 2.2–3.3) and 11.5 months (95% CI, 10.3–13.5), respectively.¹

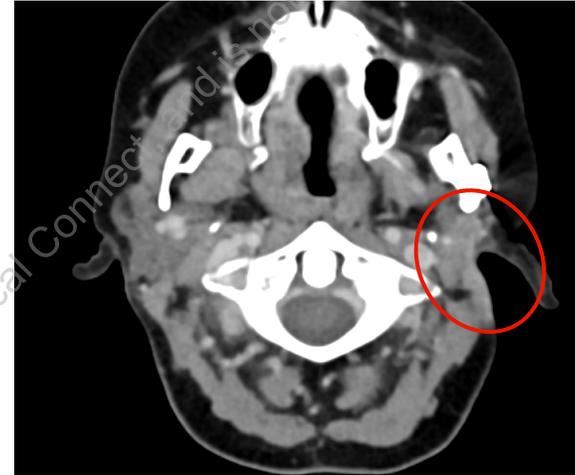
1. Harrington KJ, et al. *J Clin Oncol.* 2023;41(4):790–802.

Deep Responses Observed With Amivantamab Plus Pembrolizumab

CT Scan at Baseline



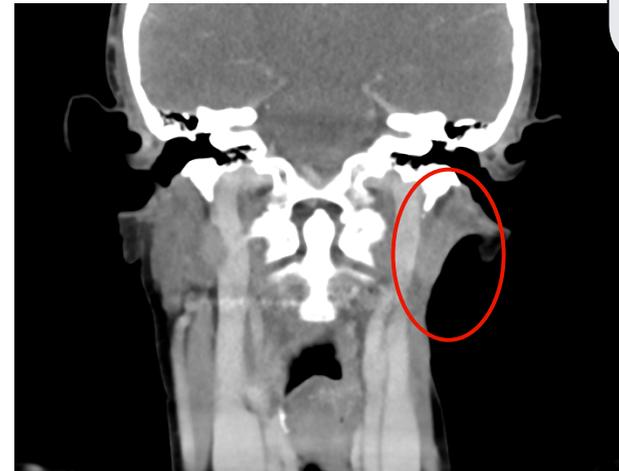
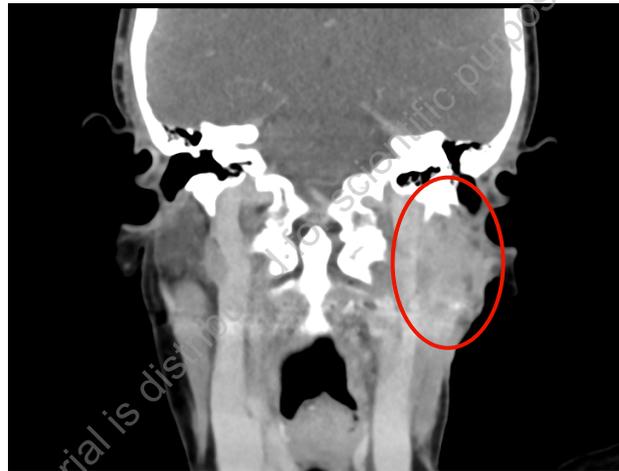
CT Scan at Week 21



Complete response
after 7 cycles of
amivantamab plus
pembrolizumab

46-year-old female with
squamous cell carcinoma
of oral cavity

Previously treated with
surgery and adjuvant
chemoradiation, with a large
recurrent tumor in left
parotid area (PD-L1 CPS=40)



Safety of Subcutaneous Amivantamab Plus Pembrolizumab

- Median treatment duration was 7.6 months (range, 0.7–12.2)
- Most common AEs were related to EGFR or MET inhibition or associated with immunotherapy, with no new safety signals
- Four (10%) participants discontinued treatment due to treatment-related AEs^a
- Administration-related reactions occurred in 6 (15%; all grade 1 or 2) participants
- Hypomagnesemia rates were low (21%), with no grade ≥3 events
- Safety profile of the combination was consistent with those of the individual agents

Treatment-emergent AEs (≥20%) by preferred term	All participants (N=39)	
	Any grade	Grade ≥3
Related to EGFR inhibition		
Rash	19 (49)	5 (13)
Paronychia	18 (46)	2 (5)
Dermatitis acneiform	15 (38)	2 (5)
Stomatitis	14 (36)	2 (5)
Related to MET inhibition		
Hypoalbuminemia	16 (41)	2 (5)
Peripheral edema	8 (21)	0
Other		
Aspartate aminotransferase increased	15 (38)	1 (3)
Alanine aminotransferase increased	14 (36)	2 (5)
Fatigue ^b	11 (28)	1 (3)
Hypothyroidism ^b	10 (26)	0
Constipation ^b	9 (23)	0
Hypomagnesemia	8 (21)	0
Pneumonia ^c	8 (21)	6 (15)

^aPneumonitis (2 participants; 1 grade 2 and 1 grade 3), hepatitis (1 participant; grade 3), and Stevens-Johnson syndrome (1 participant; grade 4). ^bOccurred in ≥15% of participants in the pembrolizumab monotherapy arm from KEYNOTE-048. ^cIn addition, pneumonitis and pneumonia aspiration were each reported in 3 (8%) participants (grade ≥3, 1 participant).

1. Burtness B, et al. *Lancet*. 2019;394(10212):1915–1928.

Conclusions

- First-line subcutaneous amivantamab plus pembrolizumab demonstrated an ORR of 56% in HPV-unrelated R/M HNSCC
 - CRs were seen in 10% of participants
 - 82% of participants had tumor shrinkage of target lesions
 - At a median follow-up of 10.4 months, median PFS was 7.7 months and median OS was not reached
 - 80% of participants were alive at 9 months
- The safety profile of the combination was tolerable and consistent with that of each individual agent; no new safety signals were identified

Subcutaneous amivantamab plus pembrolizumab and carboplatin will be evaluated for R/M HNSCC in a first-line, phase 3 trial, which is currently enrolling globally



Previously untreated, HPV-unrelated, R/M HNSCC^a

R
1:1

**Subcutaneous amivantamab plus
pembrolizumab plus carboplatin (n≈250)**

**5-FU plus pembrolizumab
plus cisplatin OR carboplatin (n≈250)**

ClinicalTrials.gov Identifier: NCT07276399.

^aThere will be no enrollment restrictions based on PD-L1 CPS status. Carboplatin was added to enable eligibility irrespective of CPS status.

For more information on OrigAMI-5,
please scan this QR code.



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Acknowledgments

- Participants who were enrolled in the study and their families and caregivers
- Physicians and nurses who cared for participants and staff members who supported this clinical trial
- Staff members at the study sites and involved in data collection/analyses
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OrigAMI-4 is currently enrolling at 55 sites from 11 countries/regions

