

Amivantamab + pembrolizumab + carboplatin in first-line recurrent/metastatic head & neck squamous cell cancer (1L R/M HNSCC)

Results from the phase 1b/2 OrigAMI-4 study

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Disclosures

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Background

- In KEYNOTE-048, 1L pembrolizumab + 5-FU + platinum demonstrated an ORR of 36%, with a median PFS of 5.0 mo (12-mo PFS rate, 19%) and a median OS of 13.6 months (12-mo OS rate, 55%) in CPS PD-L1 ≥ 1 R/M HNSCC¹
- Amivantamab, an EGFR-MET bispecific antibody, has demonstrated antitumor activity in R/M HNSCC after ICI and platinum-based chemotherapy and as 1L treatment combined with pembrolizumab in the OrigAMI-4 study (ClinicalTrials.gov Identifier: NCT06385080)^{2,3}
- MET is a compensatory escape and resistance pathway to anti-EGFR therapy⁴

Here, we present early efficacy and safety of the triplet regimen of 1L amivantamab + pembrolizumab + carboplatin^a from the phase 1b/2 OrigAMI-4 study

^aUp to 6 cycles.

CPS, combined positive score; HPV, human papillomavirus; ICI, immune checkpoint inhibitor.

1. Burtneß B, et al. *Lancet*. 2019;394(10212):1915–1928. 2. Burtneß B, et al. *J Clin Oncol*. 2026;44(24):2271–2277. 3. Kao HF, et al. *Clin Cancer Res*. 2026. doi: 10.1158/1078-0432.CCR-26-1372.

4. Rothenberger NJ, Stabile LP. *Cancers (Basel)*. 2017;9(4):39.



OrigAMI-4: Study Design

Eligibility criteria for Cohort 5

- R/M HNSCC
- No prior anti-EGFR or anti-PD-(L)1
- ECOG PS score of 0 or 1
- Documented PD-L1 CPS ≥ 1
- Documented HPV status for OPSCC
(both HPV+ and HPV- were allowed)

Drug administration schedule^a

- Amivantamab 2400 mg (≥ 80 kg, 3360 mg) SC Q3W
- Pembrolizumab 200 mg IV Q3W
- Carboplatin AUC 5 IV up to 6 cycles, followed by amivantamab + pembrolizumab maintenance

Cohort 1: Amivantamab monotherapy^b

Post-PD-(L)1 inhibitor and platinum-based chemotherapy^c

Cohort 2: Amivantamab + pembrolizumab^{b,d}

Treatment naïve in the R/M setting

Cohort 3: Amivantamab + paclitaxel^b

Post-PD-(L)1 inhibitor

Cohort 4: Amivantamab monotherapy^e

Post-PD-(L)1 inhibitor and platinum-based chemotherapy^c

Cohort 5: Amivantamab + pembrolizumab + carboplatin^{d,e}

Treatment naïve in the R/M setting

Cohort 6: Amivantamab + pembrolizumab^b

Treatment naïve in the locally advanced, perioperative setting

Endpoints

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

Responses were assessed by the investigator per RECIST v1.1 and confirmed via BICR

Treatment beyond progression was permitted for continued clinical benefit per investigator

Focus of this presentation

A sample size of 26 response-evaluable participants would provide $>80\%$ power to reject the null hypothesis ($\text{ORR} \leq 36\%$), assuming an ORR of 60% with a 1-sided alpha of 5%^g

OrigAMI-4 (ClinicalTrials.gov Identifier: NCT06385080); clinical cutoff: June 16, 2026. Note: All cohorts of OrigAMI-4 utilize the SC formulation of amivantamab, which is co-formulated with recombinant human hyaluronidase PH20 and manually injected in the abdomen.

^aEach cycle is 21 days (3 weeks); Cycle 1: Amivantamab 1600 mg (or 2240 mg if ≥ 80 kg) on Day 1, 2400 mg (or 3360 mg if ≥ 80 kg) on Days 8 and 15; Cycle 2 (and thereafter): 2400 mg (or 3360 mg if ≥ 80 kg) on Day 1. Pembrolizumab 200 mg and carboplatin at an AUC 5 mg/mL·min were administered IV on Day 1 Q3W, with carboplatin administered for a maximum of 6 cycles. ^bParticipants with HPV-related (HPV+ OPSCC) were excluded. ^cEligible participants must have received an anti-PD-(L)1 and platinum-based chemotherapy in combination or as separate lines of therapy for R/M disease. A participant could have received 1 or both treatments in the locally advanced disease if progression was within 6 mo. ^dParticipants who had disease progression within 6 mo of completing prior curatively intended systemic treatment for locally advanced disease were excluded. Systemic therapy completed >6 mo prior to first study treatment administration was permitted if given for locally advanced disease with curative intent, except for anti-EGFR or anti-PD-(L)1 therapy. ^eParticipants with HPV-related (HPV+ OPSCC) were included. ^fClinical benefit rate was defined as percentage of participants with confirmed response or durable stable disease (at the second disease assessment). ^gThe null hypothesis was based on an ORR of 36% as demonstrated with 1L pembrolizumab + chemotherapy in R/M HNSCC with a PD-L1 CPS ≥ 1 .¹

AUC, area under the curve; CPS, combined positive score; HPV, human papillomavirus; OPSCC, oropharyngeal squamous cell cancer; SC, subcutaneous. 1. Burtneß B, et al. *Lancet*. 2019;394(10212):1915–1928.

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Demographic and Baseline Disease Characteristics

- Among the 30 participants enrolled, 1 was deemed ineligible,^a leaving 29 response-evaluable (efficacy dataset)
 - 22 were HPV-unrelated (oral cavity, larynx, hypopharynx, and HPV-negative oropharynx)
 - 7 were HPV-related (HPV+ oropharynx)
- Median follow-up was 10.6 mo (range, 3.0–13.3), and median treatment duration was 6.3 mo (range, 0–13.3)
 - Median number of carboplatin cycles was 4.5 (range, 1–6)
- As of June 16, 2026, treatment was ongoing in 40% of participants

Characteristic, n (%)	Total population (N=30)	HPV-unrelated (n=22)
Age, median (range), years	66 (45–81)	67 (47–81)
Male / female	22 (73) / 8 (27)	16 (73) / 6 (27)
Race		
White	22 (73)	17 (77)
Asian	2 (7)	1 (5)
Other	6 (20) ^b	4 (18) ^c
ECOG PS score of 0 / 1	16 (53) / 14 (47)	11 (50) / 11 (50)
Primary tumor location		
Oral cavity	12 (40)	12 (55)
Oropharynx	11 (37) ^d	3 (14) ^e
Larynx	4 (13)	4 (18)
Hypopharynx	3 (10)	3 (14)
Location of R/M at screening		
Locoregional only	13 (43)	10 (45)
Locoregional and distant	10 (33)	7 (32)
Distant only	7 (23)	5 (23)
History of smoking ^f	21 (70)	17 (77)
CPS of 1–19 / ≥20	9 (30) / 21 (70)	6 (27) / 16 (73)

^aRetrospectively, patient history revealed a diagnosis of lymphoma. ^bOther included not reported (n=4) and multiple (n=2). ^cOther included not reported for all 4 participants. ^dOf the 11 participants with oropharyngeal cancer, p16 was negative in 4 participants.

^eAll 3 participants with oropharyngeal cancer had p16-negative tumors. ^fIncluded current and former smoking.

CPS, combined positive score; HPV, human papillomavirus.



ORR and Best Response

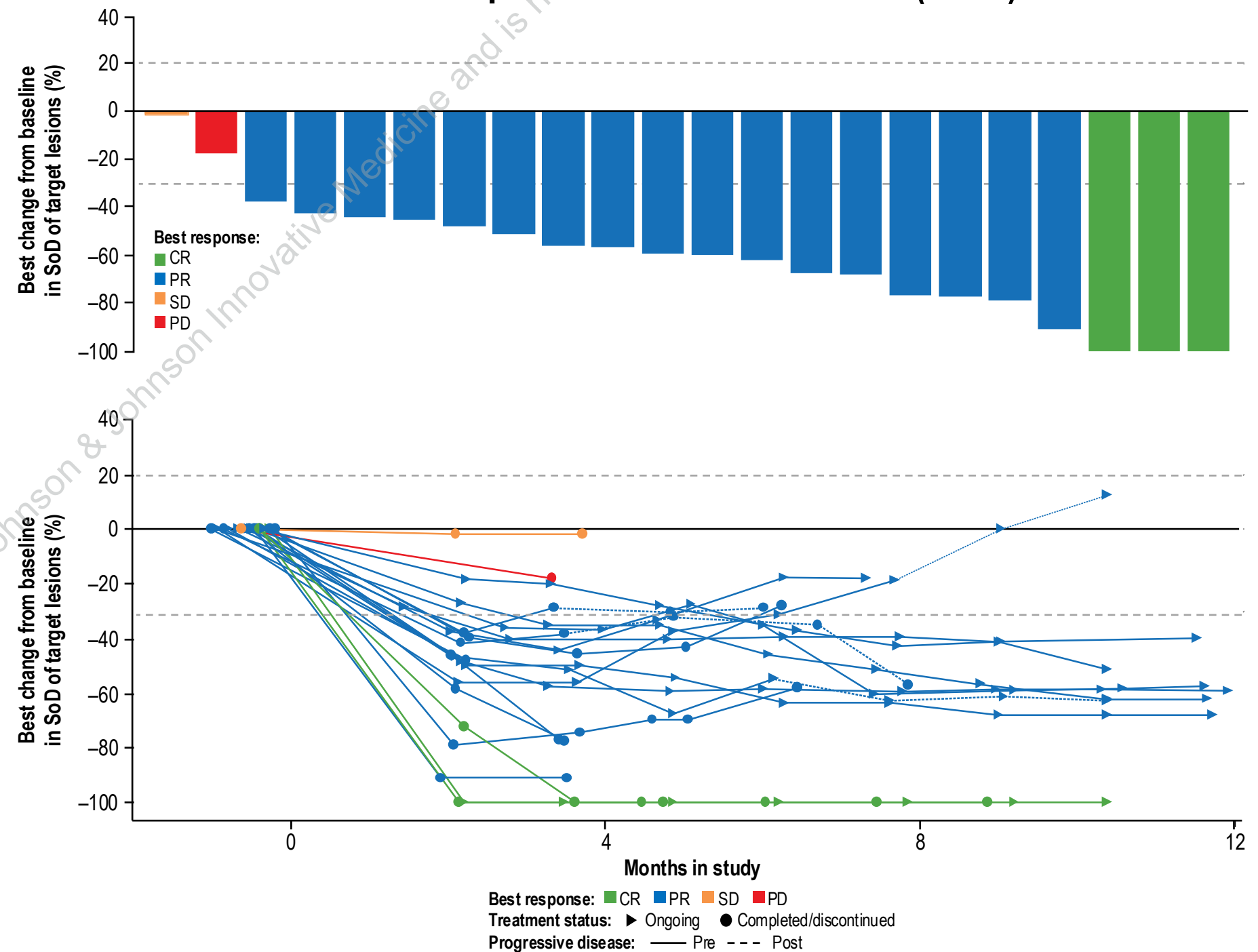
Among the 29 participants in the efficacy population, the confirmed ORR was 66% (95% CI, 46–82), meeting the prespecified statistical hypothesis

INV-assessed response ^a	HPV-unrelated (n=22)	HPV-related ^b (n=7)
Confirmed ORR, % (95% CI)	77 (55–92)	29 (4–71)
Confirmed response, n (%)		
CR	3 (14)	0
PR	14 (64)	2 (29)
SD	4 (18)	2 (29)
PD	1 (5)	2 (29)
NE	0	1 (14)
Time to first response, wk (range) ^c	9.4 (8.3–28.0)	18.1 (9.1–27.1)
Clinical benefit rate, % (95% CI) ^d	82 (60–95)	57 (18–90)

- All participants (100%) with HPV-unrelated disease had tumor shrinkage of their target lesions
- Among confirmed responders with HPV-unrelated disease (n=17), median DoR was NR (95% CI, 4.0–NR), with 65% ongoing

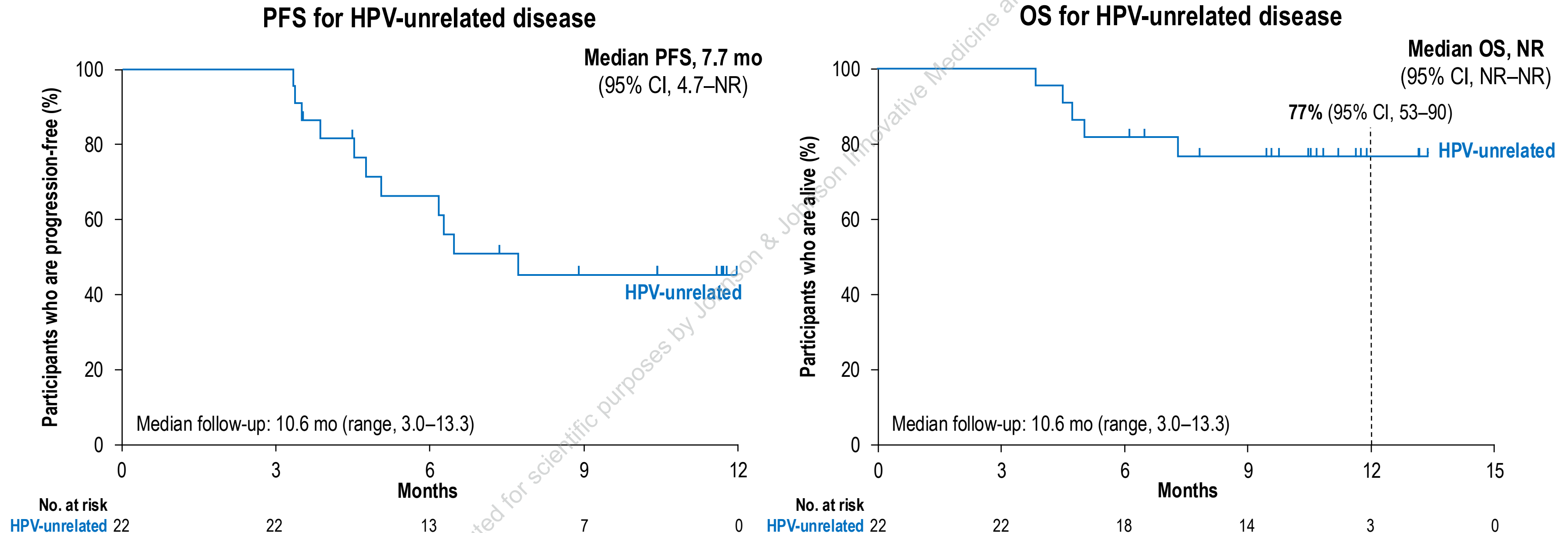
^aDisease assessments began at Week 9 (+1 week) and were conducted every 6 weeks (±1 week) up to 1 year, then every 9 weeks (±1 week) after the first year in Cohort 5. ^bPrimary tumor location was oropharynx and p16 or high-risk ISH HPV+. ^cTime to first response was calculated from the first dose to the first documented response for participants who achieved CR or PR. ^dClinical benefit rate was defined as the percentage of participants who achieved confirmed complete or partial response, or durable stable disease at the second disease assessment. HPV, human papillomavirus; INV, investigator; ISH, in situ hybridization; NR, not reached; SoD, sum of diameters.

Best Response for HPV-unrelated (n=22)



PFS and OS

- 77% of participants with HPV-unrelated HNSCC were alive at 1 year



- In the HPV-related subgroup (n=7), median PFS was 4.6 mo and median OS was NR

HPV, human papillomavirus; NR, not reached.

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Safety

- Safety profile of the triplet combination was consistent with previous reports of the individual components,^{1–4} and AEs were mostly grade 1 or 2
- Administration-related reactions due to amivantamab occurred in 13% of participants; none were grade ≥ 3
- Treatment-related AEs leading to discontinuation of all study agents occurred in 1 (3%) participant
- Treatment-related AEs leading to discontinuation of any study agent^a occurred in 8 (27%) participants
- Grade 5 AEs occurred in 4 participants (myocardial infarction, pneumonia, urinary tract infection, and respiratory failure); none were attributed to treatment

Treatment-emergent AEs ($\geq 30\%$ all grades) by preferred term, n (%)	N=30	
	All grades	Grade ≥ 3
Related to EGFR inhibition		
Stomatitis	17 (57)	3 (10)
Dermatitis acneiform	11 (37)	3 (10)
Rash	11 (37)	0
Related to MET inhibition		
Hypoalbuminemia	19 (63)	5 (17)
Peripheral edema	13 (43)	1 (3)
Other		
Anemia	22 (73)	7 (23)
Thrombocytopenia	19 (63)	5 (17)
Lymphopenia	15 (50)	6 (20)
Decreased weight	15 (50)	4 (13)
Hypomagnesemia	15 (50)	1 (3)
Nausea	14 (47)	5 (17)
Hypokalemia	14 (47)	2 (7)
Hypocalcemia	12 (40)	1 (3)
Constipation	12 (40)	0
Fatigue	11 (37)	2 (7)
Neutropenia	11 (37)	2 (7)
Leukopenia	11 (37)	1 (3)
Hyponatremia	11 (37)	0
Increased aspartate aminotransferase	10 (33)	0
Vomiting	9 (30)	4 (13)
Increased lipase	9 (30)	1 (3)

^a7 participants discontinued amivantamab, 2 pembrolizumab, and 2 carboplatin.

1. Burtneß B, et al. *Lancet*. 2019;394(10212):1915–1928. 2. Burtneß B, et al. *J Clin Oncol*. 2026;44(24):2271–2277. 3. Harrington KJ, et al. *Oral Oncol*. 2025;171:107791.

4. Kao HF, et al. *Clin Cancer Res*. 2026. doi: 10.1158/1078-0432.CCR-26-1372.

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Conclusions

- Cohort 5 met its prespecified primary endpoint; notably, participants with HPV-unrelated R/M HNSCC achieved a confirmed ORR of 77% with 1L amivantamab + pembrolizumab + carboplatin^a
 - The confirmed ORR of 77% was >2-fold that of the historical ORR with pembrolizumab-chemotherapy (36%)¹
- At a median follow-up of 10.6 mo, median OS was NR in HPV-unrelated disease, with 77% of participants alive at 1 year
- Safety profile was tolerable and consistent with previous reports of the individual agents,^{1–4} with no high-grade administration-related reactions
- The ongoing phase 3 OrigAMI-5 trial (ClinicalTrials.gov Identifier: NCT07276399) is evaluating the 1L triplet regimen of amivantamab + pembrolizumab + carboplatin versus pembrolizumab + 5-FU + platinum in HPV-unrelated disease (CPS all comers)

1L subcutaneous amivantamab + pembrolizumab + carboplatin^a demonstrated clinically meaningful and broad antitumor activity in HPV-unrelated R/M HNSCC

^aUp to 6 cycles. HPV, human papillomavirus; NR, not reached.

1. Burtness B, et al. *Lancet*. 2019;394(10212):1915–1928. 2. Burtness B, et al. *J Clin Oncol*. 2026;44(24):2271–2277. 3. Harrington KJ, et al. *Oral Oncol*. 2025;171:107791.

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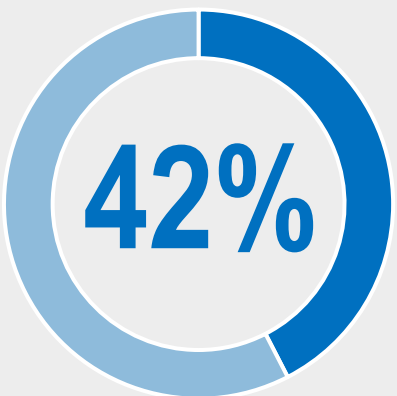


Summary of Amivantamab Activity in HPV-Unrelated R/M HNSCC

OrigAMI-4 Cohort 1

**2L+ amivantamab monotherapy
(n=102)¹**

ORR^a



Historical benchmark: cetuximab ORR=24%³

**2L+ amivantamab monotherapy received
US FDA Breakthrough Therapy Designation^c**

**The results of OrigAMI-4 Cohort 1 have been
submitted to the FDA and are under review**

OrigAMI-4 Cohort 2

**1L amivantamab + pembrolizumab
(n=39)²**

ORR^b

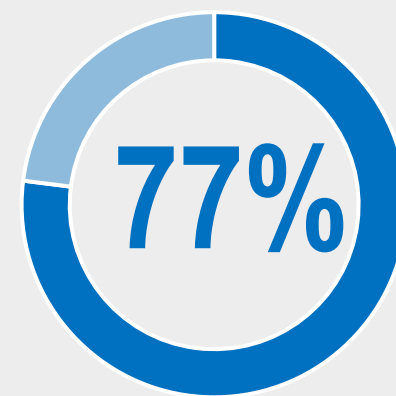


Historical benchmark: pembro ORR=19%–25%^{4,5}

OrigAMI-4 Cohort 5

**1L amivantamab + pembrolizumab +
carboplatin (n=22)**

ORR^b



Historical benchmark: pembro-chemo ORR=36%⁵

OrigAMI-5

Previously
untreated,
R/M HNSCC^d

R
1:1

Subcutaneous amivantamab + pembrolizumab + carboplatin (n≈250)

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

^aPer BICR. ^bPer investigator assessment. ^cBreakthrough Therapy Designation was based on preliminary results from Cohort 1 of OrigAMI-4. ^dNo enrollment restriction based on CPS.

CPS, combined positive score; HPV, human papillomavirus.

1. Burtress B, et al. *J Clin Oncol*. 2026;44(24):2271–2277. 2. Kao HF, et al. *Clin Cancer Res*. 2026. doi: 10.1158/1078-0432.CCR-26-1372. 3. Fayette J, et al. *Clin Cancer Res*. 2025;31(13):2617–2627.

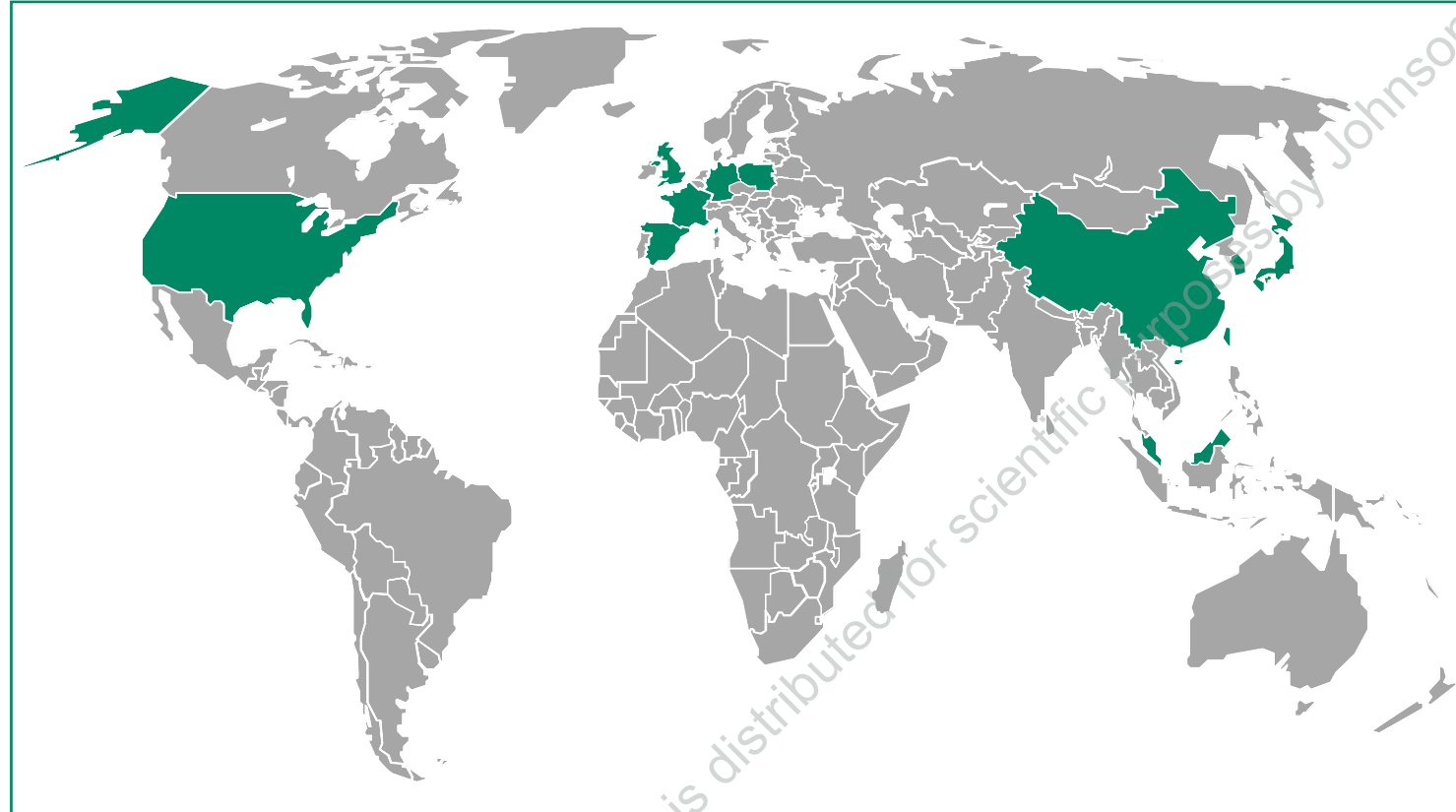
4. Licitra L, et al. *J Clin Oncol*. 2026;44(12):1098–1107. 5. Burtress B, et al. *Lancet*. 2019;394(10212):1915–1928. 6. Harrington KJ, et al. *Oral Oncol*. 2025;171:107791.



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OrigAMI-4 is currently enrolling at 56 sites from 11 countries/regions as of July 2026



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