

Amivantamab in recurrent/metastatic head & neck squamous cell cancer after disease progression on checkpoint inhibition and chemotherapy

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

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Declaration of Interests

Honoraria: AbbVie (Inst); ALX Oncology (Inst); AstraZeneca (Inst); BeiGene (Inst); Bicara Therapeutics (Inst); BMS (Inst); Boehringer Ingelheim (Inst); Exelixis (Inst); Flamingo Pharma (Inst); GlaxoSmithKline (Inst); Johnson & Johnson (Inst); Merck Serono (Inst); Merus (Inst); MSD (Inst); Nanobiotix (Inst); PDS Biotechnology (Inst); PsiVac Ltd (Inst); Replimune (Inst); Scenic Biotech

Consulting or Advisory Role: AstraZeneca (Inst); BMS (Inst); Boehringer Ingelheim (Inst); Merck Serono (Inst); MSD (Inst); Nanobiotix (Inst); Replimune (Inst)

Speakers' Bureau: BMS (Inst); Merck Serono (Inst); MSD (Inst)

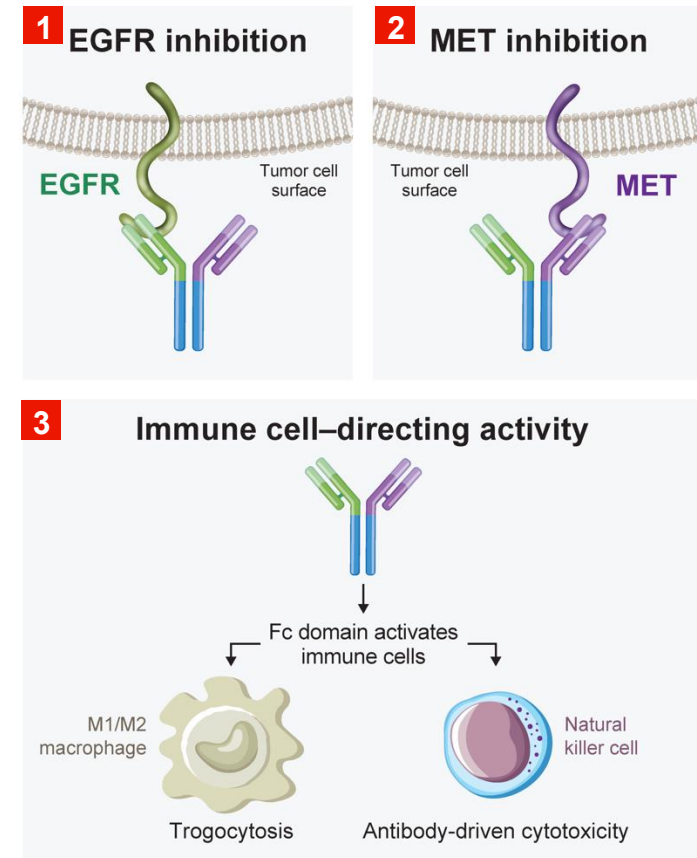
Research Funding: AstraZeneca (Inst); Boehringer Ingelheim (Inst); Replimune (Inst)



Amivantamab in Head & Neck Squamous Cell Carcinoma

- Cetuximab monotherapy demonstrated response rates of up to 24% among participants with HPV-unrelated^a R/M HNSCC after disease progression on checkpoint inhibitor and platinum-based chemotherapy¹
 - Median survival in this setting is poor (6–9 months)^{1–4}
- EGFR and MET overexpression occur in 80%–90% of HNSCC tumors^{5,6}
- Amivantamab, an EGFR-MET bispecific antibody, has a triple mechanism of action: (1) EGFR inhibition, (2) MET inhibition (important escape pathway to anti-EGFR), and (3) immune cell-directing activity^{7,8}

Amivantamab's triple action mechanism



We evaluated subcutaneous amivantamab monotherapy Q3W in HPV-unrelated R/M HNSCC after disease progression on checkpoint inhibitor and platinum-based chemotherapy

^aParticipants with human papillomavirus-positive (HPV+) oropharyngeal cancer were excluded. HNSCC, head & neck squamous cell carcinoma; R/M, recurrent/metastatic.

1. Fayette J, et al. *Clin Cancer Res.* 2025;31(13):2617–2627. 2. Ferris RL, et al. *N Engl J Med.* 2016;375(19):1856–1867. 3. Soulières D, et al. *Lancet Oncol.* 2017;18(3):323–335. 4. Cohen EEW, et al. *Lancet.* 2019;393(10167):156–167. 5. Rothenberger NJ, et al. *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.



OrigAMI-4 Study Design

Eligibility Criteria

- Recurrent/metastatic (R/M) head and neck squamous cell carcinoma
- No prior anti-EGFR therapy
- ECOG PS score: 0 or 1

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

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^b 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

Focus of this presentation

Endpoints

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

Responses were assessed by the investigator per RECIST v1.1

- **Safety population (n=86):** participants who received ≥ 1 dose of amivantamab monotherapy
- **Efficacy population (n=38):** participants who have had ≥ 2 disease assessments^d or discontinued before for any reason

Clinicaltrials.gov identifier: NCT06385080. **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.

^aEach cycle is 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.

^bCoh 3A (dose confirmation cohort of n=11 participants) will be presented during the H&N Poster Session on October 20 at noon CET (1352P).

^cClinical benefit rate defined as percentage of confirmed responders or durable stable disease (at the second disease assessment).

^dFirst disease assessment occurred 6 weeks after first dose, then every 6 weeks (± 1 week) for the first year and every 9 weeks (± 1 week) thereafter.

ECOG PS, Eastern Cooperative Oncology Group performance status.



Demographics and Baseline Disease Characteristics

- As of 1-July-2025, 86 participants have been dosed, with median follow-up of 3.5 months (range, 0–13.4)
- All participants had received prior checkpoint inhibitor (ie, anti-PD-1 or anti-PD-L1) and prior platinum-based chemotherapy
 - All (100%) had at least 1 prior line, with 43% having 2 prior lines
- As of data cutoff, treatment was ongoing in 53 of 86 (62%)

Characteristic, n (%)	Safety population (n=86)
Age, median (range)	63.5 years (30–81)
Male / female	65 (76) / 21 (24)
Race	
Asian	39 (45)
White	37 (43)
Other ^a	10 (12)
ECOG PS score 0 / 1	28 (33) / 58 (67)
Primary tumor location	
Hypopharynx	13 (15)
Larynx	21 (24)
Oropharynx	10 (12)
Oral cavity	42 (49)
Site of recurrence/metastasis ^b	
Bone	14 (17)
Head and neck	51 (62)
Liver	5 (6)
Local lymph node	33 (40)
Distant lymph node	20 (24)
Lung	45 (55)
Skin	1 (1)
Other	17 (21)

^aOther includes: 1 Black or African-American, 6 not reported, and 3 unknowns.

^bParticipants (n=82) can be counted in more than 1 category.

ECOG PS, Eastern Cooperative Oncology Group performance status.



Safety

- Median treatment duration was **2.7 months** (range, 0–11.3)
- Individual AEs were largely related to EGFR or MET inhibition and primarily grade 1 or 2
- Rate of administration-related reactions was low (7%; all grade 1 or 2), consistent with the **subcutaneous** formulation of amivantamab^{1,2}
- Discontinuation rate due to treatment-related AEs^a was low (2%)
- Overall safety profile was consistent with prior reports of amivantamab monotherapy

Treatment-emergent AEs (≥10%) by preferred term, n (%)	Safety population (n=86)	
	All grades	Grade ≥3
Related to EGFR inhibition		
Stomatitis	20 (23)	1 (1)
Dermatitis acneiform ^b	17 (20)	6 (7)
Rash ^b	16 (19)	2 (2)
Paronychia ^b	15 (17)	1 (1)
Diarrhea	13 (15)	0
Pruritus ^b	11 (13)	2 (2)
Related to MET inhibition		
Hypoalbuminemia	27 (31)	2 (2)
Peripheral edema	12 (14)	1 (1)
Other		
Fatigue	27 (31)	4 (5)
Anemia	15 (17)	5 (6)
Hypocalcemia	13 (15)	0
ALT increased	11 (13)	3 (3)
Nausea	11 (13)	0
Weight decreased	11 (13)	1 (1)
Decreased appetite	10 (12)	0
Dyspnea	10 (12)	2 (2)
AST increased	9 (10)	2 (2)
Lymphopenia	9 (10)	4 (5)

^aTreatment-related AEs were paronychia and elevated alkaline phosphatase. ALT, alanine aminotransferase; AST, aspartate aminotransferase.

^bProphylactic dermatologic management (COCOON protocol) was not mandatory in OrigAMI-4.

1. Lim SM, et al. Presented at: IASLC World Conference on Lung Cancer (WCLC); Sept 6-9, 2025; Barcelona, Spain.

2. Nadal E, et al. Presented at: European Medical Society of Oncology (ESMO) Annual Meeting; Oct 17-21, 2025; Berlin, Germany (1960P).

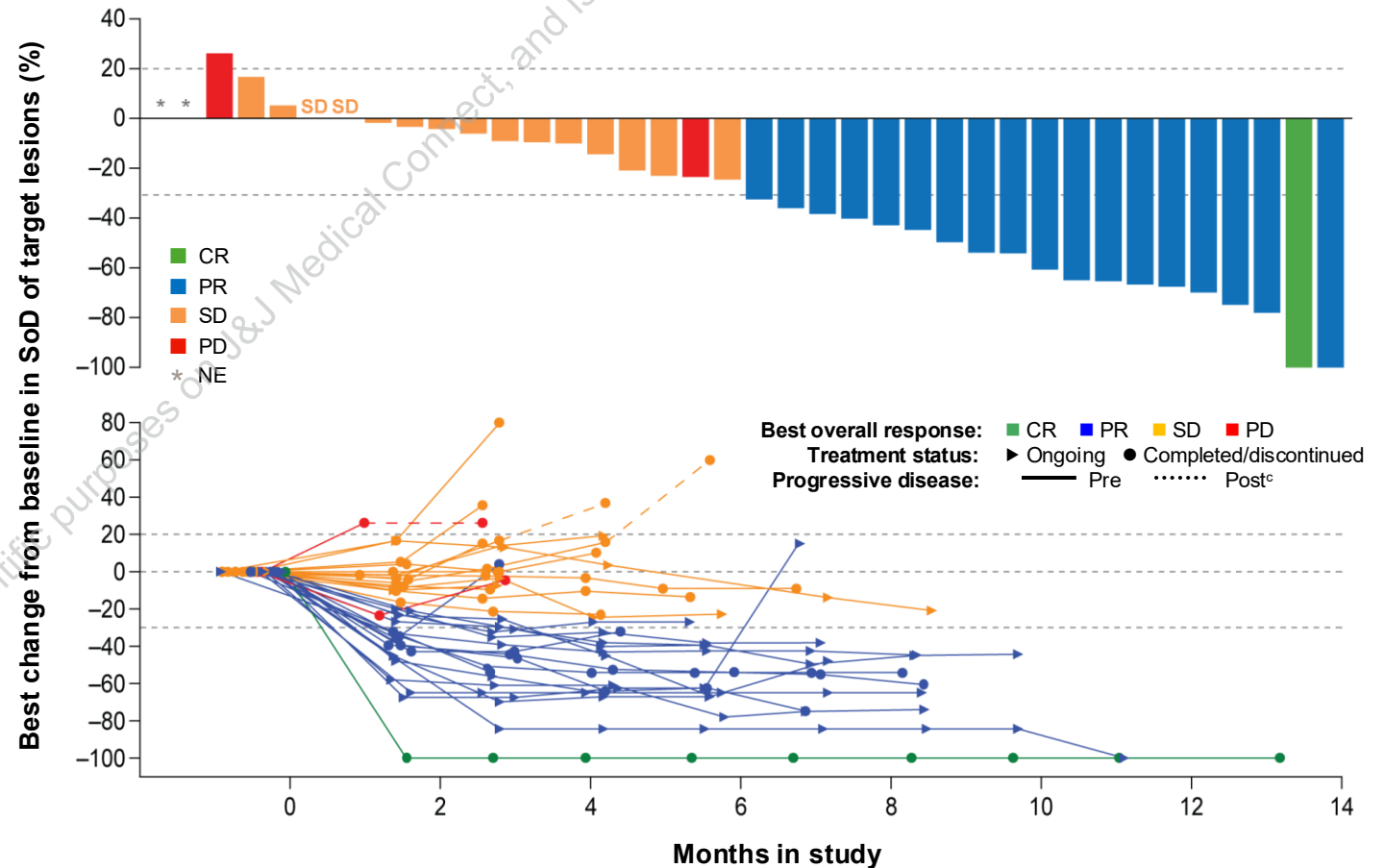


ORR and Best Response

Median follow-up^a = 8.3 months
(range, 1.1–13.4)

INV-assessed	Efficacy population (n=38) ^a
ORR	45% (95% CI, 29–62)
Best response, n (%)	
CR	1 (3)
PR	16 (42)
SD	17 (45)
PD	2 (5)
Not evaluable	2 (5)
Time to first response ^b	6.4 weeks
Clinical benefit rate	76% (95% CI, 60–89)

- A majority (82%) experienced tumor shrinkage of target lesions



^aAs of data cutoff, 38 participants had ≥ 2 disease assessments (or discontinued for any reason) and were included in the efficacy analysis. ^bAmong all responders. ^cTreatment beyond progression was allowed if participant continued to derive clinical benefit. NE, not evaluable; SoD, sum of diameters.

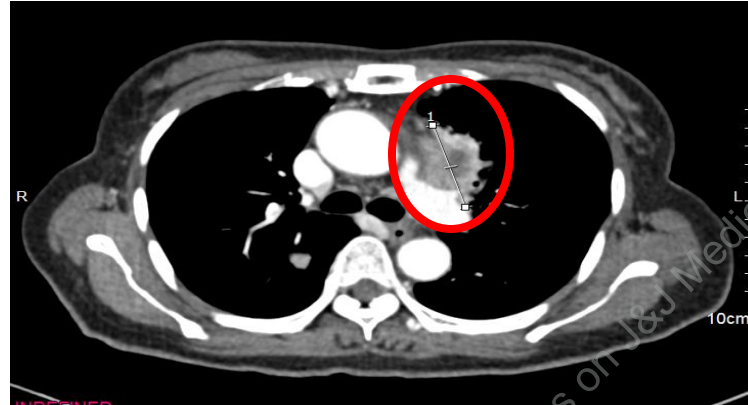


Rapid Antitumor Activity of Amivantamab

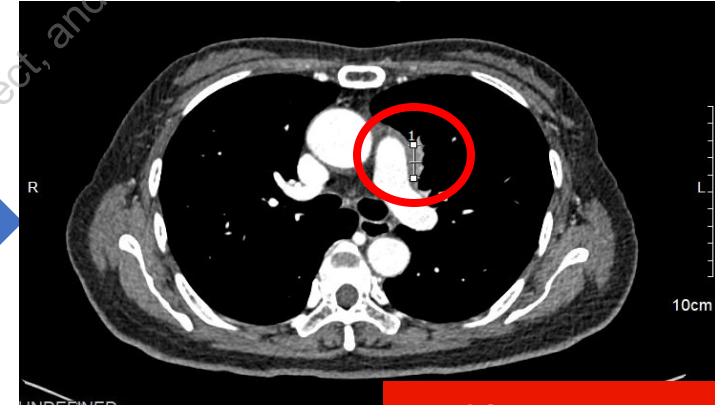
48-year-old female
with oral cavity cancer
and metastases in the
lung

Previously treated
with surgery,
cisplatin/radiation,
and nivolumab

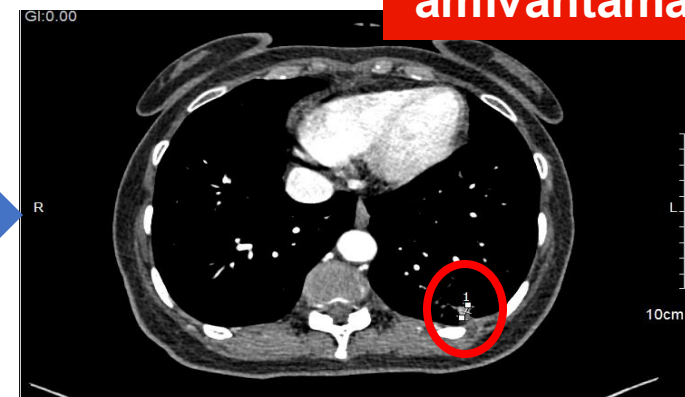
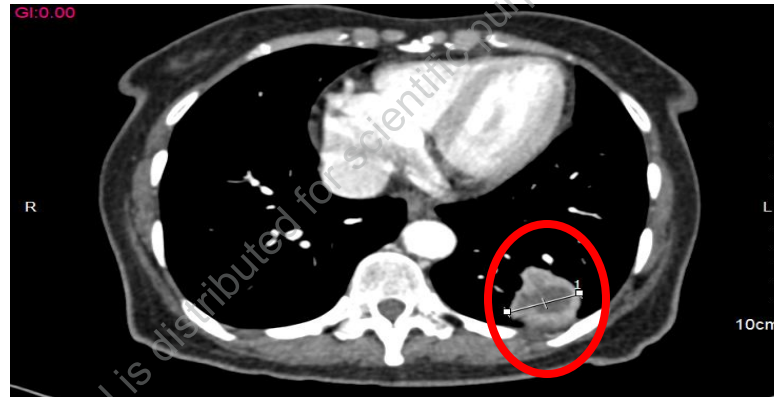
CT Scan at Baseline



CT Scan at Week 7

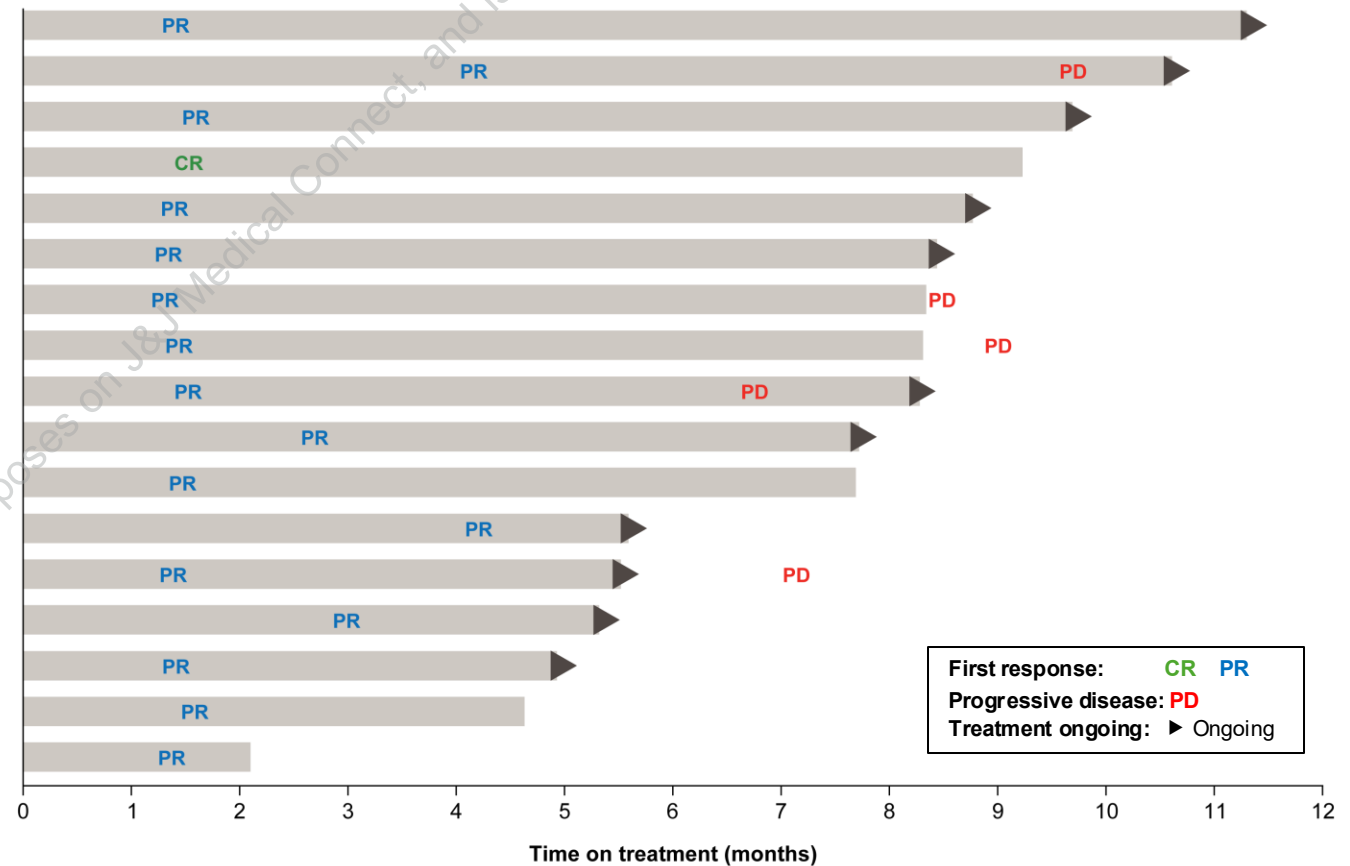


**65% tumor decrease with
amivantamab in 6 weeks**



Durability

- Among the 17 confirmed responders, median DoR was 7.2 months (95% CI, 5.3–NE)
 - 65% remain on treatment
 - 47% have a response duration ≥ 6 months
- Among the 38 participants in the efficacy population, 16 (42%) remain on amivantamab monotherapy
 - Median PFS: 6.8 months (95% CI, 4.2–9.0)
 - Median OS: not reached (95% CI, 7.7–NE)



Conclusions

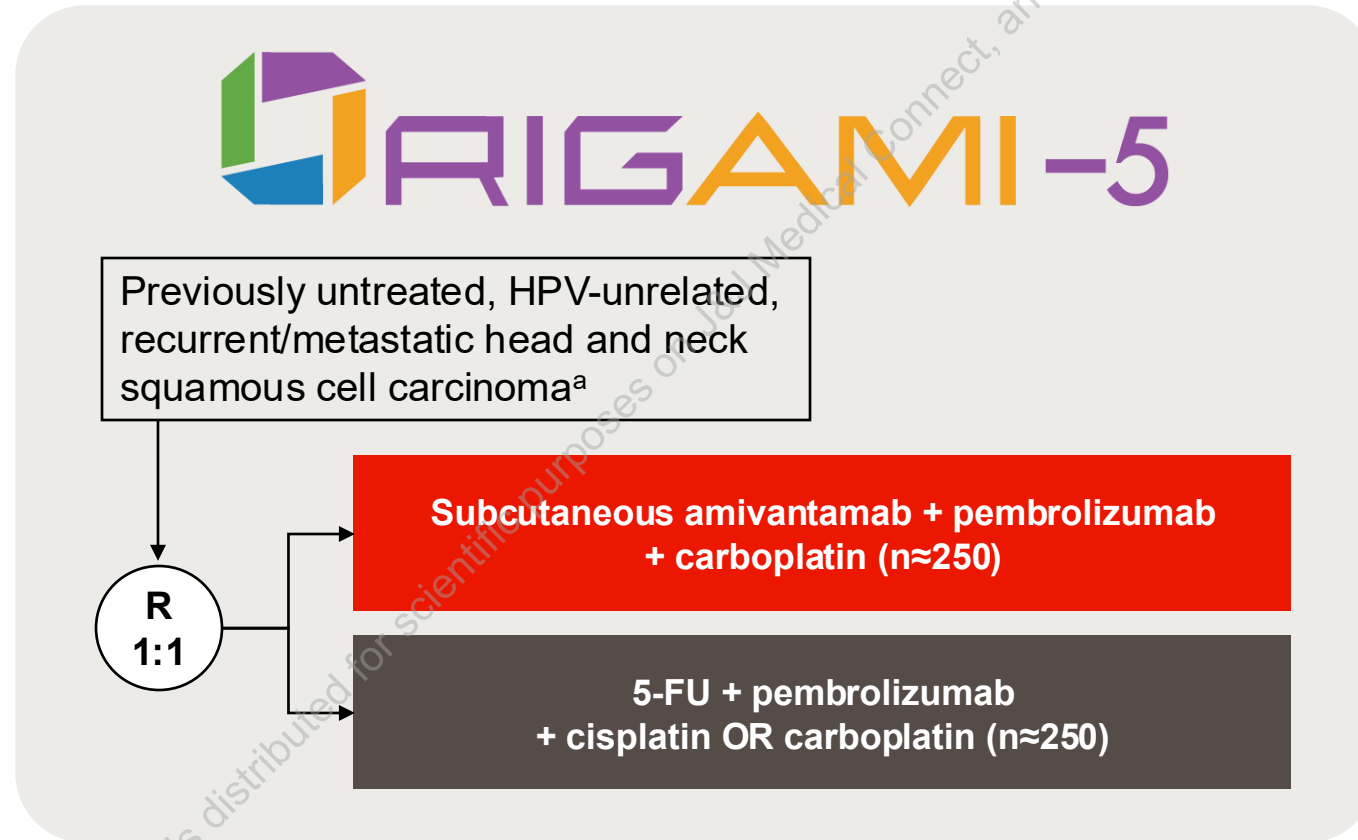
- **Subcutaneous** amivantamab monotherapy Q3W demonstrated an ORR of 45% in HPV-unrelated R/M HNSCC after disease progression on prior checkpoint inhibitor and platinum-based chemotherapy
 - Responses were rapid (6.4 weeks to first response) and durable (median 7.2 months)
 - Median PFS was 6.8 months, and median OS was not reached
- The early safety profile was consistent with prior amivantamab studies: most common treatment-emergent AEs were related to EGFR and MET inhibition, with no new safety signals identified
 - With the use of **subcutaneous** amivantamab, 7% reported administration-related reactions (none grade ≥ 3)
- Amivantamab has now demonstrated antitumor activity across multiple solid tumors: non-small cell lung cancer, colorectal cancer, and head and neck cancer



Amivantamab monotherapy demonstrated rapid and durable responses in 2L+ R/M HNSCC after disease progression on checkpoint inhibitor and platinum-based chemotherapy



Subcutaneous amivantamab plus pembrolizumab and carboplatin is proceeding to first-line, phase 3 development



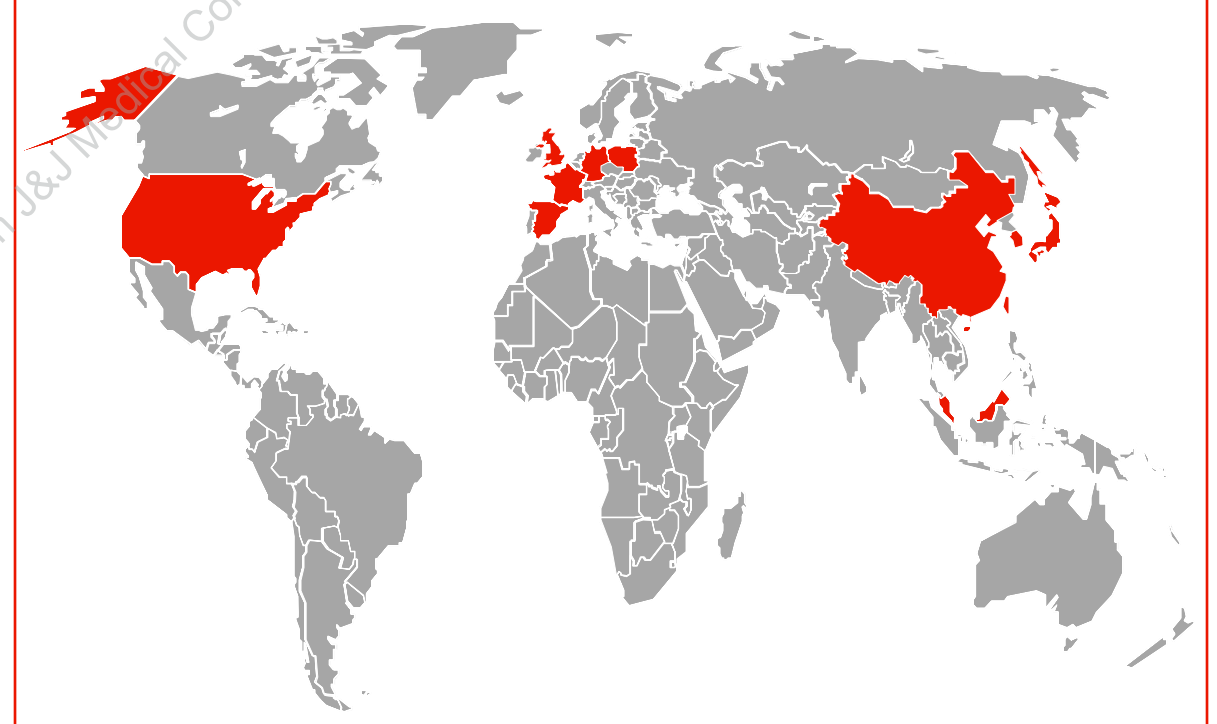
^aNo enrollment restrictions based on CPS score.



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
- Medical writing assistance was provided by Katharine Fang, PhD, (Johnson & Johnson), with support from Lumanity Communications Inc. and funded by Johnson & Johnson

OrigAMI-4 is currently enrolling at 55 sites from 11 countries/regions



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