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Subcutaneous amivantamab in recurrent/metastatic head and neck squamous cell cancer after disease progression on checkpoint inhibitor and chemotherapy: Preliminary results from the phase 1b/2 OrigAMI-4 study

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ABSTRACT

Overexpression of EGFR and MET occurs in a high proportion of recurrent and/or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). Amivantamab, an EGFR-MET bispecific antibody with immune-cell directing activity, is approved in *EGFR*-mutated advanced non-small cell lung cancer and is being evaluated in phase 3 trials for other solid tumors. Cohort 1 of OrigAMI-4 (NCT06385080) enrolled adult participants with human papillomavirus–unrelated R/M HNSCC with disease progression on/after prior checkpoint inhibitor and platinum-based chemotherapy. Subcutaneous amivantamab was administered at 1600 mg (2240 mg for ≥ 80 kg body weight) on Cycle 1 Day 1 and 2400 mg (3360 mg for ≥ 80 kg body weight) thereafter. Primary end point was investigator-assessed objective response rate (ORR). As of July 1, 2025 (median follow-up, 3.5 months [range, 0–13.4]), 86 participants (median age, 63.5 years; 45 % Asian; 43 % White) received ≥ 1 dose of subcutaneous amivantamab. Subcutaneous amivantamab was well tolerated. Administration-related reactions were reported in 7 % (n = 6/86) of participants; no new safety signals were observed. In the efficacy population (n = 38; median follow-up, 8.3 months [range, 1.1–13.4]), confirmed ORR was 45 % (95 % CI, 29 %–62 %), median time to first response was 6.4 weeks (range, 5.7–18.3), and median duration of response was 7.2 months (95 % CI, 5.3–NE). The clinical benefit rate (responder or durable stable disease) was 76 % (95 % CI, 60 %–89 %). Median progression-free survival was 6.8 months (95 % CI, 4.2–9.0). Subcutaneous amivantamab as second-/

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third-line treatment among participants with R/M HNSCC demonstrated rapid and durable antitumor activity. The safety profile of subcutaneous amivantamab was consistent with previous studies.

Introduction

Head and neck squamous cell carcinoma (HNSCC) is one of the most common types of cancers globally [1]. Following curative-intent treatment for HNSCC, approximately 10 %–20 % of patients with early-stage disease and 50 % of patients with locally advanced disease experience recurrent and/or metastatic (R/M) HNSCC [2,3]. Recommended first-line therapies for patients with R/M HNSCC include anti-programmed death 1 (anti–PD-1) checkpoint inhibitors as monotherapy or with chemotherapy, chemotherapy alone, or combination chemotherapy and cetuximab [4–6]. Combination therapy with first-line checkpoint inhibitor plus chemotherapy or cetuximab plus chemotherapy in the phase 3 KEYNOTE-048 study both provided objective response rates (ORRs) of 36 % in the total population [4]. For patients who have received anti–PD-1 checkpoint inhibitors and platinum-based chemotherapy, second- and third-line treatments have limited efficacy, with response rates ranging from 15 %–24 % [5,7–10]. Thus, a significant unmet medical need remains for second- and third-line treatment options to improve clinical outcomes for patients with R/M HNSCC.

In patients with HNSCC, overexpression of epidermal growth factor receptor (EGFR) and mesenchymal epithelial transition (MET) factor receptor occurs in 80 %–90 % of cases and is correlated with poorer prognosis [11,12]. Furthermore, MET activation has been shown to confer resistance to EGFR inhibitors in HNSCC [13]. Amivantamab is an EGFR-MET bispecific antibody with 3 distinct mechanisms of action: targeting EGFR, targeting MET, and immune-cell directing activity [14,15]. Intravenous amivantamab is approved in the United States, the European Union, and in other countries for use across a variety of treatment settings in *EGFR*-mutated advanced or metastatic non-small cell lung cancer (NSCLC) [16,17]. Subcutaneous amivantamab is approved in the European Union for NSCLC [18]. In addition, amivantamab is being investigated in phase 3 trials for the treatment of colorectal cancer (ClinicalTrials.gov identifiers: NCT06662786 [OrigAMI-2] and NCT06750094 [OrigAMI-3], supported by promising results in the phase 1b/2 OrigAMI-1 trial [19]). Amivantamab is also proceeding to first-line phase 3 development in R/M HNSCC. Given the mechanism of action, known biochemical dysregulation in R/M HNSCC, and proven benefit of EGFR inhibitors in HNSCC [20], amivantamab may be a promising treatment option for patients with R/M HNSCC.

Here, we present the preliminary results from Cohort 1 of the OrigAMI-4 study, which investigated the safety and efficacy of subcutaneous amivantamab in participants with human papillomavirus (HPV)–unrelated R/M HNSCC with disease progression on prior checkpoint inhibitor and platinum-based chemotherapy.

Materials and methods

Trial design and oversight

OrigAMI-4 (ClinicalTrials.gov identifier: NCT06385080) is a global, multicenter, open-label, multiarm, phase 1b/2 trial of subcutaneous amivantamab as a monotherapy and in addition to standard-of-care therapeutic agents involving participants with R/M HNSCC. This analysis presents safety and efficacy results of subcutaneous amivantamab monotherapy from Cohort 1 (Fig. 1).

Imaging (computed tomography [CT] or magnetic resonance imaging [MRI]) was conducted at screening, 6 weeks (+1 week) after Cycle 1 Day 1, and then every 6 weeks (±1 week) thereafter for 1 year. After 1 year, imaging was conducted every 9 weeks (±1 week). Brain MRI (or CT if MRI was contraindicated) was conducted every 12 weeks (±1 week) if brain metastases were present at baseline, and as clinically indicated if brain metastases were absent at baseline.

OrigAMI-4 was conducted in accordance with the provisions of the Declaration of Helsinki, Good Clinical Practice guidelines (as defined by the International Council for Harmonisation), and applicable regulatory and country-/territory-specific requirements. The protocol was approved by the local institutional review boards and independent ethics committees of the participating centers. Participants provided written informed consent prior to study participation.

Participants

All enrolled participants in Cohort 1 were 18 years of age or older with histologically or cytologically confirmed R/M HNSCC that was considered incurable by local therapies (Fig. 1). Additional inclusion criteria included primary tumor locations of the oropharynx, oral cavity, hypopharynx, or larynx; an Eastern Cooperative Oncology Group performance status score of 0 or 1; and disease progression on or after prior

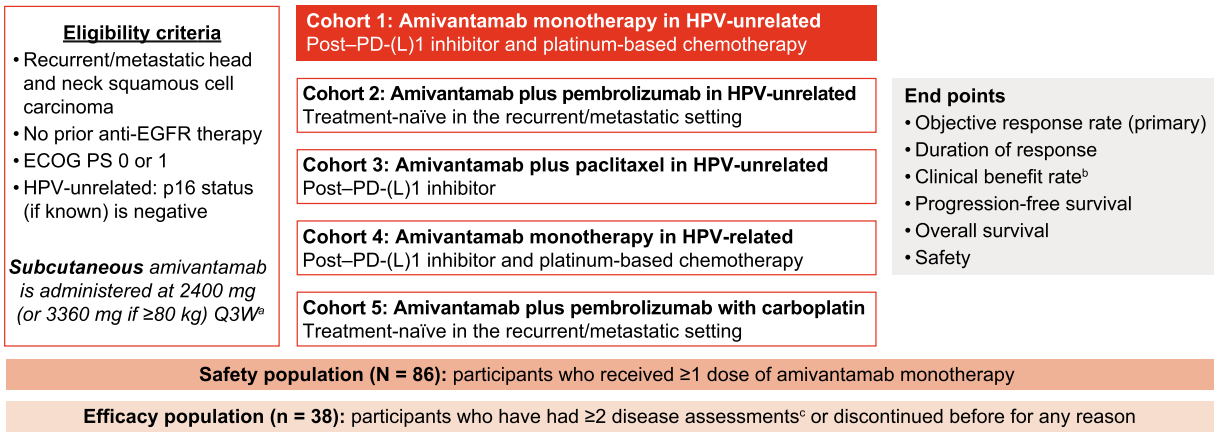

Fig. 1. OrigAMI-4 study design. ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HPV, human papillomavirus; PD-(L)1, programmed death-(ligand) 1; Q3W, every 3 weeks. [a]Each cycle is 21 days (3 weeks). Subcutaneous amivantamab administered at 1600 mg (or 2240 mg if > 80 kg) on Cycle 1 Day 1; at 2400 mg (or 3360 mg if > 80 kg) on Cycle 1 Day 8 and Day 15; and at 2400 mg (or 3360 mg if > 80 kg) on Cycle 2 Day 1 and thereafter. [b]Clinical benefit rate was defined as percentage of confirmed responders or durable stable disease (≥ 11 weeks). [c]First 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.

treatment with anti–programmed death-(ligand) 1 (anti–PD-[L]1) checkpoint inhibitor and platinum-based chemotherapy. Participants with a primary tumor located in the oropharynx were required to have p16 testing documenting the tumor to be p16 negative. Participants were excluded if they had previously received anti-EGFR therapy or received more than 2 prior lines of systemic therapy in the R/M setting.

Trial treatment

Amivantamab co-formulated with 2000 U/mL of recombinant human hyaluronidase PH20 was administered subcutaneously in the abdomen. On Cycle 1 Day 1, subcutaneous amivantamab was administered at a dose of 1600 mg (or 2240 mg for ≥ 80 kg body weight). For the remainder of Cycle 1, subcutaneous amivantamab was administered once weekly at a dose of 2400 mg (or 3360 mg for ≥ 80 kg body weight). Starting on Cycle 2 Day 1 and thereafter, subcutaneous amivantamab was administered once every 3 weeks at a dose of 2400 mg (or 3360 mg for ≥ 80 kg body weight). Prophylactic management of dermatologic adverse events (AEs) was not mandatory but was left to the discretion of the treating investigator.

End points

The primary end point was ORR as defined by investigator assessment using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Secondary end points included the clinical benefit rate (CBR), time to response, duration of response (DoR), progression-free survival (PFS) per RECIST v1.1 as determined by investigator, overall survival (OS), and incidence of AEs.

Statistical analysis

The safety population was defined as participants who received at least 1 dose of subcutaneous amivantamab. In this analysis, the efficacy population was defined as participants who received at least 1 dose of subcutaneous amivantamab and had ≥ 2 disease assessments or discontinued treatment for any reason.

ORR was defined as the proportion of participants who achieved either a confirmed complete response (CR) or confirmed partial response (PR). DoR was defined as the time from CR or PR until the date of progression or death. CBR was defined as the percentage of participants who achieved confirmed CR, PR, or durable (at the second disease assessment, typically ≥ 11 weeks) stable disease (SD). Time to response, DoR, PFS, and OS were estimated using the Kaplan-Meier method.

Here, we present results of an unplanned interim data analysis. However, participant accrual remains ongoing for this trial, and the final analysis of the full Cohort 1 population will be conducted once the dataset is available. The null hypothesis was an ORR ≤ 10 %, which was based on the available published data on the efficacy of cetuximab monotherapy in the post-platinum setting for R/M HNSCC at the time of OrigAMI-4 protocol development [21–23]. An initial sample size of 30 participants was estimated to provide over 80 % power to reject the null hypothesis assuming an ORR of 30 % with a 1-sided alpha of 5 %; however, Cohort 1 was expanded based on promising activity of amivantamab. The final analysis for Cohort 1 will be based on the updated sample size of 80 response-evaluable participants from 100 treated participants, which will provide over 99 % power to reject the null hypothesis (ORR is ≤ 10 %) assuming an ORR of 30 % with a 2-sided alpha of 0.05.

Results

A total of 86 participants were enrolled, received at least 1 dose of subcutaneous amivantamab, and were included in the safety population. The median age of participants was 63.5 years (range, 30–81; Table 1). Most of the participants were male (76 %), Asian (45 %) or White (43 %), had primary tumors located in the oral cavity (49 %), and had R/M disease located in the head and neck (62 %), lung (55 %), and/or local lymph nodes (40 %). All (100 %) participants had received prior systemic therapy for R/M HNSCC, which included anti–PD-(L)1 checkpoint

Table 1
Baseline demographic and clinical characteristics of the safety and efficacy populations.

Characteristic	Cohort 1	
	Safety population (N = 86)	Efficacy population (n = 38[a])
Age		
Median (range), years	63.5 (30–81)	67 (30–79)
Category, n (%)		
< 65 years	46 (53)	16 (42)
≥ 65 to < 75 years	30 (35)	16 (42)
≥ 75 years	10 (12)	6 (16)
Sex, n (%)		
Female	21 (24)	11 (29)
Male	65 (76)	27 (71)
Race, n (%)		
Asian	39 (45)	17 (45)
White	37 (43)	19 (50)
Black or African American	1 (1)	0
Not reported/unknown	9 (10)	2 (5)
Region, n (%)		
Eastern Asia	36 (42)	15 (39)
North America	27 (31)	14 (37)
Europe	21 (24)	7 (18)
Southeastern Asia	2 (2)	2 (5)
Body weight		
Median (range), kg	61 (40–96)	63 (43–96)
Category, n (%)		
< 80 kg	78 (91)	35 (92)
≥ 80 kg	8 (9)	3 (8)
Eastern Cooperative Oncology Group performance status, n (%)		
0	28 (33)	14 (37)
1	58 (67)	24 (63)
Time from initial head and neck diagnosis to first dose, median (range), months	22 (3–270)	27 (4–270)
Time from metastatic disease diagnosis to first dose, median (range), months	10 (0–43)	12 (1–42)
Primary tumor location, n (%)		
Hypopharynx	13 (15)	4 (11)
Larynx	21 (24)	10 (26)
Oropharynx[b]	10 (12)	4 (11)
Oral cavity	42 (49)	20 (53)
Stage at screening, n (%)		
III	2 (2)	2 (5)
IVA	18 (21)	9 (24)
IVB	12 (14)	4 (11)
IVC	54 (63)	23 (61)
Site of recurrence/metastasis, n (%)[c]		
Bone	14 (17)	7 (21)
Head and neck	51 (62)	16 (47)
Liver	5 (6)	0
Local lymph node	33 (40)	11 (32)
Distant lymph node	20 (24)	9 (26)
Lung	45 (55)	21 (62)
Skin	1 (1)	1 (3)
Other	17 (21)	7 (21)
Participants with ≥ 1 prior therapy, n (%)[c]		
Prior systemic therapy	86 (100)	38 (100)
Prior radiotherapy	76 (88)	35 (92)
Prior related surgery	71 (83)	33 (87)

Note: totals may not sum to 100 % due to rounding.
[a] n = 34 for time since metastatic disease diagnosis to first dose and site of recurrence/metastasis.
[b] All 10 (100 %) participants with oropharynx cancer had confirmed p16-negative status.
[c] Participants could be counted in more than 1 category.

inhibitor and platinum-based chemotherapy, and 39 (45 %) participants had received prior taxane-based chemotherapy for R/M disease.

As of the data cutoff of July 1, 2025, the median follow-up for the safety population was 3.5 months (range, 0–13.4), and the median duration of subcutaneous amivantamab treatment was 2.7 months (range, 0–11.3). A total of 38 participants reached their second disease assessment (or had discontinued treatment before for any reason) and were included in the efficacy population. Treatment was ongoing in the remaining 48 participants; these remaining participants had either not had their first disease assessment or had insufficient follow-up to reach their second disease assessment. Reasons for discontinuation of treatment included progressive disease in 23 (27 %) and AEs in 9 (10 %) participants; 1 (1 %) participant refused further treatment.

Safety

Overall, the safety profile of subcutaneous amivantamab in participants with R/M HNSCC was consistent with prior reports of amivantamab [24,25]. Among 86 participants in the safety population (Fig. 1), 79 (92 %) participants had at least 1 treatment-emergent adverse event (TEAE), which was either grade 1/2 (in 39 [45 %] of 86 participants) or grade ≥ 3 (in 40 [47 %] of 86 participants); serious TEAEs were reported in 29 (34 %) participants (Table 2). The most frequent (≥ 10 %) TEAEs related to EGFR inhibition included stomatitis (23 %), dermatitis acneiform (20 %), rash (19 %), and paronychia (17 %); TEAEs related to MET inhibition included hypoalbuminemia (31 %) and peripheral edema (14 %). The most common (≥ 5%) grade ≥ 3 TEAEs were dermatitis acneiform (7 %) and anemia (6 %). All other grade ≥ 3 TEAEs occurred in < 5 % of participants. Administration-related reactions to subcutaneous amivantamab were reported in 6 (7 %) participants and were either grade 1 (n = 4, 5 %) or grade 2 (n = 2, 2 %).

TEAEs leading to amivantamab dose interruption, reduction, or discontinuation were reported in 37 (43 %), 15 (17 %), and 6 (7 %) participants, respectively. TEAEs leading to amivantamab discontinuation that were deemed unrelated to study treatment included pneumonia aspiration and myocardial ischemia (n = 1), pneumonia aspiration (n = 1), cerebrovascular accident (n = 1), sudden death (n = 1), and cardiac arrest and post-procedural hemorrhage (n = 1). Amivantamab discontinuation due to treatment-related AEs was low (2 %); one case was due to paronychia and the second case was due to elevated alkaline phosphatase.

Table 2
Summary of frequent TEAEs (≥ 10 %).

Event	N = 86 n (%)	
Any TEAE	79 (92)	
Grade ≥ 3 TEAE	40 (47)	
Serious TEAE	29 (34)	
Any TEAE leading to:		
Dose interruption	37 (43)	
Dose reduction	15 (17)	
Discontinuation	6 (7)	
TEAEs (≥10 %) by preferred term	**All grades n (%)**	**Grade ≥ 3 n (%)**
Related to EGFR inhibition		
Stomatitis	20 (23)	1 (1)
Dermatitis acneiform[a]	17 (20)	6 (7)
Rash[a]	16 (19)	2 (2)
Paronychia	15 (17)	1 (1)
Diarrhea	13 (15)	0
Pruritus	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)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; EGFR, epidermal growth factor receptor; MET, mesenchymal epithelial transition; TEAE, treatment-emergent adverse event.

[a] Dermatitis acneiform and rash are subcategories of the grouped rash term, which occurred in 41 (48 %) of participants. The subcategories of dermatitis acneiform and rash are not mutually exclusive, and participants could have more than 1 type of rash.

Efficacy

At the time of the data cutoff, the median follow-up time was 8.3 months (range, 1.1–13.4) among the 38 participants in the efficacy population (Fig. 1). The baseline demographics and clinical characteristics of the efficacy population were similar to the overall safety population (Table 1). Among the efficacy population, 17 participants had 1 prior line of therapy, and 19 participants had 2 prior lines in the R/M setting. The majority (23 of 38 [61 %]) of participants received prior immunotherapy with platinum-based chemotherapy (18 of 23 had taxane or fluorouracil in addition); 8 of 38 (21 %) received prior immunotherapy with non–platinum-based chemotherapy, and 7 of 38 (18 %) received immunotherapy as monotherapy either before or after platinum-based chemotherapy. Among the 34 of the 38 participants with site of recurrence data, 5 (15 %) had only locoregional disease, 10 (29 %) had only distant disease, and the majority (19 [56 %]) had both. A total of 16 of the 38 (42 %) participants remain on amivantamab treatment.

The investigator-assessed confirmed ORR was 45 % (95 % confidence interval [CI], 29 %–62 %), and the confirmed CBR was 76 % (95 % CI, 60 %–89 %; Table 3). CR was observed in 1 (3 %) participant, and PR was observed in 16 (42 %) participants (Fig. 2). A majority of participants (31 of 38 [82 %]) experienced tumor shrinkage of target lesions. Among all responders, the median time to response was 6.4 weeks

Table 3
Summary of efficacy outcomes.

End point	Efficacy population (n = 38)[a]
Median (range) follow-up, months	8.3 (1.1[b]–13.4)
ORR, % (95 % CI)[c]	45 (29–62)
Best response, n (%)	
CR	1 (3)
PR	16 (42)
SD	17 (45)
PD	2 (5)
Not evaluable	2 (5)
CBR, % (95 % CI)[d]	76 (60–89)
Median (95 % CI) DoR, months[e]	7.2 (5.3–NE)
DoR ≥ 6 months, n (%)[e]	8 (47)
Median (95 % CI) PFS, months	6.8 (4.2–9.0)

CBR, clinical benefit rate; CI, confidence interval; CR, complete response; DoR, duration of response; NE, not estimable; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease.

[a] Efficacy population was defined as participants with ≥ 2 disease assessments (or discontinued for any reason).

[b] The lower value in the range was from a censored observation.

[c] ORR was defined as the percentage of participants achieving confirmed CR or PR.

[d] CBR was defined as the percentage of participants achieving confirmed CR, PR, or durable SD at the second assessment.

[e] DoR was defined as the time from confirmed CR or PR until the date of progression or death and was measured among the 17 confirmed responders.

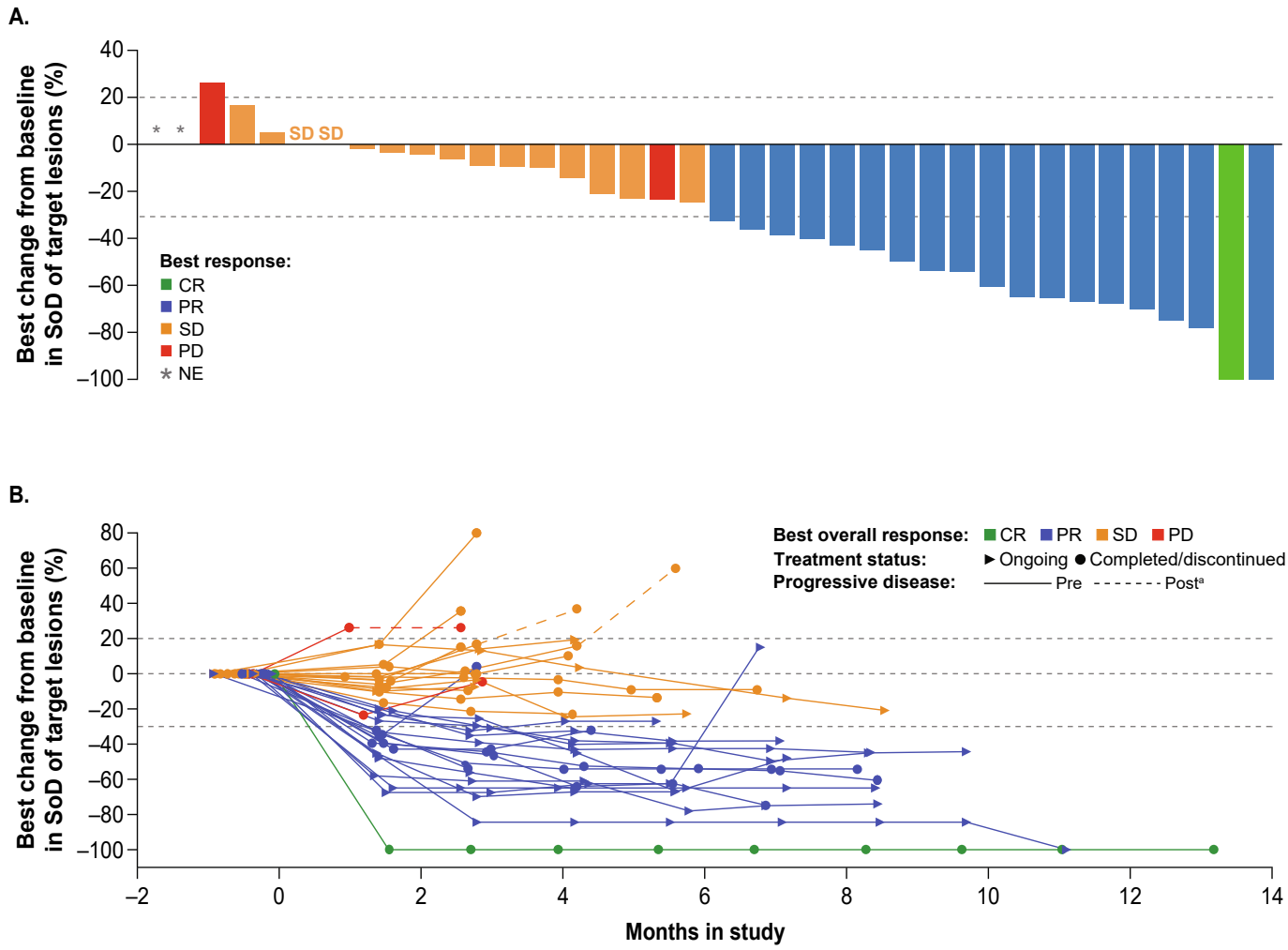

Fig. 2. Antitumor activity of amivantamab monotherapy. (A) Waterfall plot showing best responses by best change from baseline in SoD of target lesions. (B) Spider plot showing duration of response and best responses by best change from baseline in SoD of target lesions. CR, complete response; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease; SoD, sum of diameters. Note: Results are from the efficacy population, which includes participants who received ≥ 1 dose of the study drug and had ≥ 2 postbaseline disease assessments. [a]Treatment beyond progression was allowed if a participant continued to derive clinical benefit.

(range, 5.7–18.3). Among the 17 confirmed responders, the median DoR was 7.2 months (95 % CI, 5.3–not estimable; Fig. 3), and 47 % (n = 8) of participants had a DoR ≥ 6 months. Additionally, 11 of 17 (65 %) confirmed responders remain on treatment. Median PFS was 6.8 months (95 % CI, 4.2–9.0). OS data were immature as of the data cutoff.

Discussion

In the OrigAMI-4 trial involving participants with R/M HNSCC with disease progression on prior anti–PD-(L)1 checkpoint inhibitor and platinum-based chemotherapy, treatment with subcutaneous amivantamab demonstrated clinically meaningful response rates, with a confirmed investigator-assessed ORR of 45 % and CBR of 76 %. The median time to response was rapid (6.4 weeks), and once participants achieved a response, the efficacy of amivantamab was durable (7.2 months). Overall, these data demonstrate that second- and third-line treatment with subcutaneous amivantamab monotherapy is associated with promising and durable antitumor activity among participants with previously treated R/M HNSCC. Given the promising efficacy signal observed at this interim analysis and that treatment is ongoing for the majority of participants, a final analysis of the full Cohort 1 population will be conducted and reported once the data are available.

The results presented here are encouraging when considering the efficacy of standard-of-care regimens for patients with heavily pretreated R/M HNSCC. For example, a phase 3 trial involving participants with HPV-unrelated R/M HNSCC previously treated with anti–PD-1 checkpoint immunotherapy and chemotherapy who received cetuximab reported an investigator-assessed ORR of 24 % and a DoR of 5.6 months [5]. Furthermore, among predominantly Asian participants (94 %) with R/M HNSCC and disease progression following platinum-based chemotherapy, treatment with afatinib was associated with an ORR of 28 % and median PFS of 2.9 months [26]. In a retrospective, 28-patient study in Taiwan, second- or third-line treatment of R/M HNSCC with cetuximab resulted in an ORR of 32 % and median PFS of 2.9 months [27].

Results of the OrigAMI-4 trial suggest that dual inhibition of EGFR and MET can provide additional clinical benefit when compared with EGFR inhibition alone. An important factor in the underlying biology of this disease is that MET activation is considered a driver of resistance to EGFR inhibition in HNSCC [13], similar to observations in *EGFR*-mutated NSCLC [28], where amivantamab has shown robust efficacy as first- and second-line treatment [29–31]. Additionally, targeting MET and EGFR with ficlatuzumab and cetuximab, respectively, demonstrated antitumor activity among 16 participants with HPV-negative HNSCC [32]. The strength of our results suggests that dual inhibition of EGFR and MET with subcutaneous amivantamab monotherapy can have clinical utility in patients with pretreated HPV-unrelated HNSCC, which tends to be aggressive in the recurrent and metastatic stage, is difficult to

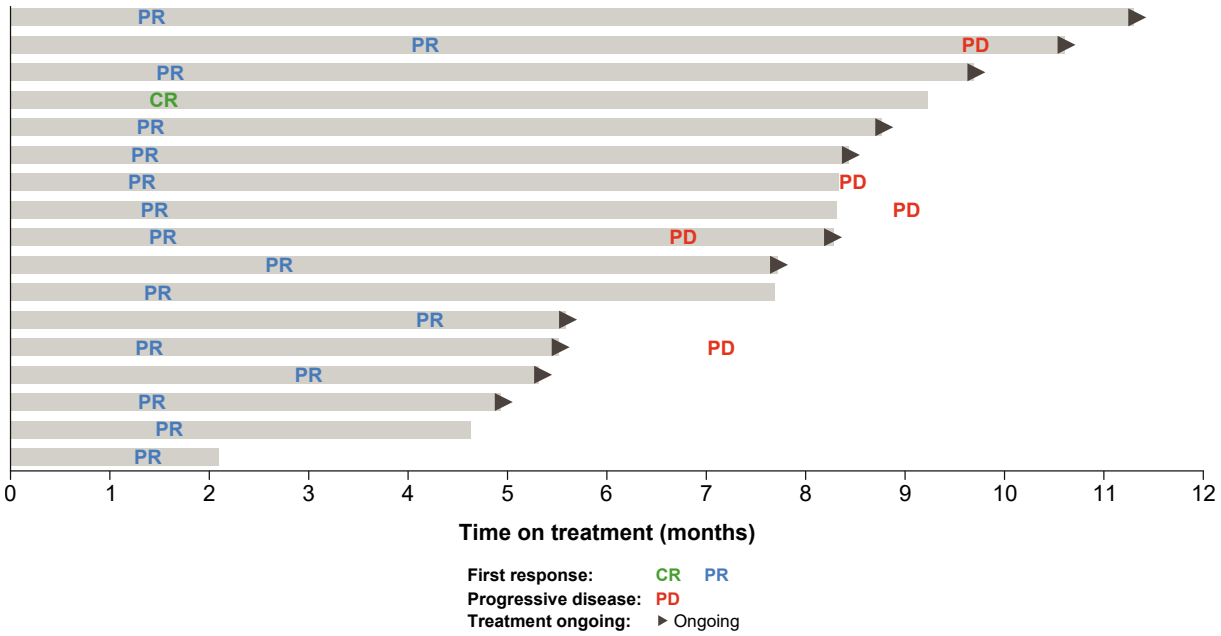

Fig. 3. Durability of amivantamab monotherapy treatment. CR, complete response; PD, progressive disease; PR, partial response.

treat, and for which the currently available treatment options are generally considered palliative [3].

The interpretation of this analysis is limited by the single-arm study design and the early analysis of 38 of the 86 participants who were included in the efficacy population. Furthermore, the safety findings should be interpreted with caution due to the limited follow-up of 3.5 months. In addition, this interim analysis is not prespecified with multiplicity control to make statistical conclusions. Because investigator-assessed ORR can be prone to assessment bias, the final analysis of the full Cohort 1 population will include ORR by blinded independent central review.

The early safety and tolerability profiles of amivantamab monotherapy in R/M HNSCC were consistent with previous reports, and no new safety signals were identified. Importantly, only 7 % of participants experienced administration-related reactions with subcutaneous administration of amivantamab, which is consistent with previous reports on the subcutaneous formulation in patients with NSCLC [24,25]. In addition, TEAEs observed with subcutaneous amivantamab were also consistent with previous reports and frequently related to EGFR and MET inhibition. The safety and tolerability profile, combined with the short administration time of subcutaneous formulation (≤ 7 min) [33], suggests that subcutaneous amivantamab may represent a safe, convenient, and efficacious second-/third-line treatment option for R/M HNSCC.

Conclusion

Subcutaneous amivantamab monotherapy was associated with promising and durable antitumor activity in this preliminary analysis among participants with HPV-unrelated R/M HNSCC who had disease progression on prior anti–PD-(L)1 checkpoint inhibitor and platinum-based chemotherapy. With these data from the OrigAMI-4 trial, amivantamab has now demonstrated antitumor activity across several solid tumor types: NSCLC [29–31], colorectal cancer [19], and head and neck cancer.

Prior presentation

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

Data sharing statement

The data sharing policy of Johnson & Johnson is available at https://innovativemedicine.jnj.com/our-innovation/clinical-trials/transparency. As noted on this site, requests for access to the study data can be submitted through the Yale Open Data Access [YODA] Project site at https://yoda.yale.edu.

CRediT authorship contribution statement

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Declaration of competing interest

Kevin J. Harrington **received honoraria** from AbbVie, ALX Oncology, AstraZeneca, BeOne Medicines, Bicara Therapeutics, Boehringer Ingelheim, Bristol Myers Squibb, Exelixis, Flamingo Pharma (UK) Ltd, GSK, Johnson & Johnson, Merck Serono, Merus, MSD, Nanobiotix, PDS Biotech, PsiVac Ltd., Replimune, and Scenic Biotech; served in a **consulting or advisory role** for AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Merck Serono, MSD, Nanobiotix, and Replimune; **participated in a speaker's bureau** for Bristol Myers Squibb, Merck Serono, and MSD; and **received research funding** from AstraZeneca, Boehringer Ingelheim, and Replimune.Ari J. Rosenberg served in a **consulting or advisory role** for Astellas Pharma Inc., Eisai, EMD Serono, Nanobiotix, Novartis, Regeneron, and Barinthus Biotherapeutics; **participated in a speaker's bureau** for Coherus Oncology; **received research funding** from AbbVie, BeOne Medicines, Bristol Myers Squibb/Celgene, EMD Serono, Hookipa Pharma, and Purple Biotech; and received **stock or stock options** from Galectin Therapeutics and Privo Technologies, Inc.Muh-Hwa Yang **received honoraria** from Merck, MSD, Ono Pharmaceutical, and Pfizer; and served in a **consulting or advisory role** for MSD and Pfizer.Jessica L. Geiger served in a **consulting or advisory role** for Astellas Pharma Inc., Exelixis, Merck, and Regeneron; and **received research funding** from Alkermes, Genentech/Roche, Merck, Merck Serono, and Regeneron. Marc Oliva **received grants or contracts for research** from AbbVie, ALX Oncology, Ascendis Pharma, Ayala Pharmaceuticals, Inc., Bayer, BeOne Medicines, Boehringer Ingelheim, Debiopharm, Elixir, Gilead, GSK, ISA Therapeutics, Merck, MSD, Nykode, Pfizer, Roche, and Transgene; **received consulting fees** from BeOne Medicines, Merck Serono, MSD, and Transgene; **received honoraria or payment** from Bristol Myers Squibb, Merck Serono, and MSD; received **travel, accommodations, and expenses** from Boehringer Ingelheim, Bristol Myers Squibb, Merck Serono, and MSD; and **participated in a data safety monitoring or advisory board** for Merck Serono, MSD, Obatica, and Transgene.Myung-Ju Ahn **received honoraria** from Amgen, AstraZeneca, Daiichi Sankyo, Merck, MSD, Takeda, and Yuhan; served in a **consulting or advisory role** for Amgen, AstraZeneca, BioNTech, Boehringer Ingelheim, Daiichi Sankyo, Johnson & Johnson, Merck, MSD, and Takeda; **holds patents/intellectual property or receive royalties** from Yuhan.Sun Min Lim **received honoraria** from Amgen, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, J Ints Bio, Eli Lilly, Merck, MSD, Oscotec, Takeda, Therapex, and Yuhan; **received research funding** from Johnson & Johnson, MSD, and Yuhan; and **participated in a safety monitoring board** for J Ints Bio, Pierre Fabre, Therapex, and Yuhan.William Ince **received honoraria** from AstraZeneca, Eisai, Ipsen, Merck Serono, and Recordati; served in a **consulting or advisory role** for Ipsen, Merck, and Recordati; **received research funding** from Merck; and received **travel, accommodations, and expenses** from Ipsen and Merck.Aarti Bhatia **received honoraria** from Clinical Care Options and Medscape; served in a **consulting or advisory role** for Adcendo, Daiichi Sankyo, and Coherus Oncology; and **received research funding** from Boehringer Ingelheim and Genentech.Siddharth Sheth **received honoraria** from Coherus Oncology, Eisai, and Inhibrx; has **participated in a speaker's bureau** for Exelixis; has **received research funding** from AstraZeneca, Exelixis, Inovio Pharmaceuticals, Merck, and Regeneron; received **travel, accommodations, and expenses** from Merus.Bhumsuk Keam has no conflict of interest.Robert Metcalf served in a **consulting or advisory role** for Avacta Group. Joshua C. Curtin is an **employee** of Johnson & Johnson and **may hold stock** in Johnson & Johnson.Kiichiro Toyoizumi is an **employee** of Johnson & Johnson and **may hold stock** in Johnson & Johnson.Mark Wade is an **employee** of Johnson & Johnson and **may hold stock** in Johnson & Johnson.Emrullah Yilmaz is an **employee** of Johnson & Johnson and **may hold stock** in Johnson & Johnson.Priya Kim is an **employee** of Johnson & Johnson and **may hold stock** in Johnson & Johnson.Remy B. Verheijen is an **employee** of Johnson & Johnson and **may hold stock** in Johnson & Johnson.Sujay Shah is an **employee** of Johnson & Johnson and **may hold stock** in Johnson & Johnson.Mahadi Baig is an **employee** of Johnson & Johnson and **may hold stock** in Johnson & Johnson.Paul L. Swiecicki **received consulting fees** from Astellas Pharma Inc., CDR-Life, Elevar, EMD Serono, GeoVax, Janssen, Prelude, Rapt Therapeutics, Regeneron, Remix, and Rgenta; **received research funding** from Ascentage Pharma and Summit Therapeutics; and **holds patents/intellectual property or receive royalties** related to ctDNA detection technology from Bio-Rad.

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Glossary

AE: adverse event
Anti–PD-1: anti–programmed death-1
Anti–PD-L1: anti–programmed death-ligand 1
CBR: clinical benefit rate
CI: confidence interval
CR: complete response
CT: computed tomography
DoR: duration of response
EGFR: epidermal growth factor receptor
HNSCC: head and neck squamous cell carcinoma
HPV: human papillomavirus
MET: mesenchymal epithelial transition
MRI: magnetic resonance imaging
NSCLC: non-small cell lung cancer
ORR: overall response rate
OS: overall survival
PD: progressive disease
PFS: progression-free survival
PR: partial response
R/M: recurrent and/or metastatic
SoD: sum of diameters
TEAE: treatment-emergent adverse event