ISRCTN98745687 https://doi.org/10.1186/ISRCTN98745687

A phase 1b/2, open-label study of amivantamab monotherapy and amivantamab in addition to standard of care therapeutic agents in participants with recurrent/metastatic head and neck squamous cell carcinoma

Submission date 05/01/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 12/03/2024	**Overall study status** Ongoing	
Last Edited 04/04/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims

This is an open-label, multicentre, phase 1b/2 study evaluating the safety, tolerability (the degree to which overt adverse effects of a drug can be tolerated by a patient), and anti-tumour activity of amivantamab (the study drug) alone, and amivantamab in addition to pembrolizumab or paclitaxel (standard care treatments) in participants with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC).

Despite recent advances in the treatment of HNSCC, patients continue to experience significant morbidity and mortality, underscoring the need to improve therapeutic approaches. Mesenchymal epithelial transition (MET) and the epidermal growth factor receptor (EGFR) are both antigens (a type of protein), both of which can be found on cancer cells. In laboratory studies, amivantamab binds to MET and EGFR on a cancer cell, and the cell cannot get the signals it needs to grow. Given the significant roles of EGFR and MET in HNSCC, amivantamab could provide targeted therapy for this population of high unmet clinical need.

Who can participate?

Adults over 18 years, who have histologically or cytologically confirmed recurrent or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC) that is considered incurable by local therapies.

What does the study involve?

Participants in this study will be enrolled into 1 of 4 treatment cohorts:

- Cohort 1: Amivantamab subcutaneous (SC) unrelated to human papillomavirus (HPV)
- Cohort 2: Amivantamab SC + pembrolizumab intravenous infusion unrelated to HPV
- Cohort 3: Amivantamab SC + paclitaxel intravenous infusion unrelated to HPV
- Cohort 4: Amivantamab subcutaneous (SC) related to HPV

• Cohort 5: Amivantamab (SC), Pembrolizumab and Carboplatin both HPV positive and negative.

Amivantamab will be administered via subcutaneous injection (i.e., under the skin).Carboplatin, paclitaxel and pembrolizumab will be administered via an intravenous (IV) infusion (i.e., directly into the vein).

The study will consist of a Screening period of up to 28 days, a Treatment period consisting of 21-day cycles (including an End of Treatment visit), and a Follow-up period.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration

Risks:
The participant information sheet(s) will contain full information on the potential side effects of study interventions.

Amivantamab:
The possible discomforts, side effects, and risks related to amivantamab treatment are not all known. As of 20th May 2023, safety data are available for approximately 1699 patients who have received amivantamab.

A full list of side effects associated with amivantamab will be included in the participant information sheet and discussed with participants during the informed consent process.

Administration-Related Reactions (ARRs) with subcutaneous administration:
When administered under the skin (subcutaneous administration), a side effect of amivantamab that may occur during or shortly after an administration is completed is called an administration-related reaction (ARR). Participants will receive premedication, including paracetamol /acetaminophen, an antihistamine, and a corticosteroid before the administration to help prevent or decrease any symptoms.

Rash:
Participants will be instructed on how to prevent and treat rashes. This will include not being in the sun unnecessarily and using SPF ≥ 30 sun protector.

Lung Inflammation:
In patients treated with amivantamab monotherapy, there have been cases of lung inflammation, including severe cases resulting in death.

Birth control and pregnancy:
The effects of amivantamab on fertility, the human embryo, the fetus, or the breast-fed infant are unknown. Potential participants cannot take part in this study if they are breastfeeding a child or are pregnant. Participants of child-bearing potential must agree not to become pregnant or donate eggs for assisted reproduction while they are in the study and for at least 10 months after the last dose of treatment. Participants of child-bearing potential must adhere to strict birth control requirements during study participation and for at least 10 months after the last dose and will be regularly tested for pregnancy. Male participants must use a condom from when they start taking the study drug until 10 months after the last dose when having sex with a female partner who is able to get pregnant and must not donate sperm.

Carboplatin, Paclitaxel and pembrolizumab:
A full list of all potential discomforts, side effects, and risks associated with carboplatin, paclitaxel and/or pembrolizumab will be provided in the participant information sheet and discussed with participants during the informed consent process.

Other study procedures:
Biopsy:
The risks associated with a biopsy will depend upon where the tumour(s) are located in the body. Typical procedures involve inserting a thin needle through the skin using images to guide exact placement (CT guided needle biopsy). Participants may be given sedation and local anesthesia as needed to make the procedure as comfortable as possible. In general, having a biopsy can cause pain, swelling, bleeding, and/or infection at the site where the biopsy needle or other instrument penetrates through the skin.
There is also the rare possibility that having this procedure may shift some cells from the tumour into the surrounding tissues. This means that the tumour may spread to that area. Participants will be monitored for these complications and treated if any occur.

Blood Draw:
Taking blood may cause pain, bruising, or irritation at the place where the needle goes into the skin. Fainting, and in rare cases infection may occur.

Electrocardiogram (ECG):
There is generally no risk of having an ECG. The sticky patches may pull the skin or cause redness or itching.

CT Scan:
CT scans do create low levels of radiation, which has a small potential to cause cancer and other defects. However, the risk associated with any one scan is small. Contrast material will be used; Participants will be told about possible side effect or allergic reaction.

MRI (including Brain MRI):
Because radiation is not used, there is no risk of exposure to radiation during MRI procedure. Participants must state if they have a metal object in their body. Contrast material will be used; Participants will be told about possible side effect or allergic reaction.

Endoscopy:
Taking this procedure may result in fever, chills, redness, swelling, or bleeding or other drainage from the IV site, belly pain, nausea, or vomiting, black, tarry, or bloody stools, trouble swallowing, throat or chest pain that gets worse.

Subcutaneous injection:
Use of a subcutaneous injection for study treatment administration, imaging, and other tests may cause discomfort, irritation, minor bruising, bleeding, or injection leakage, and rarely causes nausea, light dizziness, and air embolism.

Where is the study run from?
Janssen-Cliag International NV (Netherlands)

When is the study starting and how long is it expected to run for?
January 2024 to June 2027

Who is funding the study?
Janssen-Cliag International NV (Netherlands)

Who is the main contact?
Participate-In-This-Study@its.jnj.com

Contact information

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Scientific

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Clinical Trials Information System (CTIS)
2023-508418-40

Integrated Research Application System (IRAS)
1009340

ClinicalTrials.gov (NCT)
NCT05379595

Protocol serial number
61186372HNC2002, IRAS 1009340, CPMS 58135

Study information

Scientific Title

A phase 1b/2, open-label study of amivantamab monotherapy and amivantamab in addition to standard of care therapeutic agents in participants with recurrent/metastatic head and neck squamous cell carcinoma

Acronym
OrigAMI-4

Study objectives
Current study hypothesis:

Main objectives
In participants with recurrent or metastatic head and neck squamous cell carcinoma (R/M HNSCC), to assess anti-tumor activity of:
•Amivantamab alone in participants who have received prior platinum-based chemotherapy and programmed death receptor-1 (PD-1)/ligand 1 (PD-L1) therapy
•Amivantamab in addition to paclitaxel for participants who received prior programmed death receptor-1 (PD-1)/ligand 1 (PD-L1) based therapy
• Amivantamab in addition to pembrolizumab or in addition to pembrolizumab and carboplatin who are treatment-naïve in the R/M setting.
•To assess the recommended phase 2 combination dose (RP2CD) as well as safety and tolerability of amivantamab in addition to paclitaxel in participants who received prior PD- 1/PD-L1 therapy.

Secondary objectives
In participants with R/M HNSCC, to assess the safety, tolerability, and additional measures of efficacy of
•Amivantamab alone in participants who have received prior platinum-based chemotherapy and programmed death receptor-1 (PD-1)/ligand 1 (PD-L1) therapy. Measures of pharmacokinetics (what the body does to the drug) will also be assessed for amivantamab alone.
•Amivantamab in addition to paclitaxel for participants who have received prior programmed death receptor-1 (PD-1)/ligand 1 (PD-L1) therapy
• Amivantamab in addition to pembrolizumab or in addition to pembrolizumab and carboplatin who are treatment-naive in the R/M setting.

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Previous study hypothesis:

The primary objectives of each cohort are:
Cohort 1: To assess anti-tumour activity of amivantamab monotherapy in participants with recurrent or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC) who have received prior treatment with platinum-based chemotherapy and a PD-1/PD-L1 inhibitor.
Cohort 2: To assess anti-tumour activity of amivantamab in addition to pembrolizumab in participants with R/M HNSCC who are treatment-naïve in the R/M setting.
Cohort 3: To determine recommended Phase 2 (combination) dose(s) (RP2CDs) of amivantamab in addition to paclitaxel in participants with R/M HNSCC who have received PD-1/PD-L1 based therapy; and, to characterise safety and tolerability of amivantamab in addition to paclitaxel in participants with R/M HNSCC who have received PD-1/PD-L1 based therapy.
Cohort 3B: To assess anti-tumour activity of amivantamab in addition to paclitaxel in participants with R/M HNSCC who have received PD-1/PD-L1 based therapy.

The secondary objectives for each cohort include:
Cohort 1: To further assess anti-tumour activity of amivantamab monotherapy in participants with R/M HNSCC who have received prior treatment with platinum-based chemotherapy (PBC) and a PD-1/PD-L1 inhibitor.
Cohort 2: To further assess anti-tumour activity of amivantamab in addition to pembrolizumab in participants with R/M HNSCC who are treatment-naïve in the R/M setting.
Cohort 3B: To further assess anti-tumour activity of amivantamab in addition to paclitaxel in participants with R/M HNSCC who have received PD-1/PD-L1 based therapy.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 11/03/2024, London - Westminster Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; -; westminster.rec@hra.nhs.uk), ref: 24/LO/0090

Study design
Interventional non randomized

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma

Interventions
Current interventions, as of 31/03/2025:

Experimental: Cohort 1 Amivantamab Monotherapy (Dose Expansion)
Participants will receive subcutaneous injection of amivantamab monotherapy 1600 milligrams (mg) (2240 mg, if body weight >=80 kilograms [kg]) on Cycle 1 Day 1 and 2400 mg (3360 mg, if body weight >=80 kg) once every week (q1w) for the remainder of Cycle 1 (Days 8 and 15), and every 3 weeks (q3w) from Cycle 2 onwards.

Experimental: Cohort 2 Amivantamab + Pembrolizumab (Dose Expansion Including Safety Run-in)
Participants will receive subcutaneous injection of amivantamab 1600 mg (2240 mg, if body weight >=80 kg) on Cycle 1 Day 1 and 2400 mg (3360 mg, if body weight >=80 kg) q1w for the remainder of Cycle 1 (Days 8 and 15), and q3w from Cycle 2 onwards, along with intravenous injection of pembrolizumab 200 mg q3w (on Day 1 of each 21-day cycle).

Experimental: Cohort 3A (Dose Confirmation): Amivantamab + Paclitaxel
Participants will receive subcutaneous injection of amivantamab 1600 mg (2240 mg, if body weight >=80 kg) on Cycle 1 Day 1 and 2400 mg (3360 mg, if body weight >=80 kg) q1w for the remainder of Cycle 1 (Days 8 and 15), and q3w from Cycle 2 onwards, along with intravenous injection of paclitaxel 175 mg/m^2 q3w (on Day 1 of each 21-day cycle) in dose confirmation Cohort 3A. The recommended Phase 2 combination dose (RP2CD) of amivantamab will be determined in conjunction with study evaluation team (SET) in this dose confirmation Cohort 3A.

Experimental: Cohort 3B (Dose Expansion): Amivantamab + Paclitaxel
Participants will receive subcutaneous injection of amivantamab at the determined RP2CD in addition to intravenous injection of paclitaxel 175 mg/m^2 q3w (on Day 1 of each 21-day cycle) as confirmed by SET in Cohort 3A.

Experimental: Cohort 4 Amivantamab Monotherapy: Participants will receive subcutaneous injection of amivantamab monotherapy 1600 mg (2240 mg, if body weight >=80 kg) on Cycle 1 Day 1 and 2400 mg (3360 mg, if body weight >=80 kg) q1w for the remainder of Cycle 1 (Days 8 and 15), and q3w from Cycle 2 onwards.

Experimental: Cohort 5: Pembrolizumab + Amivantamab
+ Carboplatin (Dose Expansion). Participants will receive subcutaneous injection of amivantamab 1600 mg (2240 mg, if body weight >=80 kg) on Cycle 1 Day 1 and 2400 mg (3360 mg, if body weight >=80 kg) q1w for the remainder of Cycle 1 (Days 8 and 15), and q3w from Cycle 2 onwards in addition to intravenous injection of pembrolizumab 200 mg on Day 1 of each cycle, and carboplatin (area under the concentration-time curve [AUC] 5 milligram
per milliliter [mg/ml]*min) q3w on Day 1 of Cycles 1-6.

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Previous interventions as of 26/11/2024:

Experimental: Cohort 1 Amivantamab Monotherapy (Dose Expansion)
Participants will receive subcutaneous injection of amivantamab monotherapy 1600 milligrams (mg) (2240 mg, if body weight >=80 kilograms [kg]) on Cycle 1 Day 1 and 2400 mg (3360 mg, if body weight >=80 kg) once every week (q1w) for the remainder of Cycle 1 (Days 8 and 15), and every 3 weeks (q3w) from Cycle 2 onwards.

Experimental: Cohort 2 Amivantamab + Pembrolizumab (Dose Expansion Including Safety Run-in)
Participants will receive subcutaneous injection of amivantamab 1600 mg (2240 mg, if body weight >=80 kg) on Cycle 1 Day 1 and 2400 mg (3360 mg, if body weight >=80 kg) q1w for the remainder of Cycle 1 (Days 8 and 15), and q3w from Cycle 2 onwards, along with intravenous injection of pembrolizumab 200 mg q3w (on Day 1 of each 21-day cycle).

Experimental: Cohort 3A (Dose Confirmation): Amivantamab + Paclitaxel
Participants will receive subcutaneous injection of amivantamab 1600 mg (2240 mg, if body weight >=80 kg) on Cycle 1 Day 1 and 2400 mg (3360 mg, if body weight >=80 kg) q1w for the remainder of Cycle 1 (Days 8 and 15), and q3w from Cycle 2 onwards, along with intravenous injection of paclitaxel 175 mg/m^2 q3w (on Day 1 of each 21-day cycle) in dose confirmation Cohort 3A. The recommended Phase 2 combination dose (RP2CD) of amivantamab will be determined in conjunction with study evaluation team (SET) in this dose confirmation Cohort 3A.

Experimental: Cohort 3B (Dose Expansion): Amivantamab + Paclitaxel
Participants will receive subcutaneous injection of amivantamab at the determined RP2CD in addition to intravenous injection of paclitaxel 175 mg/m^2 q3w (on Day 1 of each 21-day cycle) as confirmed by SET in Cohort 3A.

Experimental: Cohort 4 Amivantamab Monotherapy: Participants will receive subcutaneous injection of amivantamab monotherapy 1600 mg (2240 mg, if body weight >=80 kg) on Cycle 1 Day 1 and 2400 mg (3360 mg, if body weight >=80 kg) q1w for the remainder of Cycle 1 (Days 8 and 15), and q3w from Cycle 2 onwards.

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Previous interventions:

Experimental: Cohort 1 Amivantamab Monotherapy (Dose Expansion)
Participants will receive subcutaneous injection of amivantamab monotherapy 1600 milligrams (mg) (2240 mg, if body weight >=80 kilograms [kg]) on Cycle 1 Day 1 and 2400 mg (3360 mg, if body weight >=80 kg) once every week (q1w) for the remainder of Cycle 1 (Days 8 and 15), and every 3 weeks (q3w) from Cycle 2 onwards.

Experimental: Cohort 2 Amivantamab + Pembrolizumab (Dose Expansion Including Safety Run-in)
Participants will receive subcutaneous injection of amivantamab 1600 mg (2240 mg, if body weight >=80 kg) on Cycle 1 Day 1 and 2400 mg (3360 mg, if body weight >=80 kg) q1w for the remainder of Cycle 1 (Days 8 and 15), and q3w from Cycle 2 onwards, along with intravenous injection of pembrolizumab 200 mg q3w (on Day 1 of each 21-day cycle).

Experimental: Cohort 3A (Dose Confirmation): Amivantamab + Paclitaxel
Participants will receive subcutaneous injection of amivantamab 1600 mg (2240 mg, if body weight >=80 kg) on Cycle 1 Day 1 and 2400 mg (3360 mg, if body weight >=80 kg) q1w for the remainder of Cycle 1 (Days 8 and 15), and q3w from Cycle 2 onwards, along with intravenous injection of paclitaxel 175 mg/m^2 q3w (on Day 1 of each 21-day cycle) in dose confirmation Cohort 3A. The recommended Phase 2 combination dose (RP2CD) of amivantamab will be determined in conjunction with study evaluation team (SET) in this dose confirmation Cohort 3A.

Experimental: Cohort 3B (Dose Expansion): Amivantamab + Paclitaxel
Participants will receive subcutaneous injection of amivantamab at the determined RP2CD in addition to intravenous injection of paclitaxel 175 mg/m^2 q3w (on Day 1 of each 21-day cycle) as confirmed by SET in Cohort 3A.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Cohort 1/2/3/4: Amivantamab co-formulated with recombinant human hyaluronidase (rHuPH20) [Amivantamab, Vorhyaluronidase alfa] Cohort 5: Amivantamab co-formulated with recombinant human hyaluronidase (rHuPH20) [Amivantamab, Vorhyaluronidase alfa] Biological: Pembrolizumab, Pembrolizumab will be administered intravenously. Other Names: • KEYTRUDA Drug: Carboplatin, Carboplatin will be administered intravenously. Other Names: • PARAPLATIN

Primary outcome(s)
Current primary outcome measure as of 31/03/2025:

Cohorts 1, 2, 3B, 4 and 5: Objective response rate (ORR), according to Response Criteria in Solid Tumors (RECIST) v1.1.
Cohort 3A: Incidence of dose-limiting toxicities (DLTs); and, incidence and severity of treatment-emergent adverse events (TEAEs).

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Previous primary outcome measure as of 26/11/2024:

Cohorts 1, 2, 3B and 4: Objective response rate (ORR), according to Response Criteria in Solid Tumors (RECIST) v1.1.
Cohort 3A: Incidence of dose-limiting toxicities (DLTs); and, incidence and severity of treatment-emergent adverse events (TEAEs).

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Previous primary outcome measure:

Cohorts 1, 2, and 3B: Objective response rate (ORR), according to Response Criteria in Solid Tumors (RECIST) v1.1.
Cohort 3A: Incidence of dose-limiting toxicities (DLTs); and, incidence and severity of treatment-emergent adverse events (TEAEs).

Key secondary outcome(s))
Current secondary outcome measures as of 31/03/2025:

Cohorts 1, 2,3B, 4 and 5:
1. Duration of response (DoR)
2. Clinical benefit rate (CBR)
3. Progression-free survival (PFS)
4. Overall survival (OS)
5. Incidence and severity of treatment-emergent adverse events (TEAEs).

Cohort 1 and 4:
Serum pharmacokinetic (PK) parameters including, but not limited to, maximum serum concentration (Cmax), time to reach the maximum serum concentration (tmax), area under the concentration-time curve (AUC), AUCτ, plasma/serum concentration immediately prior the next study treatment administration (Ctrough), and accumulation ratio.

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Previous secondary outcome measure as of 26/11/2024:

Cohorts 1, 2,3B and 4:
1. Duration of response (DoR)
2. Clinical benefit rate (CBR)
3. Progression-free survival (PFS)
4. Overall survival (OS)
5. Incidence and severity of treatment-emergent adverse events (TEAEs).

Cohort 1 and 4:
Serum pharmacokinetic (PK) parameters including, but not limited to, maximum serum concentration (Cmax), time to reach the maximum serum concentration (tmax), area under the concentration-time curve (AUC), AUCτ, plasma/serum concentration immediately prior the next study treatment administration (Ctrough), and accumulation ratio.

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Previous secondary outcome measure:

Cohorts 1, 2, and 3B:
1. Duration of response (DoR)
2. Clinical benefit rate (CBR)
3. Progression-free survival (PFS)
4. Overall survival (OS)
5. Incidence and severity of treatment-emergent adverse events (TEAEs).

Cohort 1 only:
Serum pharmacokinetic (PK) parameters including, but not limited to, maximum serum concentration (Cmax), time to reach the maximum serum concentration (tmax), area under the concentration-time curve (AUC), AUCτ, plasma/serum concentration immediately prior the next study treatment administration (Ctrough), and accumulation ratio.

Completion date
17/07/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 31/03/2025:

1. Have histologically or cytologically confirmed recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) that is considered incurable by local therapies
2. Acceptable prior lines of therapy will be determined according to specific cohort 1, 2, 3A, 3B, 4 and 5:
2.1. The eligible primary tumor locations are the oropharynx, oral cavity, hypopharynx, or larynx
2.2. Any known p16 status of tumor must be negative (Note: All participants with an oropharyngeal tumor must have results of p16 status, per local testing)
2.3. Participants must provide local testing results of programmed cell death ligand 1 (PD-L1) status, if available
3. Cohort 4:
3.1. Patients must have primary tumor location in oropharynx. Unknown primary tumors are not included
3.2. Primary tumor must be HPV-positive, confirmed by positive p16 test or high-risk human papillomavirus (HPV) in-situ hybridization (ISH) in tissue (current or archival)
3.3. Participants must provide local testing results of PD-L1 status, if available
4. Participants in Cohorts 1, 2, 3B, 4 and 5 must have measurable disease according to RECIST version 1.1.
5. Participants in Cohort 3A must have evaluable disease (defined as having at least 1 non-target lesion according to RECIST version 1.1
6. Toxicities from previous anticancer therapies should have resolved to baseline levels or to Grade 1 or less prior to the first dose of study treatment (except for alopecia or post-radiation skin changes [any grade], Grade less than or equal to [<=] 2 peripheral neuropathy and Grade <= 2 hypothyroidism stable on hormone replacement)
7. Have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1
8. Participant must have adequate organ and bone marrow function as follows, without history of red blood cell transfusion, platelet transfusion, or use of granulocyte colony-stimulating factor within 7 days prior to the date of the laboratory test.
8. Participants should have:
8.1. Hemoglobin >=9 grams per deciliter (g/dL)

8.2. Neutrophils >=1.5 x 10^3/mcg
8.3. Platelets >=100 x 10^3/mcg

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Previous participant inclusion criteria as of 26/11/2024:

1. Have histologically or cytologically confirmed recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) that is considered incurable by local therapies
2. Acceptable prior lines of therapy will be determined according to specific cohort 1, 2, 3A and 3B:
2.1. The eligible primary tumor locations are the oropharynx, oral cavity, hypopharynx, or larynx
2.2. Any known p16 status of tumor must be negative (Note: All participants with an oropharyngeal tumor must have results of p16 status, per local testing)
2.3. Participants must provide local testing results of programmed cell death ligand 1 (PD-L1) status, if available
3. Cohort 4:
3.1. Patients must have primary tumor location in oropharynx. Unknown primary tumors are not included
3.2. Primary tumor must be HPV-positive, confirmed by positive p16 test or high-risk human papillomavirus (HPV) in-situ hybridization (ISH) in tissue (current or archival)
3.3. Participants must provide local testing results of PD-L1 status, if available
4. Participants in Cohorts 1, 2, and 3B and 4 must have measurable disease according to RECIST version 1.1.
5. Participants in Cohort 3A must have evaluable disease (defined as having at least 1 non-target lesion according to RECIST version 1.1
6. Toxicities from previous anticancer therapies should have resolved to baseline levels or to Grade 1 or less prior to the first dose of study treatment (except for alopecia or post-radiation skin changes [any grade], Grade less than or equal to [<=] 2 peripheral neuropathy and Grade <= 2 hypothyroidism stable on hormone replacement)
7. Have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1
8. Participant must have adequate organ and bone marrow function as follows, without history of red blood cell transfusion, platelet transfusion, or use of granulocyte colony-stimulating factor within 7 days prior to the date of the laboratory test.
8. Participants should have:
8.1. Hemoglobin >=9 grams per deciliter (g/dL)
8.2. Neutrophils >=1.5 x 10^3/mcg
8.3. Platelets >=100 x 10^3/mcg

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Previous participant inclusion criteria:

1. Be at least 18 years of age at the time of informed consent.
2. Have histologically or cytologically confirmed recurrent or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC) that is considered incurable by local therapies.
3. Participants must meet the following cohort-specific requirements:
Cohort 3A: Dose Confirmation Cohort: Have evaluable disease (defined as having at least 1 non-target lesion according to RECIST v1.1). If only 1 evaluable lesion exists, it may be used for the screening biopsy as long as baseline tumour assessment scans are performed 7 or more days after the biopsy. Tumour lesions situated in a previously irradiated area are considered evaluable if progression following radiation has been demonstrated in such lesions.

Cohorts 1, 2, and 3B: Dose Expansion Cohorts: Have measurable disease according to RECIST v1.
1. If only 1 measurable lesion exists, it may be used for the screening biopsy as long as baseline tumour assessment scans are performed 7 or more days after the biopsy. Tumour lesions situated in a previously irradiated area are considered measurable if progression following radiation has been demonstrated in such lesions.
4. If available, provide adequate tumour tissue for a baseline sample following the most recent systemic anticancer therapy.
5. Participant may have a prior or concurrent second malignancy (other than the disease under study) which natural history or treatment is unlikely to interfere with any study endpoints of safety or the efficacy of the study treatment(s). Prior or concurrent second malignancies must be reviewed and agreed to with the medical monitor.
6. Toxicities from previous anticancer therapies should have resolved to baseline levels or to Grade 1 or less prior to the first dose of study treatment (except for alopecia or post-radiation skin changes [any grade], Grade lower than or equal to 2 peripheral neuropathy and Grade lower than or equal to 2 hypothyroidism stable on hormone replacement).
7. Must meet the protocol defined cohort-specific requirements (See protocol for full details).
8. Have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1.
9. Have at least 1 of the following:
a. Serum creatinine lower than or equal to 1.5 x upper limit of normal (ULN).
b. Estimated glomerular filtration rate greater than or equal to 45 millilitre per minute, based on the Modified Diet in Renal Disease (MDRD) 4-variable formula.
10. Participants are eligible if they have the following lab values:
a. Aspartate aminotransferase (AST) lower than or equal to 3 x ULN (lower than or equal to 5 x ULN if liver metastases are present)
b. ALT lower than or equal to 3 x ULN (lower than or equal to 5 x ULN if liver metastases are present)
c. Total bilirubin lower than or equal to 1.5 x ULN; participants with congenital nonhemolytic hyperbilirubinemia such as Gilbert’s syndrome can enroll if conjugated bilirubin is within normal limits.
11. Participant must have adequate organ and bone marrow function as per protocol criteria, without history of red blood cell transfusion, platelet transfusion, or use of granulocyte colony-stimulating factor within 7 days prior to the date of the laboratory test.
12. Cohort 2: Thyroid function laboratory values within the normal range.
13. While on study treatment and for 10 months after the last dose of study treatment, a participant must:
- Not breastfeed or be pregnant.
- Not donate gametes (i.e., eggs or sperm) or freeze for future use for the purposes of assisted reproduction. Participants should consider preservation of gametes prior to study treatment as anticancer treatments may impair fertility.
- Wear an external condom.
- If of childbearing potential: have a negative highly sensitive serum pregnancy test at screening and within 72 hours of the first dose of study treatment and agree to further pregnancy tests; practice at least 1 highly effective method of contraception; if oral contraceptives are used, a barrier method of contraception must also be used.
- If a participant’s partner is of childbearing potential the partner must practice a highly effective method of contraception unless the participant is vasectomised.
14. Must sign an Informed Consent Form (ICF; or their legally acceptable representative must sign) indicating that the participant understands the purpose of, and procedures required for, the study and is willing to participate in the study.
15. Be willing and able to adhere to the lifestyle restrictions specified in this protocol.

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 31/03/2025:

1. Uncontrolled illness including any medical history or current (non-infectious) interstitial lung disease (ILD)/ pneumonitis/ pulmonary fibrosis, or where suspected ILD/pneumonitis/pulmonary fibrosis cannot be ruled out by imaging at screening
2. Participant with untreated brain metastases leptomeningeal disease, or spinal cord compression not definitively treated with surgery or radiation
3. Participant with a history of clinically significant cardiovascular disease
4. Received prior chemotherapy, targeted cancer therapy, immunotherapy, or treatment with an investigational anticancer agent within 2 weeks or 4 half-lives, whichever is longer, before the first administration of study treatment. The maximum required washout is 28 days
5. Received radiotherapy for palliative purposes within 7 days of the first administration of study treatment

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Previous participant exclusion criteria as of 26/11/2024:

1. Uncontrolled illness including any medical history or current (non-infectious) interstitial lung disease (ILD)/ pneumonitis/ pulmonary fibrosis, or where suspected ILD/pneumonitis/pulmonary fibrosis cannot be ruled out by imaging at screening
2. Participant with untreated brain metastases leptomeningeal disease, or spinal cord compression not definitively treated with surgery or radiation
3. Participant with a history of clinically significant cardiovascular disease
4. Received prior chemotherapy, targeted cancer therapy, immunotherapy, or treatment with an investigational anticancer agent within 2 weeks or 4 half-lives, whichever is longer, before the first administration of study treatment. The maximum required washout is 28 days
5. Received radiotherapy for palliative purposes within 7 days of the first administration of study treatment

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Previous participant exclusion criteria:

1. Uncontrolled illness, including but not limited to all conditions specified in the protocol.
2. Medical history of (non-infectious) interstitial lung disease (ILD)/pneumonitis/pulmonary

fibrosis, or has current ILD/pneumonitis, or suspected ILD/pneumonitis/pulmonary fibrosis cannot be ruled out by imaging at screening.
3. Known allergies, hypersensitivity, or intolerance to excipients of amivantamab, recombinant human hyaluronidase (rHuPH20), or other study treatment.
4. Participant has a history of clinically significant cardiovascular disease, as specified in the study protocol.
5. Participant has, or will have, any of the following:
a. An invasive operative procedure with entry into a body cavity, within 4 weeks or without complete recovery before the first administration of study treatment.
b. Significant traumatic injury within 3 weeks before the start of the first administration of study treatment (all wounds must be fully healed prior to Day 1).
c. Expected major surgery while the investigational agent is being administered or within 6 months after the last dose of study treatment.
6. Participant with untreated brain metastases
7. Participant has a medical history or known presence of leptomeningeal disease, or participant has spinal cord compression not definitively treated with surgery or radiation.
8. HIV-positive participants are not eligible if they meet any of protocol specified criteria.
9. Active hepatitis of infectious origin.
10. Received prior chemotherapy, targeted cancer therapy, immunotherapy, or treatment with an investigational anticancer agent within 2 weeks or 4 half-lives, whichever is longer, before the first administration of study treatment. The maximum required washout is 28 days.
11. Received radiotherapy for palliative purposes within 7 days of the first administration of study treatment.
12. Requires a prohibited medication that cannot be discontinued, substituted, or temporarily interrupted during the study.
13. Received an investigational treatment (including investigational vaccines, but not including anticancer therapy) or used an invasive investigational medical device within 6 weeks before the planned first dose of study treatment.
14. Cohort 2: Prohibited immunosuppressive medication use within 7 days prior to the first administration of study treatment.
15. Cohort 2: Participant has received a live or live attenuated vaccine within 30 days prior to the first dose of study drug. Vaccines approved or authorised for emergency use and non-live vaccines are allowed.
16. Any condition for which, in the opinion of the investigator, participation would not be in the best interest of the participant (e.g., compromise the well-being) or that could prevent, limit, or confound the protocol-specified assessments.

Date of first enrolment
14/04/2024

Date of final enrolment
31/05/2026

Locations

Countries of recruitment
United Kingdom

England

France

Germany

Korea, South

Malaysia

Poland

Spain

Taiwan

Study participating centre
Imperial College London
Du Cane Road
London
United Kingdom
W12 0HS

Study participating centre
Royal Marsden Hospital
Royal Marsden Hospital
Downs Road
Sutton
United Kingdom
SM2 5PT

Study participating centre
Addenbrookes
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
The Christie Hospital
Wilmslow Road
Withington
Manchester
United Kingdom
M20 4BX

Study participating centre
University College London Hospital
University College London Hospitals NHS Foundation Trust
Department of Womens Health
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
Royal Surrey County Hospital
Egerton Road
Guildford
United Kingdom
GU2 7XX

Sponsor information

Organisation
Janssen-Cilag International NV

Funder(s)

Funder type
Industry

Funder Name
Janssen-Cliag International NV

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing policy of the Janssen Pharmaceutical Companies of Johnson and Johnson is available at https://www.janssen.com/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 yoda.yale.edu

IPD sharing plan summary

Available on request