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A Phase Ib/II, open-label study of amivantamab monotherapy and amivantamab in addition to other therapeutic agents in participants with head and neck squamous cell carcinoma

Submission date 05/01/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol
Registration date 12/03/2024	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 26/10/2026	**Condition category** Cancer	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
Head and neck squamous cell cancer (HNSCC) develops from the mucosal epithelium of the mouth, nose, and throat. HNSCC represents a significant global health concern and despite recent advances in its treatment, the overall survival rates have not substantially improved in the past few decades. While many patients initially present with localized disease, approximately 50% of patients will experience local recurrence or distant metastasis within 5 years. Amivantamab (JNJ-61186372) is a human immunoglobulin G1 (IgG1)-based antibody (a protein that helps protect the body against a foreign trigger) that simultaneously inhibits the activity of two proteins, epidermal growth factor receptor (EGFR) and mesenchymal-epithelial transition factor (MET), which are known to play crucial roles in the development and progression of HNSCC, promote tumor growth, and impact development of resistance to available therapies. The Sponsor aims to evaluate if amivantamab as monotherapy and in addition to pembrolizumab, or paclitaxel, or pembrolizumab plus carboplatin demonstrates anti-tumor activity with a tolerable safety profile.

Who can participate?
Patients >=18 years of age with head and neck squamous cell carcinoma.

What does the study involve?
The study will be conducted as below:
1. Screening (28 days)
2. Treatment Phase: Participants will receive 1 of the below study treatment(s) on Day 1 of each 21-day cycle:
• Amivantamab subcutaneous (SC)
• Amivantamab SC + pembrolizumab intravenous infusion
• Amivantamab SC + paclitaxel intravenous infusion
• Amivantamab SC + pembrolizumab and carboplatin intravenous infusion
• Amivantamab SC + pembrolizumab intravenous infusion before and after the surgery.

3. Post-treatment Follow-up Phase: Participants will be followed-up for safety until last study-related procedure or until 30 days after last dose of amivantamab SC or paclitaxel or carboplatin, or 100 days after the last dose of pembrolizumab (whichever is longer).
During the study, some tests will be performed such as blood tests, physical examinations, vital signs, and electrocardiograms. Blood samples will be taken at multiple timepoints to see how the body responds to treatment. Disease status will be checked based on solid tumor response evaluation criteria (RECIST version 1.1).

What are the possible benefits and risks of participating?
Based upon the pathophysiology of HNSCC, the mechanisms of action of amivantamab, and prior clinical experience, there is potential benefit to participants of this study in regards to improved outcomes of R/M HNSCC.
Participants may experience some benefit from participation in the study that is not due to receiving study drug, but due to regular visits and assessments monitoring overall health.
Participation may help other people with HNSCC in the future.
Participants may have side effects from the study treatments or procedures required in this study that may be mild to severe and even life-threatening, and they can vary from person to person. The potential risks include allergic and anaphylactic-like reactions and hypersensitivity, lung and skin related issues, colitis, liver toxicity, myelosuppression (condition in which bone marrow activity is decreased, resulting in fewer red blood cells, white blood cells, and platelets), renal toxicity and neurologic toxicity after getting the study drug. There are other, less frequent risks. The participant information sheet and informed consent form, which must be signed by all participants, includes a detailed section outlining the potential risks associated with study participation.
Not all possible side effects and risks related to amivantamab may be known at this moment. During the study, the Sponsor may learn new information about amivantamab. The study doctor will inform participants as soon as possible about any new information that such as unforeseen risks.
To minimise the risk associated with taking part in the study, participants will be frequently assessed for any side effects and other medical events. Participants are educated to report any such events to the study doctor, who will provide appropriate medical care. Any serious side effects that are reported to the sponsor are thoroughly reviewed by a specialist drug safety team.
There are no costs to participants to be in the study. The sponsor will pay for the study drug and tests that are part of the study. The participant will receive reasonable reimbursement for study-related costs (for example, travel/parking costs).

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 July 2033.

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

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

Contact information

Type(s)
Scientific

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ClinicalTrials.gov (NCT)
NCT05379595

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

Integrated Research Application System (IRAS)
1009340

Central Portfolio Management System (CPMS)
58135

Protocol serial number
61186372HNC2002

Study information

Scientific Title
A Phase Ib/II, open-label study of amivantamab monotherapy and amivantamab in addition to other therapeutic agents in participants with head and neck squamous cell carcinoma

Acronym
OrigAMI-4

Study objectives

Current study objectives:

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.
In participants with resectable locally advanced (L/A) HNSCC, to assess anti-tumor activity of:
• Amivantamab in addition to pembrolizumab before and after the surgery (perioperative).

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-naïve in the R/M setting.
In participants with resectable L/A HNSCC, to assess anti-tumor activity, safety and tolerability of:
• Amivantamab in addition to pembrolizumab before and after the surgery.

Previous study objectives:

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.

Original study objectives:

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

Primary study design
Interventional

Study design
Interventional non randomized

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Head and neck squamous cell carcinoma

Interventions

Current interventions as of 07/05/2026:
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 (IV) 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 millilitre [mg/ml]*min) q3w on Day 1 of Cycles 1-6.

Experimental: Cohort 6: Amivantamab + Pembrolizumab
Participants will receive subcutaneous injection of amivantamab 1600 mg (2240 mg, if body weight >=80kg) 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, along with intravenous injection of pembrolizumab 200 mg q3w (on Day 1 of each 21-day cycle) (Neoadjuvant Phase). In the adjuvant phase, pembrolizumab IV (200 mg) will be administered q3w from Adjuvant Cycle 1 Day 1 to Adjuvant Cycle 15 Day 1 and amivantamab SC 2,400mg (3,360 mg for >80 kg) will be administered q3w from Adjuvant Cycle 4 Day 1 to Adjuvant Cycle 15 Day 1.

Previous 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 1/4: Biological/Vaccine: Amivantamab co-formulated with recombinant human hyaluronidase (rHuPH20) [Amivantamab, Vorhyaluronidase alfa]; Cohort 2/6: Biological/Vaccine: Amivantamab co-formulated with recombinant human hyaluronidase (rHuPH20) [Amivantamab, Vorhyaluronidase alfa]; Biological/Vaccine: Pembrolizumab, Pembrolizumab will be administered intravenously. Other Names: • KEYTRUDA; Cohort 3: Biological/Vaccine: Amivantamab co-formulated with recombinant human hyaluronidase (rHuPH20) [Amivantamab, Vorhyaluronidase alfa]; Drug: Paclitaxel, Paclitaxel will be administered intravenously. Other Names: • TAXOL; Cohort 5: Biological/Vaccine: Amivantamab co-formulated with recombinant human hyaluronidase (rHuPH20) [Amivantamab, Vorhyaluronidase alfa]; Biological/Vaccine: 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 07/05/2026:
Cohorts 1, 2, 3B, 4 and 5: Objective response rate (ORR) – defined as the proportion of participants who achieve either a partial response (PR) or complete response (CR), as defined by investigator assessment using Response Criteria in Solid Tumors (RECIST) version 1.1
Cohort 3A: Number of participants with dose-limiting toxicities (DLT), and number of participants with treatment-emergent adverse events (TEAEs) as a measure of severity.
Cohort 6: Major pathologic response (MPR) – the participants who achieve MPR at the time of surgery.

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Previous 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 outcomes measures as of 07/05/2026:
Cohorts 1, 2, 3B, 4 and 5:
1. Duration of response (DoR)
2. Clinical benefit rate (CBR)
3. Progression-free survival (PFS)

Cohorts 1, 2, 3B, 4, 5 and 6:
1. Overall survival (OS)
2. Number of participants with treatment-emergent adverse events (TEAEs) as a measure of severity

Cohorts 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.

Cohort 6: Event-free survival (EFS)

Previous 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.

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
28/07/2033

Eligibility

Key inclusion criteria
Current inclusion criteria as of 07/05/2026:
1. Cohorts 1 to 5: Have histologically or cytologically confirmed recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) that is considered incurable by local therapies, or for Cohort 6: have histologically or cytologically confirmed locally advanced (L/A) HNSCC that is considered curable by surgery. Acceptable prior lines of therapy will be determined according to specific Cohort.
2. 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 tumour 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. Cohort 5:
4.1. The eligible primary tumor locations are the oropharynx, oral cavity, hypopharynx, or larynx
4.2. HPV status must be known (either positive or negative) for patients with primary tumor location in oropharynx with p16 test or high-risk HPV ISH in tissue

4.3. Participants must provide local testing results of PD-L1 status
5. Cohort 6:
5.1. The eligible primary tumor locations are the oropharynx, oral cavity, hypopharynx, or larynx
5.2. 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 Participants must provide local testing results of PD-L1 status
5.3. Participants must have Stage III or IVa disease (American Joint Committee on Cancer Staging Manual, 8th edition). Participants must have resectable disease
6. Participants in Cohorts 1, 2, 3B, 4 and 5 must have measurable disease according to RECIST version 1.1
7. Participants in Cohort 3A and Cohort 6 must have evaluable disease (defined as having at least 1 non-target lesion according to RECIST version 1.1
8. Cohorts 1, 2, 3A, 3B, 4, and 5 only: 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)
9. Have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1
10. 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.
11. Participants should have:
11.1. Hemoglobin >=9 grams per deciliter (g/dL)
11.2. Neutrophils >=1.5 x 10^3/mcg
11.3. Platelets >=100 x 10^3/mcg

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Previous 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
Mixed

Lower age limit
18 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
0

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
30/12/2026

Locations

Countries of recruitment
United Kingdom

England

France

Germany

Korea, South

Malaysia

Poland

Spain

Taiwan

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

Study participating centre
Addenbrookes
Addenbrookes Hospital
Hills Road
Cambridge
England
CB2 0QQ

Study participating centre
The Christie Hospital
Wilmslow Road
Withington
Manchester

England
M20 4BX

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

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

Study participating centre
The Royal Marsden Hospital
Fulham Road
London
England
SW3 6JJ

Sponsor information

Organisation
Janssen-Cilag International NV

Funder(s)

Funder type
Industry

Funder Name
Janssen-Cilag 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