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A study of amivantamab in addition to standard of care agents compared with standard of care in participants with recurrent/metastatic head and neck cancer

Submission date
12/09/2025

Recruitment status
Recruiting

Registration date
10/11/2025

Overall study status
Ongoing

Last Edited
04/12/2025

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Head and neck squamous cell carcinoma (HNSCC), is a type of solid tumour that begins in the mouth and throat. Available treatments may not work well for all participants. Thus, better therapies are required for the treatment of HNSCC in order to improve outcomes and the quality of life.

Amivantamab (JNJ-61186372) is a human immunoglobulin G1 (IgG1)-based bispecific antibody (protein that helps protect the body against foreign matter) that simultaneously inhibits the activity of two proteins, epidermal growth factor receptor (EGFR) and mesenchymal-epithelial transition (MET). Binding to EGFR and MET, turns them off, which may slow down the growth of cancer cells or kill them.

In this study, researchers want to compare the ability of amivantamab to slow down or stop the growth of tumours and overall survival when given along with pembrolizumab and carboplatin versus pembrolizumab with 5-fluorouracil (5-FU) and carboplatin or cisplatin treatment. Study will focus on participants who have treatment-naïve HNSCC (that is, have not received prior treatment).

Who can participate?
Adult patients with histologically or cytologically confirmed recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC) that is considered incurable by local therapies and meets protocol specified criteria for location and testing.

What does the study involve?
Participants first go through a screening period of up to 28 days, where doctors carry out health checks and tests.
Eligible participants are then randomly assigned to one of two treatment groups:
Group A: Receives pembrolizumab (an immunotherapy), amivantamab (the new medicine), and

carboplatin (a chemotherapy drug).
Group B: Receives pembrolizumab, 5-fluorouracil (a chemotherapy drug), and either carboplatin or cisplatin (both chemotherapy drugs).
Treatments are given by drip (intravenous infusion) or injection every three weeks. The treatment period can last up to 24 months.
After treatment, participants attend regular follow-up visits so doctors can monitor their health.

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, including all treatments administered.

Amivantamab:
The possible discomforts, side effects, and risks related to amivantamab treatment are not all known. As of May 20, 2025, safety data are available for approximately 3,486 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. Participants will be given prescriptions for specific rash treatments during treatment.

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 foetus, 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 3-14 months after the last dose of treatment. Participants of child-bearing potential must adhere to strict birth control requirements during study participation and for 3-14 months after the last dose and will be regularly tested for pregnancy. Due to the possible risk of birth defects, male and female patients should take contraceptive measures both during treatment with cisplatin and for at least 14 months after treatment has ended.

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

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

MRI:
These are undertaken within a small enclosure which can be noisy, which may cause some anxiety.

CT:
CT scans do use low levels of radiation which has a small potential to cause cancer.

Contrast agents:
May be used as a part of CT or MRI. They can cause an allergic reaction like itching, swelling, or pain at the injection site. In rare cases these can be potentially life-threatening or cause kidney damage. Participants may be given fluids or other treatments to avoid side effects.

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

When is the study starting and how long is it expected to run for?
September 2025 to June 2029

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

Who is the main contact?
Joe Taylor, JTaylo63@ITS.JNJ.com
Prof Kevin Harrington, kevin.harrington@icr.ac.uk

Lay summary under review with external organisation

Contact information

Type(s)
Public, Scientific

Contact name
Mr Joe Taylor

Contact details
50-100 Holmers Farm Way
High Wycombe
United Kingdom
HP12 4DP
+44 7393267595
jtaylo63@its.jnj.com

Type(s)
Principal investigator

Contact name

Prof Kevin Harrington

Contact details
Downs Road
Sutton
United Kingdom
SM2 5PT
+44 207 8062732
Kevin.Harrington@icr.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2025-521917-24

Integrated Research Application System (IRAS)
1012977

Central Portfolio Management System (CPMS)
67466

Protocol serial number
61186372HNC3001

Study information

Scientific Title
A phase 3, randomized, open-label, multicenter study of amivantamab in addition to carboplatin and pembrolizumab, compared to standard of care platinum and pembrolizumab and 5-FU, in participants with treatment-naïve recurrent/metastatic head and neck squamous cell carcinoma

Acronym
OrigAMI-5

Study objectives
The primary objective for this study is to compare anti-tumour activity.

The secondary objectives of this study are:
1. To further measures of clinical benefit.
2. To assess safety and tolerability.
3. To assess disease symptoms, health-related qualify of life (HRQoL), and treatment tolerability.
4. For amivantamab-treated participants only: To explore the relationship between pharmacokinetics or immunogenicity and selected endpoints in amivantamab-treated participants (including but not limited to efficacy and safety).

Ethics approval required
Ethics approval required

Ethics approval(s)
notYetSubmitted

Study design
Interventional open randomized controlled trial

Primary study design
Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Recurrent/metastatic head and neck squamous cell carcinoma

Interventions
The purpose of this study is to compare anti-tumour activity of amivantamab in addition to pembrolizumab and carboplatin versus pembrolizumab, 5 fluorouracil (FU), and platinum therapy (carboplatin or cisplatin) in participants with refractory/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). HNSCC is a type of cancer that develops in the head and neck regions, including the outer tissue layer of the mouth and throat. This study will focus on participants with HNSCC who are treatment-naive (have not received prior treatment) in the R /M setting.

Study will be conducted in 3 periods:

1. Screening period (up to 28 days)

2. Treatment period (up to 24 months): Participants will be randomly (by chance) assigned to either of the 2 arms:
- Arm A: Pembrolizumab + Amivantamab + Carboplatin:
• Dosage Level and Administration Routes:
o Pembrolizumab IV 200 mg Q3W – Intravenous Infusion
o Amivantamab SC 2400/3360 mg Q3W – Subcutaneous Injection
o Carboplatin IV AUC 5 mg/mL•min Q3W – Intravenous Infusion
• Amivantamab will be dosed weekly during Cycle 1 and Q3W starting on Cycle 2 Day 1. Pembrolizumab and carboplatin will be dosed Q3W starting from Cycle 1. The order of dosing combination agents will be: Pembrolizumab, Carboplatin, followed by amivantamab.

- Arm B: Pembrolizumab + 5-Flurouracil (5-FU) + Carboplatin or Cisplatin:
• Dosage Level and Administration Routes:
o Pembrolizumab IV 200 mg Q3W – Intravenous Infusion
o 5-FU IV 1000 mg/m2 per day for 4 days Q3W – Intravenous Infusion
o Carboplatin IV AUC 5 mg/mL•min Q3W – Intravenous Infusion
o Cisplatin 100 mg/m2 Q3W – Intravenous Infusion

The sequence of drug administration will be: pembrolizumab, followed by carboplatin/cisplatin, then 5-FU infusion. Pembrolizumab, carboplatin/cisplatin, and 5-FU will be dosed every three weeks starting on Cycle 1 Day 1. Carboplatin/cisplatin and 5-FU will be dosed for a maximum of 6 cycles. The PI will choose between carboplatin or cisplatin prior to randomization based upon physician preference and individual patient characteristic. If a patient initially receives cisplatin, investigators may switch subjects from cisplatin to carboplatin during the course of the study if

toxicities occur. If cisplatin dose was modified prior to switching, the subject may start a carboplatin dose of AUC 5 and will be eligible to receive an additional 2 dose modifications of carboplatin.

- Central randomization will be implemented in this study. Participants will be randomly assigned by a 1:1 ratio to Arm A or Arm B, based on a computer-generated randomization schedule prepared before the study by or under the supervision of the sponsor.

3. Follow-up period (until the end of study unless the participant has died, is lost to follow-up, or has withdrawn consent): Participants will be monitored for their health.

Study assessments include physical examinations, vital signs, electrocardiogram (ECG; test to record heart activity) assessments, and laboratory tests. All side effects will be recorded till the study ends (around 3 years 7 months).

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
JNJ-61186372 [Amivantamab], pembrolizumab, carboplatin, cisplatin, fluorouracil

Primary outcome(s)
Overall survival (OS) and objective response rate (ORR; using RECIST v1.1) as assessed by Blinded Independent Central Review (BICR).
OS is defined as the time from the date of randomisation to the date of death due to any cause.
ORR is defined as the proportion of randomised participants achieving a confirmed best overall response (BOR) or partial response (PR) or complete response (CR) by BICR using RECIST v1.1 criteria.

Key secondary outcome(s))
1. Progression-free survival is measured using RECIST v1.1 as assessed by blinded independent central review (BICR) at baseline and at scheduled tumour assessments throughout the study until disease progression or death
2. Duration of response is measured using RECIST v1.1 as assessed by BICR from the date of first documented response until disease progression or death
3. Objective response rate is measured using RECIST v1.1 as assessed by the investigator at baseline and at scheduled tumour assessments throughout the study
4. Incidence and severity of treatment-emergent adverse events and laboratory abnormalities are measured using CTCAE v5.0 and standard laboratory tests at baseline and throughout the treatment and follow-up periods
5. Proportion of participants with improved or stable symptoms relative to baseline is measured using the symptom scales of the EORTC QLQ-HN43 and EORTC QLQ-C30 at baseline and at scheduled PRO assessment timepoints during treatment and follow-up
6. Change from baseline in functioning and overall health-related quality of life is measured using the functioning and global health status scales of the EORTC QLQ-C30 at baseline and at scheduled PRO assessment timepoints during treatment and follow-up
7. Differences between treatment groups in tolerability are measured using the EORTC IL46 tolerability scale at scheduled PRO assessment timepoints during treatment

8. Serum amivantamab concentrations are measured using validated immunoassays at baseline, during treatment at predefined pharmacokinetic sampling timepoints, and at end of treatment
9. Serum anti-amivantamab antibodies are measured using validated immunogenicity assays at baseline, during treatment at predefined sampling timepoints, and at end of treatment

Completion date
18/06/2029

Eligibility

Key inclusion criteria
1. Be at least 18 years of age.
2. Have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.
3. Have histologically or cytologically confirmed recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC) that is considered incurable by local therapies and meets protocol specified criteria for location and testing.
4. Be treatment-naïve for systemic therapy in the R/M setting, as per protool specified criteria.
5. Have measurable disease according to RECIST v1.1. If only one 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 biopsyand if lesion remains acceptable as a target lesion after that time. Tumour lesions situated in a previously irradiated area are considered measurable if progression following radiation has been demonstrated in such lesions.
6. Consent to a screening biopsy or provide archival tissue sample per protocol-defined specifications. Participants must have a screening biopsy within 28 days prior to day 1 of the first treatment cycle, or archival tissue that was obtained within 6 months of diagnosis of R/M disease.
7. 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; Wear an external condom; If of childbearing potential, participant have a negative highly sensitive serum pregnancy test at screening and within 72 hours of the first dose of study treatment and must agree to further pregnancy tests, and practice at least 1 highly effective method of contraception; If a participant’ s partner is of childbearing potential, the partner must practice a highly effective method of contraception unless the participant is vasectomised.
8. Must sign an Informed Consent Form (ICF) indicating that the participant understands the purpose and procedures required for the study.
9. Must 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

99 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Has an uncontrolled illness.
2. Has untreated brain metastases or history of known presence of leptomeningeal disease.
3. Has a history of (non-infectious) interstitial lung disease (ILD)/pneumonitis/pulmonary fibrosis, has current ILD/pneumonitis, or where suspected ILD/pneumonitis/pulmonary fibrosis cannot be ruled out by imaging at screening.
4. Has a history of clinically significant cardiovascular disease.
5. Renal function as specified in the study protocol.
6. Hepatic function as specified in the study protocol.
7. Haematological values as specified in the study protocol.
8. Thyroid function laboratory values not within the normal range.
9. Active hepatitis of infectious origin.
10. Current or chronic history of non-infectious liver disease.
11. Have a prior malignancy (other than the disease under study) in which its natural history or treatment is likely to interfere with any study endpoints of safety or the efficacy of the study treatment(s).
12. Has known allergies, hypersensitivity, contraindications, or intolerance to excipients of any of the study treatments.
13. Has, or will have, any of the following:
a. An invasive operative procedure with entry into a body cavity, including feeding tube placement and tracheostomy, 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.
c. Expected major surgery while the investigational agent is being administered, or within 6 months after the last dose of study treatment.
14. Taken any disallowed therapies including immunosuppressive medications within 7 days prior to the first administration of study treatment.
15. 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 specified exclusions.
16. Use of live or live attenuated vaccines during study treatment, within 30 days prior to the first dose of study treatment.
17. Requires prohibited medication that cannot be discontinued, substituted, or temporarily interrupted during the study.
18. Has had radiation therapy within 2 weeks before the first administration of study treatment.
19. Has used an invasive investigational medical device or received an investigational drug (including investigational vaccines) within 6 weeks before the planned first dose of study treatment, or is currently enrolled in an investigational study, or has used investigational anti-cancer therapy within 6 months before the planned first dose of study treatment.
20. HIV-positive participants are only eligible if they meet all the protocol specific clinical requirements.

Date of first enrolment

23/10/2025

Date of final enrolment
16/06/2027

Locations

Countries of recruitment
United Kingdom

England

Australia

Austria

Belgium

Brazil

China

France

Germany

Hungary

India

Italy

Japan

Mexico

Netherlands

Poland

Portugal

Romania

Spain

Taiwan

Study participating centre

The Royal Marsden Hospital (surrey)
Downs Road
Sutton
England
SM2 5PT

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 datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository. The data sharing policy of Johnson & Johnson Innovative Medicine is available at www.innovativemedicine.jnj.com/our-innovation/clinical-trials/transparency.
As noted on this site, requests for access to the study data can be submitted through Yale Open Data Access (YODA) Project site at yoda.yale.edu.

IPD sharing plan summary
Stored in non-publicly available repository