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A phase 2b, open-label, two-cohort study of subcutaneous amivantamab in combination with lazertinib as first-line treatment, or subcutaneous amivantamab in combination with platinum-based chemotherapy as second-line treatment, for common EGFR-mutated locally advanced or metastatic non-small cell lung cancer

Submission date
28/08/2025

Recruitment status
Recruiting

Registration date
23/10/2025

Overall study status
Ongoing

Last Edited
23/10/2025

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
NSCLC is the most common type of lung cancer. NSCLC may occur due to mutations (changes) in many genes including mesenchymal-epithelial transition (MET) and EGFR. Although treatment options are available only a few patients respond to the treatment or cancer can come back after treatment. Drugs that target EGFR to attack cancer cells may be an effective way to destroy them. The study aims to assess the effectiveness of the combination of amivantamab and lazertinib as first-line treatment and combination of amivantamab and chemotherapy as second-line treatment in participants with NSCLC with specific mutation in the EGFR gene.

Who can participate?
Participants with NSCLC, with changes (mutation) in EGFR gene.

What does the study involve?
The study will include the following phases:
1.Screening Phase (up to 28 days): Participants aged 18 years or above will be screened.
2.Treatment Phase (until end of treatment): Participants will be put into one of the2 cohorts:
Cohort 1-Includes participants who have not received any prior cancer therapy.
Participants will receive amivantamab as an injection under the skin (SC) along withlazertinib orally according to the treatment schedule.
Cohort 2- Includes second-line participants who have progressed on or after EGFR-TKI cancer

therapy.
Participants will receive amivantamab as SC injection along with standardchemotherapy (carboplatin and pemetrexed) by injection into a vein as pertreatment schedule.

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3.Follow-up Phase: Participants will be followed up to monitor their overall health until theend of study, death, progression of the disease, or withdrawal of consent, whichever comesfirst.

The UK will participate in Cohort 1 only.

What are the possible benefits and risks of participating?
Based on scientific theory, taking amivantamab with lazertinib combination may help treat NSCLC. However, this cannot be guaranteed because amivantamab is still under investigation as a treatment, and it is not known whether subcutaneous amivantamab and lazertinib combination will work. Participants may experience some benefit from participation in the study that is not due to receiving amivantamab, but due to regular visits and assessments monitoring overall health. Participation may help other people with NSCLC in the future. Participants may have side effects from the drugs or procedures used in this study that may be mild to severe and even life-threatening, and they can vary from person to person. The most common, known risks are - administration-related reactions (ARRs); rash-related AEs, paronychia (tender, swollen skin around the nails); oral mucositis (mouth sores); pulmonary toxicity (lung inflammation or damage); liver chemistry abnormalities; cardiac adverse events; diarrhea; venous thromboembolic event (VTE; blood clots in veins); paresthesia (tingling or numbness); ocular toxicity (eye problems). The participant information sheet and informed consent form, which will be signed by every participant agreeing to participate in the study, includes a detailed section outlining the known risks to participating in the study. Not all possible side effects and risks related to amivantamab and lazertinib combination are known at this moment. During the study, the sponsor may learn new information about amivantamab and lazertinib combination. The study doctor will tell participants as soon as possible about any new information that might make them change their mind about being in the study, such as new risks. To minimise the risk associated with taking part in the study, participants are frequently reviewed for any side effects and other medical events. Participants are educated to report any such events to their 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 (e.g., travel/parking costs).

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

When is the study starting and how long is it expected to run for?
August 2025 to November 2030

Who is funding the study?
Janssen-Cilag International NV

Who is the main contact?
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Contact information

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1012796

ClinicalTrials.gov (NCT)
NCT06667076

Protocol serial number
61186372NSC2012

Study information

Scientific Title
A phase 2b, open-label, two-cohort study of subcutaneous amivantamab in combination with lazertinib as first-line treatment, or subcutaneous amivantamab in combination with platinum-based chemotherapy as second-line treatment, for common EGFR-mutated locally advanced or metastatic non-small cell lung cancer

Acronym
COPERNICUS

Study objectives
The primary objective of the trial is to assess the effectiveness of the combination of amivantamab and lazertinib and the combination of amivantamab and chemotherapy in participants with non-small cell lung cancer (NSCLC; a type of lung cancer with a change [mutation] in the EGFR gene*) who have a specific mutation in the EGFR gene.

*Cell surface protein that binds to epidermal growth factor. Changes (mutations) in this gene cause lung cancer.

The secondary objectives for this trial are:
1. To assess the safety of amivantamab (in both Cohorts) and lazertinib (in Cohort 1 only) and how well participants can tolerate this treatment.
2. To assess if the treatment works, how many people respond to it, and how long the response lasts.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 21/10/2025, West London & GTAC Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 2071048075; westlondon.rec@hra.nhs.uk), ref: 25/LO/0698

Study design
Interventional non-randomized

Primary study design
Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied

Common EGFR-mutated locally advanced or metastatic non-small cell lung cancer

Interventions
Amivantamab and Lazertinib Participants will receive Amivantamab(JNJ-61186372) in combination with Lazertinib (JNJ-73841937) orally in 28-day cycles until disease progression, withdrawal of consent, death, or the investigator decides to discontinue treatment, whichever comes first.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
JNJ-73841937 [Lazertinib], JNJ-61186372 [Amivantamab]

Primary outcome(s)
Progression Free Survival (PFS) PFS is defined as the time from the date of first dose of any study treatment until the date of objective disease progression or death, whichever occurs first according to response evaluation criteria in solid tumors (RECIST) version (v) 1.1 as assessed by the investigator. [Time Frame: Up to 4 Years and 6 months]

Key secondary outcome(s))
1. Number of Participants Reporting Dose Reductions, Interruptions, and Discontinuations
Participants with dose reductions, interruptions, and discontinuations will be reported. Time Frame: Up to 4 Years and 6 months
2. Number of Participants With Venous Thromboembolic Events (VTEs)
Participants with signs and symptoms (dyspnea, tachypnea, upper- or lower-extremity swelling and discoloration) of VTE events, specifically pulmonary embolism and deep vein thrombosis, will be reported as monitored by the investigators. Time Frame: Up to 4 Years and 6 months
3. Number of Participants With Dermatologic Adverse Events (AEs)
Participants with dermatologic AEs will be reported. Time Frame: Up to 4 Years and 6 months
4. Number of Participants with AEs by Severity
Severity of AEs will be graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 5.0.
Severity scale ranges from Grade 1 (Mild) to Grade 5 (Death):
Grade 1: mild
Grade 2: moderate
Grade 3: severe
Grade 4: life-threatening
Grade 5: death related to adverse event
Time Frame: Up to 4 Years and 6 months
5. Overall Survival (OS)
OS is defined as the time from the date of first dose of any study treatment until the date of death due to any cause. Time Frame: Up to 4 Years and 6 months
6. Overall Response Rate (ORR)
ORR is defined as the percentage of participants who achieve either a partial response (PR) or complete response (CR) as their best response, both confirmed and unconfirmed, as defined using RECIST v1.1. Time Frame: Up to 4 Years and 6 months
7. Clinical Benefit Rate (CBR)

CBR is defined as the percentage of participants achieving CR or PR, both confirmed and unconfirmed, or durable stable disease (SD) of a duration of at least 11 weeks as defined using RECIST v1.1. Time Frame: Up to 4 Years and 6 months
8. Duration of Response (DOR)
DOR is defined as the time from the date of first documented response (PR or CR) until the date of documented progression or death, whichever occurs first, for participants who have PR or CR. Time Frame: Up to 4 Years and 6 months
9. Time to Treatment Discontinuation (TTTD)
TTTD is defined as the date from the date of first dose of any study treatment until discontinuation of study treatment for any reason, including disease progression, treatment toxicity, or death, based on RECIST v1.1. Time Frame: Up to 4 Years and 6 months
10. Time to Subsequent Therapy (TTST)
TTST is defined as the time from the date of first dose of any study treatment until the start date of the subsequent anticancer therapy following study treatment discontinuation or death, whichever occurs first. Time Frame: Up to 4 Years and 6 months
11. Time to Symptomatic Progression (TTSP)
TTSP is defined as the time from date of first dose of any study treatment to documentation in the electronic case report form (eCRF) of any of the following (whichever occurs earlier): onset of new symptoms or symptom worsening that is considered by the investigator to be related to lung cancer and requires either a change in systemic anticancer treatment and/or clinical intervention to manage symptoms or death. Time Frame: Up to 4 Years and 6 months

Completion date
15/11/2030

Eligibility

Key inclusion criteria
1. Be 18 years of age or older at the time of informed consent.
2. Have histologically or cytologically confirmed advanced or metastatic non-small cell lung cancer (NSCLC) that is not amenable to curative intent therapy.
3. EGFR mutation must be an Ex19del or Ex21 L858R substitution, as detected by an accredited local laboratory in accordance with site standard of care.
4. Have at least 1 measurable lesion, according to RECIST v1.1, that has not been previously irradiated.
5.A participant with asymptomatic or previously treated and clinically stable brain metastases may participate in this study. Participants with a history of symptomatic brain metastases must have had all symptomatic lesions treated as clinically indicated (i.e., no current indication for further definitive local therapy).
6. Must not have received any prior systemic therapy for treatment of advanced or metastatic NSCLC or any targeted therapy for early-stage disease.
7. Be eligible for, and agree to comply with, the use of prophylactic-dose anticoagulation with a direct oral anticoagulant or a low molecular weight heparin during the first 4 months of anticancer treatment (from Day 1-120).
8. Be eligible for, and agree to comply with, the use of a proactive dermatologic regimen during the duration of anticancer treatments with amivantamab and lazertinib, or amivantamab with chemotherapy.
9. Any toxicities from prior systemic anticancer therapy must have resolved to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) Version 5.0 Grade 1 or baseline level (except as per exclusions detailed in the protocol).
10. Have an Eastern Cooperative Oncology Group (ECOG) Performance Status Score of 0 to 1.

11. Must demonstrate adequate organ and bone marrow function required for safe administration of the cohort-specific regimen, without history of growth factors, red blood cell transfusion or platelet transfusion within 7 days prior to the date of the laboratory test, as specified in the study protocol.
12. Have an estimated glomerular filtration rate (eGFR) as specified in the study protocol.
13. Meet all required hepatic laboratory values specified in the study protocol.
14. While on study treatment and for 3 months after last dose of study treatment, a participant must not breastfeed or be pregnant, must not donate gametes (i.e., eggs or sperm) or freeze for future use for the purposes of assisted reproduction, and must wear an external condom when engaging in any activity that allows for passage of ejaculate to another person. If of childbearing potential, participants must have a negative serum pregnancy test at screening and within 72 hours before the first dose of study treatment and must agree to further serum or urine pregnancy tests during the study and must practice at least 1 highly effective method of contraception.
15. Human immunodeficiency virus-positive participants are eligible if they meet all of the criteria specified in the study protocol.
16. Must sign an Informed Consent Form (ICF) that the participant understands the purpose of, and procedures required for, the study and is willing to participate in the study.
17. Be willing and independently able to adhere to the lifestyle restrictions specified in the protocol and agree to comply with the study treatment(s) and their timing requirements.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. History of uncontrolled illness, including but not limited to: uncontrolled diabetes; uncontrolled hypertension; ongoing or active infection; active bleeding diathesis; impaired oxygenation requiring continuous oxygen supplementation; refractory nausea and vomiting, chronic gastrointestinal diseases, inability to swallow the formulated product, or previous significant bowel resection that would preclude adequate absorption of study treatment; psychiatric illness or any other circumstances (including social circumstances) that would limit compliance with study requirements; any ophthalmologic condition that is clinically unstable; and active or past medical history of leptomeningeal disease.
2. Medical history of active Interstitial Lung Disease (ILD), including drug-induced ILD.
3. Had major surgery excluding placement of vascular access or tumour biopsy or had significant traumatic injury within 4 weeks before the first dose of anticancer treatments or will not have fully recovered from surgery, or has surgery planned during the time the participant is expected to participate in the study.
4. Known allergies, hypersensitivity, or intolerance to excipients of amivantamab, lazertinib, or

to rHuPH20, doxycycline, minocycline, or their excipients, or any component of the proactive dermatologic regimen.
5. Participant has a history of clinically significant cardiovascular disease.
6. Participant has uncontrolled tumour-related pain.
7. Active hepatitis B or C virus infection according to local laboratory range, on all available tests for the past 6 months or other clinically active liver disease.
8. Is currently receiving a medication or herbal supplement known to be a strong cytochrome P450 (CYP) 3A4/5 inducer and is not able to stop use for an appropriate washout period prior to C1D1.
9. Taken any disallowed therapies as noted in the study protocol before the planned first dose of study treatment.
10. Received an investigational treatment that has not been cleared (based on at least 5 half-lives of any pharmaceutical treatment) before the planned first dose of study treatment or is currently enrolled in an investigational study.
11. Has a prior or concurrent second malignancy (other than the disease under study) which natural history or treatment could likely interfere with any study endpoints of safety or the efficacy of the study treatment(s).

Date of first enrolment
23/12/2024

Date of final enrolment
31/12/2027

Locations

Countries of recruitment
United Kingdom

Belgium

Finland

France

Germany

Israel

Italy

Poland

Portugal

Saudi Arabia

Spain

Study participating centre

The Royal Marsden NHS Foundation Trust
Fulham Road
London
United Kingdom
SW3 6JJ

Study participating centre
The Royal Marsden Hospital (sutton)
Pharmacy Stores (goods Entrance)
Cotswold Road
Sutton
United Kingdom
SM2 5NF

Study participating centre
Guys and St Thomas' NHS Foundation Trust
249 Westminster Bridge Road
London
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SE1 7EH

Study participating centre
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550 Wilmslow Road
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Study participating centre
The Clatterbridge Cancer Centre NHS Foundation Trust
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Study participating centre
Torbay Hospital
Newton Road

Torquay
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TQ2 7AA

Sponsor information

Organisation
Janssen-Cilag International NV

Funder(s)

Funder type
Industry

Funder Name
Janssen Research and Development

Alternative Name(s)
Janssen R&D, Janssen Research & Development, Janssen Research & Development, LLC, Janssen Research & Development LLC, Janssen Pharmaceutical Companies of Johnson & Johnson, Research & Development at Janssen, JRD, J&J PRD

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

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 www.janssen.com/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
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes