A Phase 3, Randomized Study of Amivantamab and Lazertinib Combination Therapy Versus Osimertinib Versus Lazertinib as First-Line Treatment in Patients with EGFR Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer

Published: 15-09-2020
Last updated: 19-09-2024

This study has been transitioned to CTIS with ID 2023-506576-27-00 check the CTIS register for the current data. The hypothesis is that the amivantamab and lazertinib combination (Arm A) will demonstrate superior PFS compared with single-agent...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory tract neoplasms
Study type	Interventional

Summary

ID

NL-OMON54268

Source
ToetsingOnline

Brief title
MARIPOSA

Condition

- Respiratory tract neoplasms

Synonym
EGFR-Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer harboring EGFR

Exon 19del or L858R mutations

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: Janssen-Cilag B.V.

Intervention

Keyword: Amivantamab, Lazertinib, Non-small Cell Lung Cancer, Osimertinib

Outcome measures

Primary outcome

To assess the efficacy of the amivantamab and lazertinib combination, compared with osimertinib, in participants with EGFR mutation (Exon 19del or Exon 21 L858R substitution) positive, locally advanced or metastatic NSCLC

Endpoint

• PFS (using RECIST v1.1 guidelines), as assessed by blinded independent central review

Secondary outcome

a) To further assess the clinical benefit achieved using the amivantamab and lazertinib combination compared with osimertinib in participants with EGFR mutation positive, locally advanced or metastatic NSCLC

endpoints

• Overall survival

• Objective response rate

• Duration of response

• PFS after first subsequent therapy (PFS2)

• Time to symptomatic progression

• Intracranial PFS

b)To evaluate the safety and tolerability of the amivantamab and lazertinib

combination compared with osimertinib

endpoint

• Incidence and severity of adverse events and laboratory abnormalities

Study description

Background summary

Worldwide, lung cancer is the most commonly diagnosed cancer. In NSCLC the most prevalent actionable driver mutations result in the activation of epidermal growth factor receptor (EGFR). Osimertinib and Lazertinib are EGFR tyrosine kinase inhibitors (TKIs). Amivantamab is a novel bispecific antibody that targets the extracellular domain of both EGFR and MET and can inhibit tumor growth driven by EGFR and mesenchymal-epithelial transition (MET) receptors. Lazertinib inhibits primary activating Exon 19dell and Exon 21 L858R substitution EGFR mutations, and the EGFR T790M+ resistance mutation. The hypothesis is that the amivantamab and lazertinib combination (Arm A) will demonstrate superior PFS compared with single-agent osimertinib (Arm B). The study consists of 3 phases: Screening Phase, Treatment Phase and Follow-up Phase. Participants will undergo response evaluation criteria in solid tumors (RECIST 1.1), pharmacokinetics, and safety evaluations (adverse events, laboratory tests, vital sign measurements, physical examinations).

Study objective

This study has been transitioned to CTIS with ID 2023-506576-27-00 check the CTIS register for the current data.

The hypothesis is that the amivantamab and lazertinib combination (Arm A) will demonstrate superior PFS compared with single-agent osimertinib (Arm B).

Study design

The study will include a Screening Phase, a Treatment Phase, and a Follow-up Phase. Participants must complete screening procedures within 28 days before randomization. To be randomized, all participants must have been previously

diagnosed with NSCLC, characterized by Exon 19del or Exon 21 L858R substitution EGFR mutations.
The Treatment Phase for a participant will begin on Cycle 1 Day 1 and continue as 28 day cycles until the End of Treatment visit, approximately 30 days after discontinuation of study treatment. Participants who discontinue study treatment for any reason will be followed for survival and symptomatic progression in the Follow up Phase. The Follow-up Phase starts after the End of Treatment Visit and continues until the end of study, death, lost to follow up, or withdrawal of consent, whichever comes first.

Intervention

• Arm A: participants will be assigned to open label treatment with the combination of amivantamab (1050 mg for body weight <80 kg and 1400 mg for body weight >=80 kg by intravenous [IV] infusion, once weekly for the first 4 weeks and then once every 2 weeks) and lazertinib (240 mg orally, once daily).
• Arm B: participants will receive double blind treatment with single agent osimertinib (80 mg orally, once daily).
• Arm C: participants will receive double blind treatment with single agent lazertinib (240 mg orally, once daily).

Study burden and risks

Risks / side effects from tests:
Blood draw: Taking blood may cause bruising at the place where the needle goes into the skin. Fainting, and in rare cases infection, may occur.
ECG Risk: There is generally no risk with having an ECG. The sticky patches may pull your skin or cause redness or itching.
CT Risk: 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. If a contrast material is used, your investigator will tell you about possible side effects or allergic reaction.
MRI Risk: There are no known risks or side effects with having an MRI. If a contrast material is used, your investigator will tell you about possible side effects or allergic reaction.
MUGA Scan: The tracer used for a MUGA scan produces a very small amount of radiation. There is no significant risk from this amount of radiation. Your doctor will tell you about possible side effects or allergic reaction.
Intravenous (IV) line: Use of an intravenous line for study treatment administration, imaging and other tests may cause discomfort, irritation, minor bruising, bleeding, or injection leakage, and rarely causes nausea and light dizziness.
Radiation burden
With a CT-scan we use X-ray radiation. The radiation burden in this study is about 20 mSv per CT scan. In comparison: the background radiation in the Netherlands is about 2.5 mSv, per year.

If you often participate in scientific research with a radiation burden, you should discuss with the investigator whether participation at this time is sensible.
The radiation used during the study may cause damage to your health. This risk, however, is small. We nevertheless advise you not to participate in another scientific study with a radiation burden in the near future. There is no objection to research or treatment with radiation for medical reasons.
7. Possible advantages and disadvantages
It is important that you properly consider the possible advantages and disadvantages before you decide to participate.
Taking part in this study may improve your condition. This benefit is not guaranteed to happen and there may not be any benefit to you by being in this study. During the study, your condition may stay the same or get worse. Your participation may help future patients.
Disadvantages of participation in the study may be
- possible side effects;
- possible adverse effects/discomforts of the measurements in the study.
Participation in the study also means:
- that you lose additional time;
- an additional or an extended hospitalisation;
- (additional) testing;
- that you have appointments that you have to attend;

Contacts

Public
Janssen-Cilag

Graaf Engelbertlaan 75
Breda 4837 DS
NL
Scientific
Janssen-Cilag

Graaf Engelbertlaan 75
Breda 4837 DS
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Participant must be >=18 years of age
2. Criterion modified per Amendment 1
2.1 Participant must have newly diagnosed, histologically or cytologically confirmed, locally advanced or metastatic NSCLC that is treatment naïve and not amenable to curative therapy including surgical resection or chemoradiation.
3. Criterion modified per Amendment 1.
3.1 The tumor (meeting criteria described in Inclusion Criterion no. 2) harbors Exon 19del or Exon 21 L858R substitution, as detected by an FDA-approved or other validated test in a CLIA certified laboratory (sites in the US) or an accredited local laboratory (sites outside of the US) in accordance with site standard of care. (Note: A copy of the test report documenting the EGFR mutation must be included in the participant records and must lso be submitted to the sponsor.)
4. Criterion modified per Amendment 1.
4.1 Mandatory submission of unstained tissue from tumor meeting criteria described in Inclusion Criterion no. 2 (in a quantity sufficient to allow for central analysis of EGFR mutation status) and blood (for ctDNA, digital droplet polymerase chain reaction [ddPCR], and pharmacogenomic analysis). See Section 8.7.
5. Any toxicities from prior anticancer therapy must have resolved to Common Terminology Criteria for Adverse Events (CTCAE) Grade 1 or baseline level.
6. at least 1 measurable lesion, according to RECIST v1.1 that has not been previously irradiated.

Full details of inclusion criteria can be found in section 5.1 of the study protocol.

Exclusion criteria

1. Criterion modified per Amendment 2.

1.1 Participant has received any prior systemic treatment at any time for locally advanced stage III or metastatic stage IV disease (adjuvant or neoadjuvant therapy for stage I or II disease is allowed, if administered more than 12 months prior to the development of locally advanced or metastatic disease).
2. Criterion modified per Amendment 1.
2.1 Participant has symptomatic brain metastases. A participant with asymptomatic or previously treated and stable brain metastases may participate in this study.
3. Participant has an active or past medical history of leptomeningeal disease.
4. Criterion modified per Amendment 1.
4.1 Participant with untreated spinal cord compression. A participant that has been definitively treated with surgery or radiation and has a stable neurological status for at least 2 weeks prior to randomization is eligible provided they are off corticosteroid treatment or receiving low-dose corticosteroid treatment <=10 mg/day prednisone or equivalent.
6. Participant has an active or past medical history of ILD/pneumonitis, including drug-induced or radiation ILD/pneumonitis.
10. Participant has known allergy, hypersensitivity, or intolerance to the excipients used in formulation of amivantamab, lazertinib, or osimertinib, or any contraindication to the use of osimertinib

Full details of exclusion criteria can be found in section 5.2 of the study protocol.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	18-10-2021
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Amivantamab
Generic name:	Amivantamab
Product type:	Medicine
Brand name:	Lazertinib
Generic name:	Lazertinib
Product type:	Medicine
Brand name:	Tagrisso
Generic name:	Osimertinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	15-09-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-10-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-11-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-02-2021

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-11-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-05-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-09-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	11-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-09-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-01-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-03-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2023-506576-27-00
EudraCT	EUCTR2020-000743-31-NL

Register	ID
ClinicalTrials.gov	NCT04487080
CCMO	NL74637.056.20