A Phase 3, Open-Label, Randomized Study of Amivantamab and Lazertinib in Combination with Platinum-Based Chemotherapy Compared with Platinum-Based Chemotherapy in Patients with EGFR-Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer After Osimertinib Failure

Published: 29-09-2021
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This study has been transitioned to CTIS with ID 2023-506518-33-00 check the CTIS register for the current data. The purpose of this study is to assess the efficacy of adding lazertinib to amivantamab, carboplatin, and pemetrexed (LACP/ACP-L dosing...

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

Summary

ID

NL-OMON54075

Source
ToetsingOnline

Brief title
MARIPOSA-2

Condition

- Respiratory tract neoplasms

Synonym
locally advanced or metastatic EGFR Exon 19del or Exon 21 L858R substitution NSCLC; locally advanced lung cancer

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 failure

Outcome measures

Primary outcome

Progression-Free Survival (PFS) According to RECIST v1.1 Guidelines as Assessed

by Blinded Independent Central Review (BICR) - Up to 17 months - PFS is defined

as the time from randomization until the date of objective disease progression

or death, whichever comes first, using Response Evaluation Criteria in Solid

Tumors (RECIST) version 1.1.

Secondary outcome

Objective Response as Assessed by BICR

Up to 17 months

Objective response is defined as the percentage of participants who achieve

either a complete response (CR) or partial response (PR) as their best response

as defined by BICR using RECIST v1.1 criteria.

Overall Survival (OS)

Up to 48 months

Overall Survival is defined as the time from the date of randomization to the

date of participant's death due to any cause.

Duration of Response (DoR)

Up to 17 months

DoR is defined as the time from the date of first documented response (CR or PR) until the date of documented progression or death, whichever comes first, only for participants who achieve CR or PR.

Time to Subsequent Therapy (TTST)

Up to 17 months

TTST is defined as the time from the date of randomization to the start date of the subsequent anti-cancer therapy following study treatment discontinuation, or death whichever comes first.

Progression-Free Survival After First Subsequent Therapy (PFS2)

Up to 17 months

PFS2 is defined as the time from randomization until the date of second objective disease progression, after initiation of subsequent anticancer therapy, based on investigator assessment (after that used for PFS) or death, whichever comes first.

Time to Symptomatic Progression (TTSP)

Up to 17 months

TTSP is defined as the time from randomization 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 anticancer treatment and/or clinical intervention to manage symptoms.

Intracranial PFS

Up to 17 months

Intracranial PFS is defined as the time from randomization until the date of objective intracranial disease progression or death, whichever comes first, based on BICR using RECIST v1.1.

Number of Participants with Adverse Events (AEs)

Up to 48 months

An AE is any untoward medical occurrence in a participant participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study.

Number of Participants with Clinical Laboratory Abnormalities

Up to 48 months

Number of participants with clinical laboratory abnormalities (serum chemistry, hematology, blood coagulation, and urinalysis) will be reported.

Serum Concentration of Amivantamab

Up to 17 months

Serum samples will be analyzed to determine concentrations of amivantamab.

Plasma Concentration of Lazertinib

Up to 17 months

Plasma samples will be analyzed to determine concentrations of lazertinib.

Number of Participants with Anti-Amivantamab Antibodies

Up to 17 months

Number of participants with anti-amivantamab antibodies will be reported.

Non-Small Cell Lung Cancer - Symptom Assessment Questionnaire (NSCLC-SAQ)

Up to 17 months

NSCLC-SAQ is a 7-item PRO measure designed for use in adults to assess symptoms of advanced non-small cell lung cancer (NSCLC). The NSCLC-SAQ has a seven-day recall period. It contains five domains and accompanying items that will be identified as symptoms of NSCLC: cough (1 item), pain (2 items), dyspnea (1 item), fatigue (2 items), and appetite (1 item). Each item uses a response scale between 0 to 4, with higher scores indicating more severe symptomatology. All five of these domains must be non-missing to compute a total score, with a response range from 0 to 20 with higher scores indicating more severe symptomatology.

European Organization of Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC-QLQ-C30) Score

Up to 17 months

The EORTC QLQ-C30 includes 30 items in 5 functional scales, 1 global health status scale, 3 symptom scales, and 6 single symptom items. The responses are reported using a verbal rating scale. The item and scale scores are transformed to a 0 to 100 scale. A higher score represents greater HRQoL, better functioning, and more (worse) symptoms.

Patient Reported Outcomes Measurement Information System-Physical Function (PROMIS-PF)

Up to 17 months

PROMIS-PF is used to characterize and better understand overall health, level of physical disability, and general well-being. Physical function is a foundation for commonly used general and cancer-specific patient reported

outcomes (PRO) measures.

Study description

Background summary

Lung cancer is one of the most common types of cancer and is the most common cause of death from cancer. NSCLC accounts for approximately 85 percent (%) of lung cancers. Advanced NSCLC is a serious terminal illness that accounts for approximately 20% of all cancer mortality, and until recently had a median overall survival (OS) of approximately 1 year. Amivantamab (JNJ-61186372) is a low fucose, fully human immunoglobulin (IgG)1-based bispecific antibody directed against EGFR and mesenchymal-epithelial transition (MET) tyrosine kinase receptors. It shows clinical activity against tumors with primary activating EGFR mutations Exon 19del and Exon 21 L858R substitution. Lazertinib (JNJ-73841937; YH-25448) is an oral, highly potent, third-generation EGFR tyrosine kinase inhibitor (TKI). It selectively inhibits both primary activating EGFR mutations (Exon 19del, Exon 21 L858R substitution) and the EGFR T790M resistance mutation, with less inhibition of wild-type EGFR. The study consists of a Screening Phase (up to 28 days), a Treatment Phase (from randomization until the End of Treatment visit) and a Follow-up Phase (from End of Treatment Visit until the end of study, death, lost to follow-up, or withdrawal of consent, whichever comes first). Safety will be assessed by physical examinations, laboratory tests, vital signs, electrocardiograms, Eastern Cooperative Oncology Group (ECOG) performance status, and monitoring of adverse events (AEs). The total duration of the study is up to 48 months.

Study objective

This study has been transitioned to CTIS with ID 2023-506518-33-00 check the CTIS register for the current data.

The purpose of this study is to assess the efficacy of adding lazertinib to amivantamab, carboplatin, and pemetrexed (LACP/ACP-L dosing strategies) and amivantamab, carboplatin and pemetrexed (ACP) compared with carboplatin and pemetrexed (CP) in participants with locally advanced or metastatic epidermal growth factor receptor (EGFR) Exon 19del or Exon 21 L858R substitution non-small cell lung cancer (NSCLC) after osimertinib failure. The purpose of the extension cohort is to further describe the safety and efficacy for the ACP-L dosing schedule versus ACP with additional data.

Study design

The study consists of a Screening Phase (up to 28 days), a Treatment Phase

(from randomization until the End of Treatment visit) and a Follow-up Phase (from End of Treatment Visit until the end of study, death, lost to follow-up, or withdrawal of consent, whichever comes first). Safety will be assessed by physical examinations, laboratory tests, vital signs, electrocardiograms, Eastern Cooperative Oncology Group (ECOG) performance status, and monitoring of adverse events (AEs). The total duration of the study is up to 48 months.

Intervention

Arm A: LACP/ACP-L: LACP dosing (form study start until 6 November 2022): participants will receive lazertinib orally along amivantamab, pemetrexed and carboplatin starting on Cycle 1 Day 1 for 4 cycles (each cycle consists of 21 days). After 4 cycles, participants will received amivantamab, pemetrexed and Lazertinib as maintenance until disease progression. ACP-L dosing (from 7 November 2022 until study completion): Participants will receive amivantamab, pemetrexed and carboplatin, starting on Cycle 1 Day 1 for 4 cycles (each cycle consists of 21 days). Lazertinib in ACP-L will start on Cycle 5 Day 1 or sooner if carboplatin is discontinued before cycle 4 (each cycle consists of 21 days). Beginning with Cycle 5 Day 1, participants will receive amivantamab, pemetrexed and lazertinib as maintenance until disease progression.
Arm B CP (Carboplatin and Pemetrexed): Participants will receive Pemetrexed in combination with Carboplatin as IV infusion for up to 4 cycles (each cycle consists of 21 days). After 4 cycles, participants will receive Pemetrexed as maintenance until disease progression.
Arm C: ACP (Amivantamab, Carboplatin and Pemetrexed): Participants will receive Amivantamab, Pemetrexed, and Carboplatin as IV infusion for up to 4 cycles (each cycle consists of 21 days). After 4 cycles, participants will receive Amivantamab and Pemetrexed as maintenance until disease progression.
Arm A2 (Extension Cohort): ACP-L: Participants will receive Amivantamab and Carboplatin as IV infusion for up to 4 cycles (each cycle consists of 21 days), Lazertinib will start on C5D1 or sooner if carboplatin is discontinued earlier). After 4 cycles, participants will receive Pemetrexed, Amivantamab, Lazertinib as maintenance until disease progression.
Arm C2 (Extension Cohort): ACP: Participants will receive Amivantamab, Pemetrexed, and Carboplatin as IV infusion for up to 4 cycles (each cycle consists of 21 days). After 4 cycles, participants will receive Amivantamab and Pemetrexed as maintenance until disease progression.

Study burden and risks

Risks/discomforts tests:
Blood draw Risk: Taking blood may cause bruising irritation 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 (including Brain MRI): Because radiation is not used, there is no risk of exposure to radiation during MRI procedure. However please notify the investigator if you have a metal object inside your body e.g. pacemaker. Additionally, if a contrast material is used during MRI, your investigator will tell you about possible side effects or allergic reaction.

MUGA Scan Risk: 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 investigator will tell you about possible side effects or allergic reaction.
Intravenous (IV) line Risk: Use of an intravenous line for trial treatment administration, imaging and other tests may cause discomfort, irritation, minor bruising, bleeding, or injection leakage, and rarely causes nausea, light dizziness and air embolism.
Biopsy Risk (for optional sample): Your doctor will inform you in detail about the procedures and risks associated with the biopsy since these will depend upon where your tumor(s) are located in your body. Typical procedures involve inserting a thin needle through the chest wall using images to guide exact placement (*transthoracic needle biopsy*), or passing a scope through the mouth into the windpipe, to get close enough to the tumor to reach it with a biopsy tool (*bronchoscopy*). You will be given sedation and local anesthesia as needed to make the procedure as comfortable as possible. In general, having a biopsy can cause pain, swelling, bleeding, and/or infection at the site where the biopsy needle or other instrument penetrates through your skin. Additional risks of biopsy of tissue in the lung or chest cavity, depending on the procedure used, include coughing, blood in sputum, throat irritation, wheezing or increased difficulty breathing, need for additional oxygen to breathe, leakage of air into the chest cavity which can result in collapse of the lung, pneumonia, and very rarely, air entering the bloodstream. There is also the rare possibility that having this procedure may shift some cells from the tumor into the surrounding tissues (tissues that come into contact with the biopsy needle). This means that the tumor may spread to that particular area. You will be monitored for these complications and treated if any occur.

Fine Needle Aspirate: Complications after fine needle aspiration are rare. Minor bleeding under the skin at the biopsy site can occur. This can result in a tender, swollen area called a hematoma.

Possible advantages and disadvantages
It is important that you carefully weigh the possible advantages and disadvantages before you decide to participate.
Participating in this study may improve your condition. Whether you will benefit from participating in the study is not guaranteed, and it may also be

that you will not get any
benefit at all. During the study, your condition may stay the same or worsen.
Your participation may help future patients.
Disadvantages of participating in the study may include
- possible side effects;
- possible adverse effects/discomforts of the measurements in the study.
Participating in the study also means:
- that you will lose additional time;
- additional or prolonged hospitalization;
- (additional) tests;
- that you have appointments to keep.

Contacts

Public
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Scientific
Janssen-Cilag

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion Criteria:- Participant must have at least 1 measurable lesion, according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, that has not been previously irradiated- Participant must have histologically or cytologically confirmed, locally advanced or metastatic, non-squamous non-small cell lung cancer (NSCLC), characterized at or after the time of locally advanced or metastatic disease diagnosis by either epidermal growth factor receptor (EGFR) Exon 19del or Exon 21 L858R mutation- A participant with a history of brain metastases must have had all lesions treated as clinically indicated (that is, no current indication for further definitive local therapy). Any definitive local therapy to brain metastases must have been completed at least 14 days prior to randomization and the participant can be receiving no greater than10 milligrams (mg) prednisone or equivalent daily for the treatment of intracranial disease- Participant must have Eastern Cooperative Oncology Group (ECOG) status of 0 or 1- 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 for alopecia [any grade], Grade <= 2 peripheral neuropathy, or Grade <= 2 hypothyroidism stable on hormone replacement)- A woman of childbearing potential must have a negative serum pregnancy test at screening and within 72 hours of the first dose of study treatment and must agree to further serum or urine pregnancy tests during the study- Participant must have progressed on or after osimertinib monotherapy as the most recent line of treatment. Osimertinib must have been administered as either the first-line treatment for locally advanced or metastatic disease or in the second- line setting after prior treatment with first- or second-generation EGFR tyrosine kinase inhibitor (TKI) as a monotherapy. Participants who received either neoadjuvant and/or adjuvant treatment of any type are eligible if progression to locally advanced or metastatic disease occurred at least 12 months after the last dose of such therapy and then the participant progressed on or after osimertinib in the locally advanced or metastatic setting. Treatment with osimertinib must be discontinued at least 8 days (4 half-lives) prior to randomization (that is last dose no later than Day -8)

Exclusion criteria

Exclusion Criteria:- Participant received radiotherapy for palliative treatment of NSCLC less than 14 days prior to randomization- Participant with symptomatic or progressive brain metastases- Participant has history of or current evidence of leptomeningeal disease, or participant has spinal cord compression not definitively treated with surgery or radiation- Participant has known small cell transformation- Participant has a medical history of interstitial lung disease (ILD), including drug-induced ILD or radiation pneumonitis- Participant

has a history of clinically significant cardiovascular disease including, but not limited to diagnosis of deep vein thrombosis or pulmonary embolism within 4 weeks prior to randomization; myocardial infarction; unstable angina; stroke; transient ischemic attack; coronary/peripheral artery bypass graft; or acute coronary syndrome. Participant has a significant genetic predisposition to venous thromboembolic events. Participant has a prior history of venous thromboembolic events and is not on appropriate therapeutic anticoagulation as per National Comprehensive Cancer Network or local guidelines

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	29-08-2022
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Lazertinib
Generic name:	Lazertinib
Product type:	Medicine
Brand name:	Rybrevant
Generic name:	Amivantamab

Ethics review

Approved WMO Date:	29-09-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-11-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-01-2022
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:	30-05-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-09-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	12-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-03-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-03-2023
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:	05-05-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-09-2023
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	CTIS2023-506518-33-00
EudraCT	EUCTR2021-001825-33-NL
ClinicalTrials.gov	NCT04988295
CCMO	NL78839.056.21