LIBRETTO-431: A Multicenter, Randomized, Open-label, Phase 3 Trial Comparing Selpercatinib to Platinum-Pemetrexed Chemotherapy Plus Investigator*s Choice of Pembrolizumab in Patients with Advanced, Treatment-Naïve RET Fusion-Positive Non-Small Cell Lung Cancer

Published: 03-02-2020
Last updated: 07-09-2024

This study has been transitioned to CTIS with ID 2023-506783-14-00 check the CTIS register for the current data. The proposed Study J2G-MC-JZJC (hereafter referred to as JZJC) will evaluate selpercatinib in comparison to platinum-based (carboplatin…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON52946

Source
ToetsingOnline

Brief title
A Phase 3 Trial, Non-Small Cell Lung Cancer, J2G-MC-JZJC

Condition

- Other condition

Synonym
Lung Cancer, Non small cell Lung Cancer

Health condition

Oncology- Lung

Research involving
Human

Sponsors and support

Primary sponsor: Eli Lilly
Source(s) of monetary or material Support: Eli Lilly & Company

Intervention

Keyword: Non-Small Cell Lung Cancer, selpercatinib

Outcome measures

Primary outcome

Objectives

To compare PFS of selpercatinib and platinum-based (carboplatin or cisplatin)

and pemetrexed therapy with or without pembrolizumab in patients with advanced

or metastatic RET fusion-positive NSCLC

Endpoints

PFS per RECIST 1.1 by BICR

Secondary outcome

Objectives

To compare efficacy of selpercatinib and platinum-based and pemetrexed therapy with pembrolizumab

Endpoints

* PFS per RECIST 1.1 by BICR
* PFS per RECIST 1.1 by investigator
* ORR/DOR/DCR per RECIST 1.1 by BICR
* ORR/DOR/DCR per RECIST 1.1 by investigator
* Intracranial ORR/DOR per RECIST 1.1 by BICR
* Time to CNS progression per RECIST 1.1. by BICR
* Intracranial ORR/DOR per RANO-BM by BICR
* OS
* PFS2
* Time to deterioration in pulmonary symptoms: cough, chest pain, and dyspnea as measured by the NSCLC-SAQ

Objectives

To compare efficacy of selpercatinib and platinum-based and pemetrexed therapy with or without pembrolizumab

Endpoints

* PFS per RECIST 1.1 by investigator

* ORR/DOR/DCR per RECIST 1.1 by BICR

* ORR/DOR/DCR per RECIST 1.1 by investigator

* Intracranial ORR/DOR per RECIST 1.1 by BICR

* Time to CNS progression per RECIST 1.1. by BICR

* Intracranial ORR/DOR per RANO-BM by BICR*

* OS

* PFS2

* Time to deterioration in pulmonary symptoms: cough, chest pain, and dyspnea

as measured by the NSCLC-SAQ

Objectives

To assess safety and tolerability of selpercatinib compared to platinum-based

and pemetrexed therapy with or without pembrolizumab

Endpoints:

Including but not limited to SAEs, AEs, deaths, and clinical laboratory

abnormalities per CTCAE v5.0

Objectives:

To assess/evaluate performance of RET local laboratory tests compared to a

single central test:

Endpoints:

RET fusion status

Tertiary/exploratory:

Please refer to objectives and endpoints table/section of study protocol.

Study description

Background summary

Rationale:

Patients with RET fusion-positive non-small cell lung cancer (NSCLC) represent a population with high unmet need. Combination chemotherapy has short-term palliative potential in advanced NSCLC. While anti-programmed cell death protein 1 (anti-PD-1) monoclonal antibodies (e.g., nivolumab and pembrolizumab) have extended progression-free survival (PFS) and recently been approved for patients with NSCLC in some geographies, they may be less effective as monotherapy in tumors marked by single-gene driver oncogenic kinase alterations (including kinase fusions) with otherwise low mutation burdens and low neo-antigen production.

The identification of activating genetic alterations in specific tyrosine kinases has led to a new classification of NSCLC based on molecular genotype rather than histology. Agents targeting specific alterations such as EGFR and BRAF activating mutations and ALK and ROS1 gene fusions have demonstrated compelling efficacy in patients with cancers that harbor the respective activating genetic alteration. Selpercatinib, a selective RET tyrosine kinase inhibitor, has demonstrated a favorable safety profile and evidence of durable antitumor activity in patients with advanced RET fusion-positive patients with NSCLC (both treatment naïve and those previously treated with approved first-line chemotherapy with or without immunotherapy). As a result, selpercatinib may be of benefit as an initial treatment for advanced or

metastatic RET fusion-positive NSCLC.

Study objective

This study has been transitioned to CTIS with ID 2023-506783-14-00 check the CTIS register for the current data.

The proposed Study J2G-MC-JZJC (hereafter referred to as JZJC) will evaluate selpercatinib in comparison to platinum-based (carboplatin or cisplatin) and pemetrexed therapy with or without pembrolizumab in patients with locally advanced or metastatic RET fusion-positive NSCLC.

Study design

Overall Design:

Study JZJC is a global, multicenter, randomized, open-label, controlled Phase 3 study of selpercatinib (Arm A) compared to platinum-based and pemetrexed therapy with or without pembrolizumab (Arm B) in patients with locally advanced or metastatic, RET fusion-positive non-squamous NSCLC. Enrolled patients will be stratified based on geography (East Asian vs. non-East Asian), brain metastases per investigator assessment (presence vs. absence), and investigator*s choice of treatment if randomized to Arm B (with or without pembrolizumab and cisplatin vs. carboplatin - choice/intent of treatment regimen must be declared prior to randomization). Patients will be allowed cross over from the comparator Arm B to Arm A upon confirmation of disease progression by a blinded independent central review if they meet the eligibility criteria for crossover. The primary endpoint being evaluated is PFS per RECIST 1.1 by BICR

Disclosure Statement: This is a randomized, active treatment study with 2 arms where the participant and investigator will not be blinded, but the aggregate data in the clinical research database will be blinded to sponsor personnel.

Intervention

You will get selpercatinib or one of the medication combinations listed below. You will know which medicine you are taking. Whether you receive selpercatinib or the medications listed below will be decided by chance. The chance that you will receive selpercatinib is 2 in 3.

If you are not assigned to selpercatinib, your doctor will decide which of the following combinations you will get:
• Cisplatin plus pemetrexed with pembrolizumab
• Cisplatin plus pemetrexed without pembrolizumab
• Carboplatin plus pemetrexed with pembrolizumab

• Carboplatin plus pemetrexed without pembrolizumab

Selpercatinib- Arm A- Tablets only

Comparator- Arm B- IV injection.

Study burden and risks

During the study, you will visit the hospital approximately 3 times a month, the frequency of study visits may be higher than visits required as routine practice by your doctor for looking after your illness, but these are required for study participation. A visit will take approximately 2-4 hours during the treatment period. The follow-up visits will take 1-2 hours.

Venapunction : Yes

Biopsy: Possible

Intra-venous injection: Possible if on Arm B

Refer to section E6 and J.

Contacts

Public
Eli Lilly

Island House, Eastgate Business Park, Little Island na
Cork Co.
NL
Scientific
Eli Lilly

Island House, Eastgate Business Park, Little Island na
Cork Co.
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Histologically confirmed Stage IIIB-IIIC or Stage IV non-squamous NSCLC that is not suitable for radical surgery or radiation therapy
- A RET gene fusion in tumor and/or blood from a qualified laboratory
- Measurable disease as determined by RECIST 1.1 by the investigator
- ECOG performance status of 0-2
- Adequate hematologic, hepatic and renal function
- Willingness of men and women of reproductive potential to observe conventional and effective birth control for the duration of treatment and for 6 months after
- Written informed consent

Exclusion criteria

- Additional validated oncogenic drivers in NSCLC if known
- Prior systemic therapy for metastatic disease
- Major surgery (excluding placement of vascular access) within 3 weeks prior to planned start of selpercatinib.
- Radiotherapy for palliation within 1 week of the first dose of study treatment or within 6 months prior to the first dose of study treatment if more than 30 Gy to the lung
- Symptomatic CNS metastases, leptomeningeal carcinomatosis, or untreated spinal cord compression
- Clinically significant active cardiovascular disease or history of myocardial infarction within 6 months prior to planned start of selpercatinib or prolongation of the QT interval corrected for heart rate using Fridericia*s formula (QTcF) > 470 msec
- Active uncontrolled systemic bacterial, viral, or fungal infection or serious ongoing intercurrent illness, such as hypertension or diabetes, despite optimal treatment. Screening for chronic conditions is not required
- Clinically significant active malabsorption syndrome or other condition likely to affect gastrointestinal absorption of the study drug
- Require concomitant use of strong CYP3A4 inhibitors or inducers, proton pump

inhibitors, or medications known to cause QTc prolongation
- Known hypersensitivity to any of the excipients of the study drugs
- Pregnancy or lactation
- Active second malignancy
- Symptomatic ascites or pleural effusion - requiring chronic treatment with steroids

Exclusion Criteria for patients receiving pembrolizumab
- History of interstitial lung disease or interstitial pneumonitis
- Active autoimmune disease or any illness or treatment that could compromise the immune system

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-02-2021
Enrollment:	7
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Alimta
Generic name:	Pemetrexed
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	Cisplatin Accord
Generic name:	Cisplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Keytruda
Generic name:	Pembrolizumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Ribocarbo®-l
Generic name:	Carboplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Selpercatinib
Generic name:	Selpercatinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	03-02-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-06-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	06-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-12-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-02-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-08-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-04-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-04-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-06-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-01-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	29-06-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-07-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-10-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-10-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	CTIS2023-506783-14-00
EudraCT	EUCTR2019-001979-36-NL
CCMO	NL71634.029.19