A Phase II single-arm trial to investigate tepotinib in advanced (locally advanced or metastatic) non-small cell lung cancer with MET exon 14 (METex14) skipping alterations or MET amplification (VISION)

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This study has been transitioned to CTIS with ID 2024-512003-39-00 check the CTIS register for the current data. PART 1Cohort A (METex14 skipping alterations):• To assess the efficacy of tepotinib in subjects with locally advanced or metast. (NSCLC...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON54801

Source
ToetsingOnline

Brief title
MS200095-0022 (VISION)

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Non-small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Merck
Source(s) of monetary or material Support: pharmaceutical industry

Intervention

Keyword: METex14, non-small cell lung cancer, phase II

Outcome measures

Primary outcome

Objective response (confirmed CR or PR) determined according to RECIST Version

1.1, based on independent review (IRC).

Secondary outcome

• Anti-tumor activity

• Objective response (confirmed CR or PR) determined according to RECIST

• Version 1.1, as per Investigator

• Duration of response (DOR) as per IRC

• Duration of response as per Investigator

• Objective disease control (DCR) as per IRC

• Objective disease control as per Investigator

• Progression free survival (PFS) as per IRC

• Progression free survival as per Investigator

• Overall survival (OS).

• Patient reported outcomes (PROs)

• EQ-5D-5L

• EORTC QLQ-C30

• QLQ-LC13.

Study description

Background summary

Lung cancer remains the leading cause of cancer death in men and the second cause of cancer death in women worldwide, with 1.8 million cases and 1.6 million deaths estimated for 2012.
According to the latest mortality predictions for the year 2015 based on the 6 most populated countries in the European Union (EU), mortality rates from lung cancer are expected to exceed those from breast cancer for the first time among women in the EU. In the USA, lung cancer is the leading cause of cancer death with an estimated 221,200 new cases and 158,040 deaths in 2015, according to the National Cancer Institute. Non-small cell lung cancer (NSCLC), accounts for approximately 85% of all diagnosed lung cancer cases.

Study objective

This study has been transitioned to CTIS with ID 2024-512003-39-00 check the CTIS register for the current data.

PART 1
Cohort A (METex14 skipping alterations):
• To assess the efficacy of tepotinib in subjects with locally advanced or metast. (NSCLC), harboring the METex14 skipping alterations or MET amplif., as per objective response acc. to RECIST v.1.1, based on independent review in
• Subjects tested positive for METex14 skipping alterations, regardless of MET amplification status
• Subjects tested positive for METex14 skipping alterations based on liquid biopsy (LBx), regardless of MET amplification status
• Subjects tested positive for METex14 skipping alterations based on tumor biopsy (TBx), regardless of MET amplification status.
PART
Cohort B (MET amplification):
• To assess the efficacy of tepotinib in subjects with locally advanced or metastatic NSCLC, as per objective response (confirmed complete response [CR] or partial response [PR]) determined according to Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1, based on independent review in:
• Subjects tested positive for MET amplification in LBx, and negative for METex14
skipping alterations.

PART 2
Cohort C (confirm. part for MET ex14 skipping alterations), ref to protocol

Study design

This single-arm, open-label, Phase II trial will assess the antitumor activity and tolerability of tepotinib, a highly selective small molecule inhibitor of c-Met in subjects with advanced (Stage IIIB/IV) NSCLC harboring METex14 skipping alterations or MET amplification.

Intervention

Tepotinib 500 mg, orally, once daily in cycles of 21-day duration until progression of disease, undue toxicity or withdrawal from trial.

Study burden and risks

In a pharmaceutical trial like this one, every risk or side effect cannot be predicted. Each person*s reaction to a test drug may be different.
The most frequently observed adverse events (>=10% of patients) irrespective of severity and relationship to study drug were: Abdominal pain (pain in the stomach area); Anemia (decrease in red blood cells); Ascites (accumulation of fluid in the stomach area); AST increase (liver enzyme, a clinical laboratory parameter indicating a possible liver disease or damage); Constipation (blockage of stool); Decreased appetite; Dehydration (decreased body water); Diarrhea (loose stool); Dyspnea (labored breathing); Edema peripheral (swelling caused by excess fluid); Fatigue (feeling tired); Hypoalbuminemia (low level of albumin in the blood, which can cause swelling, muscle weakness, and cramps); Nausea (feeling sick); Vomiting (being sick).
Liver failure leading to death and decrease in platelets leading to death may occur in patients with hepatocellular cancer and extensive liver involvement from metastases in other disease settings as well. Up to now the reported events were assessed not to be related to study drug.

Contacts

Public
Merck

Frankfurter Str. 250
Darmstadt 64293
DE
Scientific
Merck

Frankfurter Str. 250
Darmstadt 64293
DE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Histologically or cytologically confirmed advanced (Stage IIIB/IV) NSCLC (all histologies including squamous and sarcomatoid);
2. Treatment naive patients in first-line or pre-treated patients with no more than 2 lines of prior therapy
3. Subjects with MET alterations, namely METex14 skipping alterations in plasma and/ or tissue, as determined by the central laboratory or by an assay with appropriate regulatory status will, be enrolled into the trial. For these subjects, sufficient tumor tissue and/or plasma is requested to allow additional testing MET amplification only in plasma defined by a positive LBx test, as determined by the central laboratory or by an assay with appropriate regulatory status. Based on the outcome of the interim analysis in 12 LBx selected subjects; MET amplification only in tissue defined by a positive TBx with a gain of at least 4 copies of the MET gene, as determined by the central laboratory or by an assay with appropriate regulatory status.
4. Signed, written informed consent by subject or legal representative prior to any trial-specific screening procedure;
5. Male or female, >= 18 years of age (or having reached the age of majority according to local laws and regulations, if the age of majority is > 18 years of age); [i.e., >= 20 years of age in Japan]);
6. Measurable disease in accordance with RECIST version 1.1;
7. Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0 or 1
8. A female subjects is eligible to participate if she is not pregnant, not breastfeeding, and at least one of the following conditions applies:
a. Not a woman of childbearing potential as defined in Appendix VIII OR
b. A woman of childbearing potential who agrees to use a highly effective contraception (i.e., methods with a failure rate of less than 1 % per year) as detailed in in Appendix VII of this protocol 2 weeks before

start of first dose of study treatment, during the treatment period and for at least 4 weeks after the last dose of study treatment. Women of childbearing potential must have a negative pregnancy test (β-HCG test in serum) prior to enrollment.
9. A male subject must agree to use and to have their female partners of childbearing potential to use a highly effective contraception (i.e., methods with a failure rate of less than 1 % per year) as detailed in Appendix VII of this protocol from the first dose of study treatment, during the treatment period and for at least 3 months after the last dose of study treatment and refrain from donating sperm during this period. Male subjects should always use a barrier method such as condom concomitantly.

Exclusion criteria

1. Subjects with characterized EGFR activating mutations that predict sensitivity to anti-EGFR-therapy, including, but not limited to exon 19 deletions and exon 21 alterations;
2. Subjects with characterized ALK rearrangements; that predict sensitivity to anti-ALK therapy
3. Subjects with symptomatic brain metastases who are neurologically unstable, and/or have required an increase in steroid dose within 2 weeks and/or have received prior stereotactic radiosurgery/gamma knife within 2 weeks and/or other prior treatment for brain metastases within 4 weeks prior to the start of therapy. Subjects with leptomeningeal disease are ineligible;

4. Any unresolved toxicity Grade 2 or more according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) from previous anticancer therapy;
5. Need for transfusion within 14 days prior to the first dose of trial treatment;
6. Prior chemotherapy, biological therapy, radiation therapy, hormonal therapy for anti-cancer purposes, targeted therapy, or other investigational anticancer therapy (not including palliative radiotherapy at focal sites) within 21 days prior to the first dose of trial treatment
7. Subjects who have brain metastasis as the only measureable lesion
8. Inadequate hematological, liver, renal, cardiac function
9. Prior treatment with other agents targeting the HGF/c-Met pathway;
10. Past or current history of neoplasm other than NSCLC, except for curatively treated non-melanoma skin cancer, in situ carcinoma of the cervix, or other cancer curatively treated and with no evidence of disease for at least 5 years (for a full list of exlustion criteria please see the study protocol)

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-04-2019
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tepotinib
Generic name:	Tepotinib

Ethics review

Approved WMO Date:	20-11-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	25-01-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	11-06-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-06-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-07-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-07-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-08-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-09-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-12-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-02-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	17-04-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-06-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-10-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-07-2022

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-01-2023
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	CTIS2024-512003-39-00
EudraCT	EUCTR2015-005696-24-NL
ClinicalTrials.gov	NCT02864992
CCMO	NL67616.056.18