Phase II study examining the activity of L19-IL2 immunotherapy and stereotactic ablative radiotherapy in metastatic non-small cell lung cancer

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The purpose of this scientific study is to verify whether immunotherapy (L19-IL2) after a standard treatment such as radiotherapy, fights the metastatic disease more efficiently than the current standard treatment alone.

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

Summary

ID

NL-OMON56015

Source
ToetsingOnline

Brief title
ImmunoSABR Phase 2 trial

Condition

- Other condition

Synonym
progressive Lung cancer

Health condition

Long kanker

Research involving

Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Europese Unie

Intervention

Keyword: immunocytokine L19-IL2, Lungcancer, PFS, Radiotherapy ImmunoSABR

Outcome measures

Primary outcome

The main objective of the trial is to test the activity of the combination of

(SAB)R and L19-IL2 in patients with metastatic NSCLC will resulting in improved

progression-free survival (PFS) compared to the SOC.

Secondary outcome

• PFS;

• Overall survival;

• Toxicity (CTCAEv4);

• Quality of Life (EORTC QLQ C30 v3.0, QLQ LC13 and EQ5D);

• The occurrence of OFRI / the abscopal effect using imaging, based on RECIST

criteria;

• The occurrence of an IFRI response, based on RECIST criteria.

Study description

Background summary

In the past L19-IL2 has been studied in patients with different metastasised tumours, both alone and in combination with chemotherapy. The medicine can be administered alone or in combination with chemotherapy and radiotherapy with

acceptable side effects. In a part of the patient population it also has the effect of (temporarily) stopping the disease. Previous non-human subjects research appears to show that the combination of radiation and L19-IL2 works much better on the radiated and non-radiated tumours, than each of the treatments separately. The purpose of this study is to verify how efficient this combined treatment is in people to fight the cancer.

Study objective

The purpose of this scientific study is to verify whether immunotherapy (L19-IL2) after a standard treatment such as radiotherapy, fights the metastatic disease more efficiently than the current standard treatment alone.

Study design

A standard treatment for patients known with maximum 5 metastases is high-dose radiotherapy. Patients who 6 to 10 metastases get radiotherapy without the high-dose. Radiation will be applied to maximum 5 metastases and minimal 1 metastasis in the experimental arm.

Intervention

blood sampling , stool sampling + translational research
Biopsy

Study burden and risks

Standard of care for patients with metastatic NSCLC without targetable drive mutations is a palliative systemic treatment (chemotherapy, immunotherapy). With this, progression-free survival and overall survival in this patients group are poor.
The ultimate aim of the combination of (SAB)R and L19-IL2 is to prolong PFS and OS by inducing an immune response which would be able to keep this systemic disease controlled. Known/potential risks additional to the standard of care treatment include:

The side effects of the standard treatment will be discussed with the patient by the treating physician(s).
The side effects of the radiation may differ for each site on thebody that is radiated.

Possible side effects of radiation include:
Nausea, vomiting and diarrhoea when the abdomen is radiated, or local pain and discomfort when bones or soft tissue are radiated. When radiating the lungs/chest a cough, shortness of breath or broken ribs may occur.

The side effects of the study treatment with L19-IL2 are:
Fever with cold shivers, fatigue, nausea, vomiting, weakness, (peripheral) oedema (accumulation of fluid elsewhere in the body), skin rash, production of more fluid, pain in the torso, itching, increased kidney function values, high blood pressure, lack of oxygen, and pain in the tumour region.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

The study population consists of adult, squamous and non-squamous, non-small cell lung cancer patients with Stage IV metastatic disease (up to 10 metastases).

Exclusion criteria

• More than 10 metastatic lesions
• More than 2 brain metastatic lesions
• Two brain metastases with a cumulative diameter larger than 5 cm.
• Patients with non-infectious pneumonitis, uncontrolled thyroid disease pleuritis, pericarditis peritonitis carcinomatosis, severe pleuritis and pleuritis carcinomatosis
• Patients who received live vaccines 30 days or fewer prior to enrolment.(Patient can still participate after this is reached.)
• Patients who are already actively participating in another study
• Previous radiotherapy to an area that would be re-treated by (SAB)R resulting in overlap of the high dose areas
• Patients that need (maintenance) chemotherapy during ImmunoSABR in the E-arm
• Pregnancy or breast feading; it is well known that ED-B, the target of both L19-IL2, is expressed in a variety of fetal tissues. Furthermore, anti-PD(L)1 treatment may increase the risk of immune-mediated disorders. Therefore it will be contra indicated for pregnant or lactating women.
• Non-sterilised, sexually active male patient with a female partner who is of child-bearing age, must use two acceptable birth control methods like a condom combined with spermicidal cream or gel from the first dose of study medicine
• Women of childbearing potential (WOCBP) and WOCPD partners of male patients must be using, from the screening to three months following the last study drug administration and 45 months after last dose of antanti-PD(L)1 maintenance treatment, effective contraception methods ((a) IUD (IUD) or intrauterine hormone delivery system (IUS), b) combined (with estrogen and progesterone) hormonal contraception associated with ovulation inhibition (oral, intravaginal, transdermal), c) hormonal contraception with progesterone only associated with ovulation inhibition (oral, injectable, implantable),
• Whole brain radiotherapy (WBRT) is not allowed, although it is accepted when given at least 3 weeks prior to randomisation or after the treatment period. Patients with stable brain metastases are not excluded.
• Excluded are those with (non-)infectious pneumonitis and uncontrolled thyroid disease,. as well as infectious pericarditis, infectious pleuritis or infectious peritonitis. Patients become eligible once treated and stable (thyroid disease) or recovered (note: patients with a medical history of

immunotherapy induced pneumonitis grade 3 or higher are always excluded). Patients with pericarditis carcinomatosa, pleuritis carcinomatosa or peritonitis carcinomatosa are excluded (based on Dingemans et al, JTO 2019; Lievens et al, R&O 2021). Patients with a small amount of pericardial, pleural or peritoneal fluid, and no diagnosis of malignant cells in this fluid (at least once evaluation), or with so little fluid that cytological evaluation is not possible and/or without other findings suggestive for malignancy (i.e. no pericardial, pleural or peritoneal thickening) are eligible
• History of immunotherapy related toxicity grade 3 or higher , except for controlled endocrine toxicity.
• Other active malignancy or malignancy within the last 2 years (except localised skin basal/squamous cell carcinoma, non-muscle invasive carcinoma of the bladder or in situ carcinoma from any site).
• Concomitantly administered glucocorticoids may decrease the activity of IL2 and therefore should be avoided. However, patients who develop life-threatening signs or symptoms may be treated with dexamethasone until toxicity resolves or reduces to an acceptable level (generally grade 1 and 2, however must be based at the research physician*s discretion).
• History of allergy to intravenously administered L19-IL2/proteins/peptides/antibodies/ radiographic contrast media.
• HIV positive; active HIV infection, or active hepatitis B or C (assessed in local lab). For HBV serology: the determination of HBsAg, anti-HBsAg-Ab and anti-HBCAg-Ab is required. In patients with serology documenting previous exposure to HBV (i.e., anti-HBs Ab with no history of vaccination and/or anti-HBc Ab), negative serum HBV-DNA is required. For HCV: HCV RNA or HCV antibody test. Subjects with a positive test for HCV antibody but no detection of HCV RNA indicating no current infection are eligible.
• Systemic treatment with either corticosteroid (>10 mg daily prednisone equivalents) or Interferon alpha or immunosuppressive medications within 14 days prior to randomisation. Topical or inhalation steroids are allowed. If a patient needs to take unexpectedly immunosuppressive medication during the trial, it will be allowed but decreasing the dose as soon as possible is strongly advised.
• Prior history of organ transplant, including autologous stem cell transplant.
• Acute or sub-acute coronary syndromes within the last year, acute inflammatory heart disease, heart insufficiency NYHA > 2, or irreversible cardiac arrhythmias.
• A known impaired cardiac function defined as left ventricular ejection fraction (LVEF) < 50 % (or below the study site*s lower limit of normal) as measured by MUGA or ECHO.
• Uncontrolled hypertensive disease; (systolic blood pressure (SBP) >=160 or diastolic blood pressure (DBP) >=100 mm Hg during two measurements).
• Uncontrolled and symptomatic hypotensive disease; (systolic blood pressure (SBP) <85 or diastolic blood pressure (DBP) <55 mm Hg during two measurements).
• History or evidence of active autoimmune disease.
• Severe diabetic retinopathy (neoangiogenesis targeted by L19 outside

the tumour).
• Major trauma, including oncologic surgery, but excluding smaller procedures like the placement of porth-à-cath or surgical biopsy, within 4 weeks prior to randomisation (neoangiogenesis targeted by L19 outside a tumour).
• Any underlying mental, medical or psychiatric condition which in the opinion of the investigator will make administration of study drug hazardous or hinder the interpretation of study results. Unstable or serious concurrent uncontrolled medical conditions.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	10-01-2020
Enrollment:	56
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	L19-IL2
Generic name:	L19-IL2 (L19 Interleukin-2, Darleukin

Ethics review

Approved WMO

Date:	09-01-2019

Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	03-04-2019
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-07-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-10-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-04-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-05-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	13-09-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	24-09-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	16-09-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-10-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	24-04-2024
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
EudraCT	EUCTR2018-002583-11-NL
ClinicalTrials.gov	NCT03705403
CCMO	NL67629.068.18

Study results

Date completed:	06-01-2025

Summary results

Trial ended prematurely