Track and treat in NSCLC (TATIN) - ctDNA guided treatment of early resistance to targeted treatment in patients with EGFR positive NSCLC

Published: 10-01-2019
Last updated: 31-12-2024

Primary objectives• To identify the percentage of patients in which a drug resistant clone can be detected with ctDNA before the emergence of radiological progression.• To determine the success rate of crizotinib and osimertinib combination...

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

Summary

ID

NL-OMON48173

Source
ToetsingOnline

Brief title
TATIN

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Lung cancer, non-small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis

Source(s) of monetary or material Support: Roche GmbH

Intervention

Keyword: ctDNA, EGFR positive NSCLC, MET amplification, osimertinib

Outcome measures

Primary outcome

The number of patients with a resistant clone detected before radiological progression will be calculated as a percentage of total number of patients.
The success rate of crizotinib treatment to eliminate resistance due to MET amplification will be calculated as the percentage of patients with disappearance of MET amplification in a subsequent ctDNA sample (not necessarily the first ctDNA following MET directed treatment) of the total number of patients with MET amplification detected in the ctDNA.

Secondary outcome

The Lag time between ctDNA based detection of a resistant clone and radiological progression will be calculated as a median with 95% confidence interval. This parameter will be calculated for all resistance mechanisms combined, as well as for the individual resistance mechanisms.
The time to re-appearance of the MET amplification clone after successful elimination after crizotinib treatment will be calculated as a median with 95% confidence interval.

Study description

Background summary

The current strategy is to test for treatment resistance at the time of radiological progression and design subsequent treatment based on the mechanism of resistance. However, upon disease progression patients tend to deteriorate quickly and 30% - 40% of patients will not be in the clinical condition to receive next line treatment. Therefore, there is a potential for early resistance identification and directing treatment against it in order to improve patient outcome.
Next Generation Sequence (NGS) technology rapidly evolves and it is now feasible to use circulating tumor DNA (ctDNA) as a BioSource for comprehensive analysis of the molecular make up of tumors. ctDNA based techniques are able to detect the emergence of drug resistance mechanisms with high sensitivity and prior to radiological progression.

Study objective

Primary objectives
• To identify the percentage of patients in which a drug resistant clone can be detected with ctDNA before the emergence of radiological progression.
• To determine the success rate of crizotinib and osimertinib combination treatment to eliminate MET amplification, defined by disappearance of the MET amplification clone in a subsequent ctDNA sample.

Secondary objectives
• Lag time between ctDNA based detection of a resistant clone and radiological progression.
• Correlation of ctDNA results with that of the tumor biopsy upon radiological progression.
• The time to disappearance of the MET amplification clone after crizotinib initiation as detected by ctDNA.
• The time to re-appearance of MET amplification as detected by ctDNA or tumor biopsy in case of radiological progression after successful elimination with crizotinib treatment.

Study design

Patients with EGFR mutation positive NSCLC who are eligible for osimertinib treatment will be treated with osimertinib. At baseline and every eight weeks during treatment blood will be drawn to analyse ctDNA with Avenio ctDNA (Expanded panel) to detect all known EGFR TKI resistance mechanisms. Patients will also be monitored with CT every eight weeks.
With the exception of MET amplification, detection of resistant clones by ctDNA will be followed over time until radiological progression. Upon radiological progression, a tumor biopsy will be performed according to routine clinical care for EGFR mutation positive patients, and a comparable Avenio FFPE panel will be analysed on the tissue sample for comparison. Tissue and ctDNA based resistance profiling will be compared.

When MET amplification is detected by ctDNA at any time, the patient will be treated with crizotinib 250 mg bi-daily in combination with osimertinib 80 mg once daily for as long as MET amplification can be detected with (8-weekly assessment of) ctDNA. Crizotinib treatment will be discontinued when MET amplification becomes undetectable with the Avenio ctDNA panel, while continuing osimertinib treatment.

Intervention

All subjects will receive continuous daily treatment with osimertinib 80mg once daily.

Study burden and risks

The disadvantage of participating in this study is that more blood will be taken than normal.

Contacts

Public
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121
Amsterdam 1066CX
NL
Scientific
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121
Amsterdam 1066CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Histologically confirmed metastatic NSCLC, characterized by a sensitizing exon 19 deletion or exon 21 L858R EGFR mutation., 2. WHO performance status 0-2., 3. Eligible for osimertinib treatment according to the label and according to the treating physician., 4. Patients must be >=18 years of age.

Exclusion criteria

1. Patients with symptomatic central nervous system metastases who are neurologically unstable. Unstable brain metastases except for those who have completed definitive therapy and have had a stable neurological status for 2 weeks after completion of definitive therapy. Patients may be on corticosteroids to control brain metastases if they have been on a stable dose for 2 weeks prior to the start of study treatment and are clinically asymptomatic.

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	23-07-2019
Enrollment:	100
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Tagrisso
Generic name:	Osimertinib
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Xalkori
Generic name:	Crizotinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	10-01-2019
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	12-07-2019
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	12-08-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-12-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-12-2024
Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2018-004798-29-NL
CCMO	NL67847.031.18

Study results

Date completed: 09-12-2023

Results posted: 22-10-2024

First publication
01-01-1900

URL result
URL
Type
ext
Naam
www.annalsofoncology.org
URL