Fluid phase biopsy (circulating tumour DNA and serum tumour markers) in patients with non-small cell lung cancer.

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In advanced NSCLC & in first stage of study in locally advanced NSCLC:To assess the kinetics of STMs and ctDNA in plasma before, during and after treatment for NSCLC.Second stage of study in locally advanced NSCLC:To determine the prognostic...

Ethical review	Approved WMO
Status	Pending
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON45168

Source
ToetsingOnline

Brief title
Fluid phase biopsy in NSCLC.

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: Ministerie van OC&W

Intervention

Keyword: circulating tumour DNA, NSCLC, serum tumour markers

Outcome measures

Primary outcome

Primary endpoint - advanced NSCLC & first study stage in locally advanced NSCLC:

• Levels of ctDNA, in amplifiable copies per millilitre of plasma, determined

before start of treatment, at multiple days during and after treatment

Primary endpoint - second study stage in locally advanced NSCLC:

• Association of ctDNA levels with progression free survival at one year

Secondary outcome

• Percentage of patients with detectable ctDNA levels in plasma

• Type and frequency of mutated genes in ctDNA found

• Association of STMs levels with progression free survival at one year

• Correlation of levels of ctDNA and STMs with locoregional and distant control

• Correlation of levels of ctDNA and STMs with tumour burden

o As assessed by gross tumour volume (GTV) before treatment

o As assessed by response evaluation on CT-scan according to RECIST version1.112

• Correlation of ctDNA kinetics with STMs kinetics

Study description

Background summary

Levels of serum tumour markers and circulating tumour DNA (ctDNA) in plasma could reflect the clinical course of disease and its response to treatment in

patients with locally advanced NSCLC treated with concurrent chemoradiotherapy and in patients with stage IV disease treated with systemic therapy. In addition, identification of molecular pathways activated in NSCLC could provide targets for new treatments and/or
guide current treatment options.

Study objective

In advanced NSCLC & in first stage of study in locally advanced NSCLC:
To assess the kinetics of STMs and ctDNA in plasma before, during and after treatment for NSCLC.

Second stage of study in locally advanced NSCLC:
To determine the prognostic value of change in ctDNA levels during treatment with regard to treatment response in patients with (locally) advanced NSCLC (early response marker).

Study design

Plasma samples will be collected prospectively before, during and after treatment. Besides, ctRNA will be isolated from blood platelets from a subset of patients with a know/suspected translocation. Both patients with locally advanced NSCLC and with advanced NSCLC can be included in the study. For patients with locally advanced NSCLC, the study involves two stages that will be performed consecutively. The first stage is explorative in nature assessing the biological variation in the quantity of mutations in ctDNA and the biological variation in STM throughout treatment.

The data collected in this first study stage will help to determine the optimal collection points for the second study stage, which is a validation phase testing the value of ctDNA and STMs as early response marker. The second stage will only be initiated once the first stage is completed successfully. Upon disease progression, patients will be asked to have a tumor biopsy (optional part of the study).

Study burden and risks

Extra blood will be drawn only at regularly planned blood drawls. For patients with locally advanced NSCLC in the first stage of this study this will be: once before start of treatment (16 ml), at ten different moments during treatment (each drawl 8 ml blood and only once 16 ml) and at maximally five moments after end of treatment (16ml each). In the second stage of this study the number of blood drawls during treatment will be reduced to a maximum of three, the exact amount of blood to be drawn in this second study stage will be determined after completion of the first study stage. For patients with advanced stage NSCLC, blood will be drawn (16 ml) at baseline, 3-weekly during treatment and 6-weekly

after treatment until disease progression.

It is optional to take a tumour biopsy at disease progression. Patients may have discomfort due to taking biopsies. Biopsies will be taken from metastases that are easily accessible (mainly subcutaneous and lymph node metastases) and will be performed by means of ultrasound guidance by an experienced radiologist.

In this study, tumor and germline DNA will be analyzed using sequencing techniques. Therefore, there is a small possibility of detection of unsolicited findings, i.e. germline DNA variants that confer an increased risk of developing malignancies or other diseases both for the patient and his/her family. Patients should be informed and offered genetic counselling in case of revelation of a variant that is clinically relevant and medically actionable. However, the analysis of ctDNA / ctRNA is not part of an established workflow and methods have not been validated yet. Therefore, it is not realistic to expect that reporting of the data to the patient will take place in the present trial. The patient information form will be adapted to allow described counselling and to prevent too high expectations.

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

Inclusion criteria locally advanced stage disease (for both stage 1-2):
1. 18 years of age, or above
2. Histologically or cytologically confirmed diagnosis of NSCLC
3. Stage II/III non-operable disease, without malignant pleural effusion
4. Indication for concurrent chemoradiotherapy (NKI-AVL: 66Gy in 24 fractions with daily low dose cisplatin 6mg/m2; University Hospital Leuven: 66Gy in 33 fractions with 3 weekly dose cisplatin 75mg/m2)
5. Performance score: WHO 0-2 at study entry
6. Signed written informed consent;Inclusion criteria advanced stage NSCLC
1. 18 years of age, or above
2. Histologically or cytologically confirmed diagnosis of NSCLC
3. Advanced stage disease
4. Indication for treatment
5. Performance score: WHO 0-2 at study entry
6. Signed written informed consent

Exclusion criteria

Unwillingness to participate in study

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2013
Enrollment:	1190
Type:	Anticipated

Ethics review

Approved WMO Date:	03-12-2013
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	08-05-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-06-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-11-2017
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
CCMO	NL45524.031.13