Can tumor uptake of [18F]afatinib in NSCLC patients be quantified, and does [18F]afatinib uptake identify patients who will benefit from afatinib therapy ?

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract neoplasms
Study type	Observational invasive

Summary

ID

NL-OMON47284

Source
ToetsingOnline

Brief title
[18F]afatinib in NSCLC

Condition

- Respiratory tract neoplasms

Synonym
lung cancer, lung carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Boehringer Ingelheim

Intervention

Keyword: [18F]afatinib, afatinib therapy, NSCLC, predictive biomarker

Outcome measures

Primary outcome

1. Tracer pharmacokinetic modeling for [18F]afatinib.

2. Procedure optimization

3. Difference between tumor [18F]afatinib uptake and EGFR mutational status

4. Correlation between tumor [18F]afatinib uptake and tumor response to

afatinib therapy using RECIST 1.1.

Secondary outcome

N.a.

Study description

Background summary

Non-small cell lung cancer (NSCLC) patients that harbour an activating epithelial growth factor receptor (EGFR) mutation are best treated with EGFR tyrosine kinase inhibitors (TKI). First, second and third generation EGFR TKI have shown efficacy in the common EGFR mutations, i..e. the exon 19 deletion and exon 21 point mutation L858R. Afatinib, a second generation EGFR TKI, has also shown efficacy in the *uncommon* EGFR mutations L861Q, G719X and S768I. Moreover, for these indications the FDA approved the use of afatinib.
However, identifying EGFR mutation positive patients can be challenging because obtaining representative tumor biopsies for DNA analysis may be difficult or even impossible in some patients due to difficult to reach tumor sites.
Positron emission tomography (PET) using radiolabelled afatinib, i.e. [18F]afatinib, as a tracer, may overcome the limitations associated with obtaining representative biopsies.
The aim of our study is to evaluate whether [18F]afatinib and PET could identify patient groups that are sensitive to afatinib. We hypothesized that tumour [18F]afatinib uptake would be higher in the sensitive groups, i.e.

higher in the TKI-naïve EGFR (common and uncommon) mutation positive group as compared to the wild type group.

Study objective

1. To define the optimal pharmacokinetic tracer model for [18F]afatinib.
2. To determine the optimal simplified measure for quantifying tumor [18F]afatinib uptake
3. To assess [18F]afatinib uptake differences between patients (1) with wild type EGFR, (2) EGFR mut+, TKI-resistant EGFR mut+ (3) with and (4) without T790M mutations.
4. To assess whether [18F]afatinib uptake is predictive for tumor response to afatinib in patients with wild type EGFR and EGFR mut+, prior to TKI therapy and after resistance occurs to a 1st generation TKI.

Study design

Prospective observational study with invasive intervention

Intervention:
There will be 2 subsequent steps involving 4 and 11 patients, respectively, in order to find the optimal PET scanning conditions.

Step 0: Dosimetric measures for safety are legally required in new PET tracers, therefore the first patient will be used for dosimetry. The data obtained is not intended for the purpose of this study.

Step 1: The first 4 patients will undergo a low dose CT scan, followed by a dynamic [15O]H2O PET scan and thereafter a prolonged (90 + 30 minutes) dynamic [18F]afatinib PET scan. Arterial sampling will be performed.

After step 1, kinetic analysis of the prolonged dynamic PET data will be performed to determine the best scanning interval for a whole body static PET scan.

Step 2: The subsequent 8 patients (regardless of the groups they are in) will undergo 2 scanning procedures on subsequent days for determining test-retest repeatability. A low dose CT scan, followed by a dynamic [15O]H2O PET scan and thereafter a 60-min dynamic [18F]afatinib PET scan will be done, followed by a break (duration will be determined by step 1). After this, a low dose CT and a 40-min static [18F]afatinib whole body PET scan will be made. Arterial sampling will be performed.

Study burden and risks

Patients in step 1 will be lying for a total of approximately 2.5 hours on the

scanner, a pause of 30 minutes is scheduled to break up this period. A venous cannula will be inserted in an arm vein to inject the tracers. After local anaesthesia, a cannula will be inserted the radial artery to drawn blood, both continuously and at seven time point manually. Per patient no more than 115cc blood will be drawn. There will be a total radiation burden of 5.7 mSv.

Patients in step 2 will undergo two scanning procedures on subsequent days. Patients will be lying for approximately 2 hours on the scanner, a break is scheduled to make the procedure easier. A cannula will be inserted in an arm vein (tracer injection) and in the radial artery to drawn blood, both continuously and at 7 time point manually. Per patient no more than 230cc blood will be drawn over the whole of day 1 and 2 together. There will be a total radiation burden of 16.8 mSv for both days together.

During follow up visits all assessments using CT-thorax and laboratory analyses will be similar to routine care during regular chemotherapy, and will therefore not be an extra burden.

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

- Age above 18 years
- Patient is planned to receive afatinib after scanning
- Histologically proven NSCLC, with EGFR mutational status (as determined by high resolution melting and DNA sequencing)
- Life expectancy of at least 12 weeks
- Malignant lesion of at least 1.5 cm diameter within the chest as measured by CT
- Performance status Karnofsky index >60%
- Written informed consent

Exclusion criteria

- Claustrophobia
- Pregnant or lactating patients
- Patients having metal implants in the thorax that could cause an attenuation artefact (e.g. pacemakers)
- Concurrent treatment with experimental drugs
- Anaemia (Hb < 6.0 mmol/L)
- Coumarin therapy

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-04-2015
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	18F-afatinib
Generic name:	18F-afatinib

Ethics review

Approved WMO Date:	04-11-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-07-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-04-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-07-2017
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-12-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-07-2019
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

ID: 23934
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2012-002849-38-NL
CCMO	NL46671.029.13
OMON	NL-OMON23934