Sorafenib pharmacokinetics in non small cell lung cancer patients: an in;vivo study using positron emission tomography

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To assess sorafenib pharmacokinetics and biodistribution, K-Ras mutational status, tumor uptake and tumor response in NSCLC patients.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON37648

Source
ToetsingOnline

Brief title
[11C]sorafenib kinetics in NSCLC patients

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: [11C]sorafenib, kinetics, non small cell lung carcinoma, positron emission tomography

Outcome measures

Primary outcome

[11C]sorafenib pharmacokinetics

Secondary outcome

1. Comparison of venous versus arterial sampling

2. Reproducibility of [11C]sorafenib PET-CT measurements

3. Relationship between K-Ras mutations and [11C]sorafenib pharmacokinetics in

tumor tissue

4. Study the relation between tumor blood flow and [11C]sorafenib uptake in

tumors

Study description

Background summary

Sorafenib is used in second-line treatment of renal cell carcinoma and hepato-cellular carcinoma. In non small cell lung carcinoma (NSCLC) patients sorafenib is being evaluated in phase II trials. Sorafenib targets, amongst others, VEGF and b-Raf. B-Raf is an effector in the Ras-Raf pathway. Patients harboring a K-Ras mutation are hypothetically more sensitive to sorafenib, because of the overstimulation of this pathway. Sorafenib is labeled with the positron emitter 11-Carbon. Positron emission tomography (PET) studies using [11C]sorafenib would provide a unique means to measure [11C]sorafenib pharmacokinetics, tumor uptake and tumor response in vivo. By relating PET measurements with tumor response, it will be possible to investigate the potential role of [11C]sorafenib and PET as a tool for predicting sorafenib therapy and consequently an important step in personalizing therapy.

Study objective

To assess sorafenib pharmacokinetics and biodistribution, K-Ras mutational status, tumor uptake and tumor response in NSCLC patients.

Study design

An observational study with invasive measurements.

Study burden and risks

Risk associated with participation in this study are related to 1) radiation exposure; 2) idiosyncratic reaction to the tracer [11C]sorafenib; 3) intravenous and arterial cannulation; 4) blood sampling; 5) discomfort during scanning; 6) bleeding due to biopsy.

1. Radiation exposure
A PET-CT scan is a regular diagnostic imaging technique. Each study will be conducted in compliance with the radiation safety of the department. Based on the calculations with Olinda software that whole body radiation from intravenous injection of 370 Mbq [15O]H2O and 370 Mbq [11C]sorafenib is approximately 0.4 mSv and 2 mSv respectively. In addition a low dose CT scan performed during PET scanning has a radiation dose of 1 mSV as calculated with the *ImPACT CT patient dosimetry calculator*. Patients will undergo 2 combined [15O]H2O/[11C]erlotinib PET-CT scans. The total amount of radiation burden is 6.8 mSv during the entire study, which is below the general accepted amount of radiation burden of 10 mSv. To compare, every person living in the Netherlands receives a natural background radiation dose of 2-2,5 mSv per year.

2. Idiosyncratic reaction of the tracer [11C]sorafenib
Due to the fact that only sub-pharmacological doses of [11C]sorafenib are administered in PET studies, no [11C]sorafenib-induced side effects will be expected in this study. A physician will be present during PET scanning.

3. Intravenous and arterial cannulation.
There is a very small risk of infection and bleeding associated with intravenous and arterial catheters, which are prevented by proper techniques. The venous cannulas and arterial cannulas (under local anaesthetics) will be placed by highly qualified medical doctors of the Department of Nuclear medicine & PET Research. However, occasionally these cannulas may cause a haematoma.

4. Blood sampling.
Adverse events of blood sampling will be minimised by exclusion of subjects with low haemoglobin levels (haemoglobin level must be > 6 mmol/l). No more than 286 ml blood will be withdrawn during the two PET scans.

5. Discomfort during PET scanning.
It may be uncomfortable to lie motionless in the camera and it may cause some subjects to feel anxious. Subjects will be made acquainted with the surroundings beforehand. Our staff will be available to provide support, reduce anxiety, optimise the comfort of the subject and remove the subject from the scanner if requested.

6. Bleeding due to biopsy.
There is a small risk of bleeding during taking biopsy. To minimise these risks, biopsies will be taken by highly qualified medical doctors of the Department of Pulmonary Diseases.

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

• Patients age of 18-70 years;
• Patients with advanced non small cell lung cancer harboring a K-Ras mutation;
• 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%;
• Laboratory requirements;
• Written informed consent

Exclusion criteria

• Claustrophobia;
• Pregnant or lactating patients;
• Patients having metal implants (e.g. pacemakers);
• Concurrent or previous treatment with experimental drugs
Anemia

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-06-2012
Enrollment:	12
Type:	Anticipated

Medical products/devices used

Product type:	Medicine

Brand name:	nvt
Generic name:	[11C]sorafenib

Ethics review

Approved WMO Date:	09-12-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-05-2012
Application type:	First submission
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2011-005564-24-NL
CCMO	NL38072.029.11