Imaging of [11C]erlotinib pharmacokinetics in non small cell lung cancer patients; an in vivo study with positron emission tomography

Published: 14-09-2009
Last updated: 04-05-2024

Primary Objective: To study the tumour pharmacokinetics of [11C]erlotinib in NSCLC patients in vivo and relating uptake with EGFR mutations, obtained from tumour biopsies. Secondary Objective(s): 1. to define the test-retest reproducibility of [11C]...

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

Summary

ID

NL-OMON32923

Source
ToetsingOnline

Brief title
Imaging of [11C]erlotinib kinetics in non small cell lung carcinoma

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: Cyclotron BV Amsterdam

Intervention

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

Outcome measures

Primary outcome

Primary study parameters/outcome of the study:

Change in [11C]erlotinib kinetics in EGFR mutated non small cell lung carcinoma

(NSCLC) compared to non mutated EGFR NSCLC.

Secondary outcome

Secundary study parameters/outcome of the study:

1. Validation of the PET-CT study

2. Compare the venous and arterial plasma kinetics of [11C]erlotinib

3. Study the relationship between tumor blood flow and [11C]erlotinib kinetics

in tumor tissue

Study description

Background summary

Over the last decade PET/CT has emerged as an important tool for staging, diagnosis, early response measurement and tumour surveillance during follow-up. In routine clinical studies use is made of [18]FDG, an analogue of glucose, which allows for imaging glucose metabolism. Although enhanced glucose metabolism is seen in most tumours, abnormal metabolism is not specific for malignancies and there is a continuing search for other, more tumour specific, tracers. One example is erlotinib, a small molecule which belongs to a group of

cancer drugs known as epidermal growth factor receptor (EGFR) inhibitors by inhibition of the enzyme tyrosine kinase. Erlotinib is under investigation as a possible treatment for many tumor types, including pancreatic cancer, ovarian cancer and head and neck cancer. Clinical trials were performed with monotherapy or combination therapy with erlotinib in NSCLC. However, often the efficacy of these agents is limited due to T790M mutation in the EGFR coding gene. This mutation is thought to cause resistance by sterically blocking binding of tyrosine kinase inhibitors, such as erlotinib. From phase III clinical studies it has been concluded that addition of EGR-TKI*s, such as erlotinib and gefitinib, to standard chemotherapy, does not improve survival (Giaccone et al., Herbst et al. 2004, Herbst et al., 2005). As it was discovered that genetic mutations are associated with sensitivity to erlotinib, it is interesting to study the relationship between EGFR mutations and clinical response in patients with NSCLC (Lynch et al., Pao et al.). Furthermore, EGFR expression may be important for both tumour growth and survival. In some reports, EGFR overexpression has been correlated with chemoresistance and poor prognosis (Selvaggi et al., Buchholz et al, Wang et al). Taken together, it will be very interesting to have knowledge about tumoral EGFR density and mutations. Positron emission tomography (PET) may be a useful technique to visualize and quantitate these items. This study will give insight in the relationship between EGFR mutation status and density, [11C]erlotinib pharmacokinetics and tumor accumulation, and tumor response. This study will therefore provide clues to come to optimized personalized targeted therapy.

Study objective

Primary Objective:

To study the tumour pharmacokinetics of [11C]erlotinib in NSCLC patients in vivo and relating uptake with EGFR mutations, obtained from tumour biopsies.

Secondary Objective(s):
1. to define the test-retest reproducibility of [11C]erlotinib PET measurements in lung cancer patients.
2. to validate the use of venous instead of arterial blood samples for metabolite analysis and measurement of plasma radioactivity concentrations.
3. to develop a tracer kinetic model for quantitative analysis of [11C]erlotinib PET studies.
4. to study the relation between tumor blood flow and [11C]erlotinib uptake in tumors

Study design

This is an observational feasibility 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]erlotinib; 3) intravenous canulation; 4) blood sampling; 5) discomfort during scanning; 6) bleeding due to biopsy

1. Radiation exposure
The total amount of radiation burden will be 6.8 mSv during the entire study.

2). Idiosyncratic reaction of the tracer [11C]erlotinib
No [11C]erlotinib-induced side effects will be expected in this study.

3). Intravenous canulation.
There is a very small risk of infection and bleeding or haematoma.

4). Blood sampling.
No more than 250 ml blood will be withdrawn.

5). Discomfort during PET scanning.
It may be uncomfortable to lie motionless in the camers and it may cause some subjects to feel anxious.

6) Bleeding due to biopsy.
There is a small risk of bleeding during taking tumor biopsy.

Contacts

Public
Vrije Universiteit Medisch Centrum

De Boelelaan 1117
1007 MB Amsterdam
NL
Scientific
Vrije Universiteit Medisch Centrum

De Boelelaan 1117
1007 MB Amsterdam
NL

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 non small cell lung cancer planned to receive erlotinib
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
Haemoglobin level < 6 mmol/l

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-11-2009
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	[11C]erlotinib

Ethics review

Approved WMO Date:	14-09-2009
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-09-2009
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
Other	CWO-VICI Pro 09/14
EudraCT	EUCTR2009-012403-25-NL
CCMO	NL28161.029.09