Demonstrating Pemetrexed induced Thymidylate Synthase inhibition in non-small cell lung cancer in vivo: a pilot study.

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The aim of the present study is to investigate whether a 4 hr time lapse between the first dose of pemetrexed in NSCLC is associated with increased FLT uptake, in responding patients.

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

Summary

ID

NL-OMON32208

Source
ToetsingOnline

Brief title
Alimta study

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
NSCLC

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: 18F-FLT, Alimta, NSCLC, PET

Outcome measures

Primary outcome

Change of 18F-FLT uptake as measured with time lapse of 4 hrs after pemetrexed.

18F-FLT changes versus clinical response measured with RECIST.

Secondary outcome

Not applicable

Study description

Background summary

Thymidylate synthase is a key enzyme for de novo synthesis of DNA and as such a target for anticancer drug development. In a mouse model (fibrosarcoma) it has been shown that 3'-deoxy-3'-[(18)F]fluorothymidine (18F-FLT) positron emission tomography (PET) allows for early measurement of thymidylate synthase inhibition effectuated by 5-FU (Perumal M, Cancer Res 2006): effective TS-inhibition resulted in a 1.8 fold increase of 18F-FLT cellular uptake.
Hence, 18F-FLT PET appears suited for noninvasive assessment of thymidylate synthase inhibition in tumours.
Conceptually, 18F-FLT PET could thus be used to predict the efficacy of pemetrexed, amongst others an inhibitor of TS, in non-small cell lung cancer (NSCLC) therapy.
Pemetrexed has several side-effects such as nausea, anemia, bone marrow depression, stomatitis, pharyngitis, rash. This unnecessary toxicity in non-responding patients might be strongly reduced if effectiveness would be predictable, e.g. from PET measurements.

Study objective

The aim of the present study is to investigate whether a 4 hr time lapse between the first dose of pemetrexed in NSCLC is associated with increased FLT uptake, in responding patients.

Study design

Single centre, prospective observational study including 12 eligible patients with NSCLC (tumor size at least 3 cm) who will be scanned with 18F-FLT PET on two separate occasions: first within 7 days prior to pemetrexed therapy, the second 4 hrs after the first therapeutic dose of pemetrexed. Personal characteristics will be registered, (age, sex, bodyweight, height, drug use). The standard follow-up measurements (CT scan, laboratory tests) will be performed every 6 weeks after the first therapeutic dose of pemetrexed.

Study burden and risks

The total amount of blood taken for investigation is 120 ml. The total amount of radiation burden: 10 mSv.

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

Patient age 18 years or older
Histological diagnosis of NSCLC
Scheduled for treatment with pemetrexed
Tumour diameter min. 3cm (to minimize partial volume effects) within the chest
Able to remain supine for 60 minutes
Written informed consent

Exclusion criteria

Pregnant or lactating patients
Claustrophobia
Patients having metal implants (e.g. pacemakers)

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	26-09-2008
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO Date:	23-07-2008
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
CCMO	NL23639.029.08