Movember substudy

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON26162

Source
NTR

Health condition

matastasized castrate resistent prostate cancer

Sponsors and support

Primary sponsor: VU university Medical Center
Source(s) of monetary or material Support: Movember foundation

Intervention

Outcome measures

Primary outcome

A pharmacokinetic model for [18F]FDHT; an appropriate simplified quantitative method for [18F]FDHT; concordance of DCE-MRI and [15O]-water parameters.

Secondary outcome

not apllicable

Study description

Background summary

Abstract: A study on the pharmacokinetics of [18F]-fluordihydrotestosterone in patients with metastasized castrate resistant prostate cancer

Rationale:
[18F]Fluorodihydrotestosterone ([18F]FDHT) is a relatively new oncological tracer used to perform Positron Emission Tomography y ([18F]FDHT PET) scans. A series of radiotracers has been developed to visualize the androgen receptor of which 16β-[18F]-fluoro-5α-dihydrotestosterone was selected for clinical evaluation (1). Dihydrotestosterone is the predominant form of testosterone in the prostate gland. Biodistribution studies in rats and baboons showed prostate-to-blood activity concentration ratios up to 7:1, and androgen receptor binding. The activity of FDHT in the region of the prostate peaked at 30-90 minutes post injection. At 60 minutes there was a high ratio of prostatic activity to soft tissue, blood and bone (>6:1, >3.5:1 and >7:1 respectively) (2). Uptake decreases after the administration of cold testosterone. However, time course studies have not been conducted in relation to treatment and response. A noninvasive method for measuring changes in the androgen receptor (AR) in metastatic prostate cancer may be particularly important for assessing the effects of drugs that act through or directly on the androgen receptor. The androgen receptor is of particular importance in advanced prostate cancer. The AR axis remains functional even in the androgen-independent state by a variety of mechanisms, including mutation, overexpression, and ligand-independent activation, among others (3-10). Scher et al. have shown a positive [18F]FDHT signal in at least some of the metastases in about 85% of patients with castrate resistant metastasized prostate cancer (11).

Accurate quantification of the [18F]FDHT signal is important beyond visual image interpretation. For quantification of PET tracers, non-linear regression analysis is the gold standard. However, its complexity makes it unsuitable for application in daily clinical practice; moreover, it is not compatible with the whole body acquisitions typically required in patients with metastasized disease. Simplified measures applicable in whole body settings can and should be validated versus the reference technique. Perfusion related parameters are often important in pharmacokinetic modeling. Sofar, we have used 15O-water PET to measure these variables. However, [15O]-water PET requires an on-site cyclotron, and this is not available in the majority of hospitals. Alternatively, DCE-MRI is a clinically available, and it measures perfusion-related parameters as well. However, it needs to be shown how these DCE-MRI parameters correlate with [15O]-water PET. We expect that, upon validation, incorporation of DCE-MRI will provide an even more comprehensive multiparametric quantitative image since this adds information on permeability and perfusion and with higher spatial resolution than is feasible with PET.
Taken together, a profound understanding of the [18F]FDHT pharmacokinetics could lead to an optimization of the [18F]FDHT PET diagnostic potential; integration of DCE MRI and PET parameters would allow for a clinically feasible method with PET-MRI. This is essential to improve the quality of the imaging research towards personalized therapy strategies for prostate cancer patients.

Objective: The aims of the present study are to create a tracer kinetic model for quantification of [18F]FDHT, to simultaneously validate a simplified quantitative method, and to investigate the concordance of MRI- and PET-based perfusion related parameters.

Study design: a monocenter, prospective observational study in 10 patients with

metastasized castrate resistant prostate cancer. Dihydrotestosterone uptake [18F]FDHT,

perfusion ([15O]-water), and DCE-MRI parameters will be measured quantitatively. Accuracy of

blood and plasma activity concentration, plasma metabolite measurements derived from

arterial and venous samples as well as the reliability of using Image Derived Input Functions

(IDIF) for quantification of [18F]FDHT kinetics will be tested. Dynamic PET and MRI scanning will

be performed using 2 tracers for PET ([15O]-water and [18F]FDHT) and 1 contrast agent for MRI

(Gadovist)

Study population: Patients with metastasized castrate resistant prostate carcinoma.

Intervention: A 10 min PET study after intravenous (iv) administration of [15O]-water,

followed by a second 30 min dynamic PET study directly after [18F]FDHT administration, and a

30 min skull base-mid thigh half body acquisition. Analysis of arterial and venous samples to

ensure that arterial and venous samples provide the same information for calibrating and

correcting input functions for use of [18F]FDHT kinetic quantification. The DCE-MRI protocol

consist of a fast T1-weighted MRI sequence (duration ~5 sec) which is repeated for about 6

minutes while the contrast agent is injected intravenously via an injection pump. Prior to the

dynamic scan, a series of pre-scans are acquired, which are needed to calculate the intrinsic T1

relaxation time of the imaged tissue. These scans allow the absolute quantification of the

contrast agent concentration in tissue.

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Study objective

Taken together, a profound understanding of the [18F]FDHT pharmacokinetics could lead to an optimization of the [18F]FDHT PET diagnostic potential; integration of DCE MRI and PET parameters would allow for a clinically feasible method with PET-MRI. This is es-sential to improve the quality of the imaging research towards personalized therapy strategies for prostate cancer patients.

Study design

We expect to complete the patient inclusion in 4 months. Data analysis and document writing will require 4 months

Intervention

A 10 min PET study after intravenous (iv) administration of [15O]-water, followed by a second 30 min dynamic PET study directly after [18F]FDHT administration, and a 30 min skull base-mid thigh half body acquisition. Analysis of arterial and venous samples to ensure that arterial and venous samples provide the same information for calibrating and correcting input functions for use of [18F]FDHT kinetic quantification. The DCE-MRI proto-col consist of a fast T1-weighted MRI sequence (duration ~5 sec) which is repeated for about 6 minutes while the contrast agent is injected intravenously via an injection pump. Prior to the dynamic scan, a series of pre-scans are acquired, which are needed to calculate the intrinsic T1 relaxation time of the imaged tissue. These scans allow the absolute quanti-fication of the contrast agent concentration in tissue.

Contacts

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Eligibility criteria

Inclusion criteria

- Patients with mCRPC eligible for the GAP2-FDHT study

- Written informed consent

- Patients able to remain supine for 70 minutes

Exclusion criteria

- Claustrophobia

- Multiple malignancies

- Use of anticoagulantia

- Renal failure (GFR <30ml/min/1,73m2)

- Known hypersensitivity to Gadovist

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	02-06-2014

Enrollment:	10
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL4364
NTR-old	NTR4504
Other	2014-001600-21 EUdraCT : 49008 ABR

Study results