Measuring c-Abl levels in Parkinson's Disease: A first in human PET study using [18F]FB610

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Ethical review	Approved WMO
Status	Pending
Health condition type	Movement disorders (incl parkinsonism)
Study type	Observational invasive

Summary

ID

NL-OMON51436

Source
ToetsingOnline

Brief title
[18F]FB610 PET in PD

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's disease

Research involving
Human

Sponsors and support

Primary sponsor: 1st Biotherapeutics Inc.
Source(s) of monetary or material Support: 1st biotherapeutics inc.

Intervention

Keyword: c-Abl, disease, Parkinson's, PET

Outcome measures

Primary outcome

The main study parameters are the [18F]FB610 binding as a measure of c-Abl in PD patients and healthy volunteers, to assess the radiation dose and assess its safety, and to identify the most suitable tracer kinetic method for quantification of [18F]FB610 binding.

Secondary outcome

Secondary study parameters include the difference between binding of the radioligand [18F]FB610 in PD patients and healthy volunteers to determine whether c-Abl expression may be increased in PD patients.

Study description

Background summary

Parkinson's disease is the second most common neurodegenerative disease. With the new radiotracer [18F]FB610, the levels of the non-receptor tyrosine kinsae enzym c-Abl can be measured. c-Abl activation plays a role in alfa-synuclein accumulation and parkin inactivation, which lead to accumulation of pathological substrates of parkin. These processess lead to neurodegeneration in Parkinson*s disease. In this study we investigate the safety and dosage of this new radiotracer. Additionally, we aim to investigate whether this tracer can differentiate individuals with Parkinson's disease from healthy control subjects. In the future, this tracer could help identify patients who are eligbile for medical trials with c-Abl inhibitors.

Study objective

The primary objectives of this study are to assess the safety and estimate the radiation dose of the radioligand [18F]FB610, and to assess the optimal kinetic model for quantification of the tracer uptake. Secondary objectives are to

determine whether binding of radioligand [18F]FB610 can differentiate PD patients and healthy volunteers and to assess the potential of [18F]FB610 for patient selection for medical trials with c-Abl inhibitors.

Study design

This is an observational cross-sectional study. All subjects will undergo a 90 minute [18F]FB610 PET scan after injection of [18F]FB610 with continuous arterial blood sampling, which is necessary for kinetic modelling. The dose of [18F]FB610 will be 185 MBq.

Study burden and risks

In total there will be three visits at Amsterdam UMC: a first (screening) visit, an MRI scan and a PET scan. Some participants with PD will need an extra visit for a DAT-SPECT. During the screening study visit, the medical history will be recorded, a neurological examination will be performed, questionnaires and cognitive tests will be administered, and blood samples will be taken. There are no risks associated with MRI acquisition after MRI safety screening. The risks associated with PET scanning are limited, but the subjects will have radiation burden, which will be no more than 10 mSv. During the PET scan arterial blood samples will be taken, with a total of approximately 224 ml blood. In PD patients and in healthy volunteers this is not associated with risks. Insertion of arterial catheter can be painful. No immediate benefits for the subjects are to be expected from participation in this study. However, an indirect effect in the future is plausible for PD subjects, since more knowledge about the pathophysiological mechanisms of the disease may lead to improvement in therapy.

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

- Participant understands the study procedures in the informed consent form and is willing and able to comply with the study prescriptions
- Signed informed consent form
- Diagnosis of PD according to the Movement Disorder Society (MDS) clinical diagnostic criteria (applicable to participants with Parkinson's Disease)
- Abnormal DAT-SPECT (applicable to participants with Parkinson's Disease)
- Age 40 years or older
- Medically healthy with no abnormalities at short neurological and physical examination (applicable to healthy volunteers)

Exclusion criteria

- Inability to undergo MRI, e.g. metal objects in or around the body, claustrophobia or inability to lie still in the scanner
- Inability to undergo PET-CT with administration of radioligand [18F]FB610, including inability to lie still for 90 minutes.
- (History of) other relevant neurological disease
- (History of) malignancy
- Known significant cardiac disease
- Relevant history of severe drug allergy or hypersensitivity
- Inadequate renal function: creatinine clearance <60 ml/min
- Liver dysfunction: in male subjects ALAT >45 U/L and ASAT >35 U/L, in female subjects ALAT >34 U/L and ASAT>31 U/L
- Loss or donation of blood over 500 mL within four months prior to study visits
- In male subjects Hb < 8.0 g/dL, in female subjects Hb < 7.0 g/dL
- Pregnancy or breast feeding
- Medications that, in the opinion of the PI or designee, may interfere with

the study, such as benzodiazepines. It is allowed for PD patients to use dopaminergic medication.
- Exposure to previous radiation leading to an annual cumulative dose of more than 10 mSV if participating in this protocol

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:	Pending
Start date (anticipated):	01-10-2024
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	[18F]FB610
Generic name:	[18F]FB610

Ethics review

Approved WMO

Date:	26-10-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	14-02-2023
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	EUCTR2022-002228-11-NL
CCMO	NL81730.029.22