Validating in vivo quantification of tau with [18F]AV-1451 PET

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This protocol is a follow-up of a previously submitted protocol (Evaluation of [18F]AV-1451 kinetic modelling in patients with Alzheimer*s Disease and healthy controls, protocol nr. 2014.519), in which the optimal (simplified) kinetic model for [18F...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Encephalopathies
Study type	Observational invasive

Summary

ID

NL-OMON47001

Source
ToetsingOnline

Brief title
TRT AV-1451

Condition

- Encephalopathies
- Dementia and amnestic conditions

Synonym
Alzheimer's Disease, dementia

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: ZonMw,Eli Lilly

Intervention

Keyword: Alzheimer's Disease, kinetic modelling, PET, Tau

Outcome measures

Primary outcome

The main outcome is the test-retest variability of the previously defined

simplified tracer kinetic model to quantify specific binding of [18F]AV-1451.

Secondary outcome

not applicable

Study description

Background summary

Alzheimer*s disease (AD) is the most common cause of dementia in the elderly. Current biomarkers frequently used to probe AD pathology encompass markers of amyloid pathology. However, the other core pathological component of AD, tau pathology, is key to take into account when studying AD. First, A* plaques are only moderately correlated with cognition, while the severity of cognitive impairment is highly associated with the burden of neocortical neurofibrillary tangles (NFTs) with hyperphosporylated tau. Second, several studies have suggested that tau * and not A* * is the first neuropathological sign of AD. Finally, approximately a quarter of cognitively normal subjects show abnormal neurodegenerative markers while amyloid PET and/or CSF are normal. These subjects progress frequently to MCI of dementia, suggesting a different underlying pathology, such as tau.
Tau pathology can now be studied in-vivo with the PET tracer [18F]AV-1451. Binding of this tracer co-localizes with NFTs, but not with amyloid plaques, and there is increased [18F]AV-1451 uptake in AD patients compared to controls. As such, [18F]AV-1451 has great potential as a prognostic marker in preclinical and clinical stages of AD. The overall aim of this proposal is to fully develop [18F]AV-1451 as a tau marker that can be used for accurate and early diagnosis of AD, for prognostic purposes. This requires validation of previously defined (simplified) kinetic models for [18F]AV-1451 and assessing test-retest variability of these measures.

Study objective

This protocol is a follow-up of a previously submitted protocol (Evaluation of [18F]AV-1451 kinetic modelling in patients with Alzheimer*s Disease and healthy controls, protocol nr. 2014.519), in which the optimal (simplified) kinetic model for [18F]AV-1451 will be developed. We aim to validate this model, by assessing test-retest variability. The objectives of this project are:
1) To assess test-retest variability of the previously defined tracer kinetic model to quantify specific binding of [18F]AV-1451

Study design

This study includes 7 healthy elderly controls and 8 patients with AD or MCI due to AD. [18F]AV-1451 is injected intravenously and immediately following injection, a dynamic 60 minute PET scan will be performed. An additional dynamic 50 minute PET scan will occur approximately 80 minutes following injection. Procedures are repeated after 1 week.

Study burden and risks

1. Radiation exposure
Subjects receive 2 PET-scans with [18F]AV-1451. Before every scan, a low dose CT scan is made. The radiation exposure is 12,4 mSv each year. The total amount of radiation for this study is 12,4 mSv.
2. Idiosyncratic reaction to the tracer
The following adverse effects have been reported: headache, diarrhea, dysguesia
3. Placement of the intra-venous catheter
There is a very small risk of infection and bleeding associated with catheters.
4. Discomfort during scanning
It may be uncomfortable to lie motionless in the PET scanner. Subjects may expierence myalgia.

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

Healthy volunteers:
1. At least 50 years of age;
2. Have no evidence of cognitive impairment as indicated by a cognitive neurologist;
3. Subjects, who in the opinion of the principal investigator, can tolerate the [18F]AV1451 PET scan procedures.;MCI due to AD subjects:
1. At least 50 years of age;
2. Have a clinical diagnosis of MCI (Albert, 2011)
3. Have positive A* biomarkers on PET and/or CSF
4. Have a Mini Mental State Examination (MSSE) of 18 or higher;
5. Subjects, who in the opinion of the principal investigator, can tolerate the [18F]AV1451 PET scan procedures.;AD patients:
1. At least 50 years of age;
2. Have a clinical diagnosis of probable AD (McKhann, 2011)
3. Have a Mini Mental State Examination (MMSE) of 18 or higher;
4. Subjects, who in the opinion of the principal investigator, can tolerate the [18F]AV-1451 PET scan procedures.

Exclusion criteria

1. Has contra indications for MRI scanning and therefore can not receive brain MRI
2. Has evidence of structural abnormalities such as major stroke or mass on MRI that is likely to interfere with interpretation of a PET scan;
3. Has a history of severe traumatic brain injury (TBI);
4. Is a female of childbearing potential who is not surgically sterile, not refraining from sexual activity or not using reliable methods of contraception for up to 24 hours after scanning procedures. Females of childbearing potential must not be pregnant or breastfeeding at screening.

5. Has a relevant history of severe drug allergy or hypersensitivity (relevant severe drug allergies should be determined by the Principal Investigator or Co-Principal Investigator, and any questions about a subject*s eligibility can be directed to Avid Radiopharmaceuticals Inc.);
6. Has ever participated in an experimental study with a tau or amyloid targeting agent, unless it can be documented that the subject received only placebo during the course of the trial.
7. Has been injected with a previously administered radiopharmaceutical within 6 terminal half-lives OR when total yearly radiation exposure exceeds 10 mSv.

Study design

Design

Study phase:	2
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-03-2017
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[18F]AV-1451
Generic name:	[18F]AV-1451

Ethics review

Approved WMO

Date:	15-02-2016

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-11-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-02-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-03-2018
Application type:	Amendment
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	EUCTR2015-004230-10-NL
CCMO	NL54572.029.15