Tau Imaging in Tauopathies; Alzheimer's disease and Non-AD dementias

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To 1) clinically validate the novel PET-tracer [18F]AV1451 for tau pathology as a diagnostic and prognostic marker in tauopathies, 2) to examine the (change in) (regional) binding of [18F]AV1451 across tauopathies, and the relationships between (...

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

Summary

ID

NL-OMON50757

Source
ToetsingOnline

Brief title
TITAN

Condition

- Encephalopathies
- Dementia and amnestic conditions

Synonym
dementia, Tauopathy

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, PET, Tau, Tauopathies

Outcome measures

Primary outcome

(Change in) the amount and distribution of specific [18F]AV1451 binding in DLB

and AD

Secondary outcome

- Neuropsychological performance (over time);

- DLB specific questionnaires

- Gray matter volumes on MRI (over time);

- CSF protein levels (over time);

- Amyloid-beta PET tracer binding (when available).

- FDG tracer binding

- EEG measurements

Study description

Background summary

The most common cause of dementia, Alzheimer*s disease, is pathologically characterized by aggregated amyloid-beta and hyperphosphorylated tau proteins. Several other neurodegenerative diseases that can underlie dementia also present with tau pathology such as Dementia with lewy bodies.

The success of amyloid PET-tracers such as Pittsburgh compound B, [18F]Florbetapir, [18F]Flutemetamol and [18F]Florbetaben, prompted the search for a tau-specific PET-tracer and has led to the recent introduction of the tau tracer [18F]AV1451. The possibility to visualize and quantify tau pathology in vivo has the potential to greatly facilitate research on tau pathology inducing AD dementia and other non-AD dementias. For example, assessment of regional uptake patterns of tau, which are distinct across tauopathies, may improve

diagnostic accuracy and may help to identify tauopathies in an early stage. Second, in contrast to Amyloid-beta, the spread of tau-pathology has been shown to be tightly correlated with neurodegeneration and cognitive deterioration, indicating that (longitudinal) [18F]AV1451 binding may help to provide insight into staging of tau pathology and serve as a prognostic marker for disease progression. Finally, PET-imaging with [18F]AV1451 would contribute to the development of new tau-targeted treatments by providing a means to identify applicable patients for clinical trials, and by offering an in-vivo surrogate marker of tau pathology.

Study objective

To 1) clinically validate the novel PET-tracer [18F]AV1451 for tau pathology as a diagnostic and prognostic marker in tauopathies, 2) to examine the (change in) (regional) binding of [18F]AV1451 across tauopathies, and the relationships between (change in) tracer binding, neurodegeneration and symptoms, and 3) to explore the predictive value of [18F]AV1451 binding for change over time in neuropsychological performance.

Study design

The present study is a longitudinal, observational study. The diagnostic intervention is a PET scan using [18F]AV1451 for in vivo visualisation and quantification of tau pathology in the human brain. This project builds on a tracer kinetic model previously developed in another project and aims to implement [18F]AV1451 in a clinical setting.

Eligible participants will be recruited from the VUmc, Erasmus MC and the UMCU. For the VUmc, participants will be recruited from the Amsterdam dementia cohort, consisting of patients of the Alzheimer center of the VU medical center. These patients have all been screened according to the VUmc standardized dementia screening protocol including physical examination, medical history, neuropsychological testing, MRI and laboratory measurements. In addition, lumbar puncture is performed to obtain measurements of Amyloid-beta, and tau in CSF for all patients, unless contraindicated. For the Erasmus medical center, patients recruitment will rely on the study titled *Early brain changes in frontotemporal dementia* (also known as the FTD-risC study; protocol number: MEC-2009-409). For the University medical center Utrecht, patients are primarily recruited from the study titled *Biomarkers in body fluids of patients with neurodegenerative disorders* (also known as the Parelsnoer study; protocol number 09-211).

After signing informed consent and screening procedures (physical examination and if necessary MRI brain), paticipants will be invited to undergo a dynamic [18F]AV1451 PET scan on a clinical PET-CT scanner and for DLB patients a static [18F]-FDGPET scan at the VU Medical Center on a PET-CT scanner.

All paticipants will receive annual clinical follow-up that includes neuropsychological examination according to the same standardized protocols as performed at baseline examination.

MCI/AD subjects will, >2 years after baseline [18F]AV1451, be asked to undergo a second [18F]AV1451 PET scan. Additionally, they will be invited to undergo a lumbar puncture at follow up.

Intervention

Name of compound : 18F-AV-1451(also known as [F-18]T807) Dose: 240 MBq (6.5mCi) Route of Administration: Intravenous (IV) bolus

Study burden and risks

Risks associated with participation in this study are related to 1) radiation exposure; 2) idiosyncratic reaction to the tracer ;
3) placement of the arterial and intra-venous catheter; 4) discomfort during PET scanning; 5) chance findings, and 6) small chance of headache after lumbar puncture.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria: , - At least 35 years of age
- Subjects must, in the opinion of the principal investigator/attending neurologist, be able to tolerate the [18F]AV1451 PET scan procedures and be competent to make a well informed decision to participate in this study.., Additional inclusion criteria per diagnostic group:, For probable AD dementia patients;
- A diagnosis of probable AD with at least intermediate likelihood according to recently proposed NIA-AA criteria27. This will be determined using PET and/or CSF evidence of A* deposition., For *MCI due to AD* patients;
- Patients must meet clinical criteria for MCI25, and;
- present with positive A* biomarkers on PET and/or CSF., For DLB patients;
- At least 50 years of age
- Patients must be included in the DEvELOP (protocol number 15/548)
- Subjects must, in the opinion of the principal investigator/attending neurologist, be able to tolerate the [18F] FDG PET scan procedures, For controls;
- No objective evidence of cognitive impairment as assessed by a multidisciplinary specialist team;
- normal MRI;

Exclusion criteria

No MRI available or possible
Abnormalities on MRI which may interfere with PET image assessment:
Is or may become pregnant in the first 24h after the PET scan
Relevant history of drug allergy or hypersensitivity
Has ever recieved a tau and/or amyloid-beta targetting agent
Has been injected with a previously administered radiopharmaceutical within 6 terminal half-lives OR the total yearly radiation exposure exceeds 10 mSv;
Has a history of moderate or severe traumatic brain injury (TBI).

Study design

Design

Study phase:	2
Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-12-2016
Enrollment:	200
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[18F]AV1451
Generic name:	[18F]AV1451
Product type:	Medicine
Brand name:	[18F]FDG
Generic name:	[18F]FDG

Ethics review

Approved WMO Date:	20-01-2016
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:	28-12-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-01-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-04-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-04-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-08-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-03-2018

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-12-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-11-2020

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	EUCTR2015-005604-29-NL
CCMO	NL55206.029.15