Longitudinal imaging of tau accumulation in the preclinical stages of AD

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Primary objective:To explore the natural time course of specific [18F]AV-1451 binding in patients with subjective cognitive decline after two and four year follow upa. To compare rate of change in [18F]AV-1451 binding according to baseline amyloid...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Dementia and amnestic conditions
Study type	Observational invasive

Summary

ID

NL-OMON50737

Source
ToetsingOnline

Brief title
LUNAR

Condition

- Dementia and amnestic conditions

Synonym
first symptoms of Alzheimer's disease, preclinical Alzheimer's disease

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: ZonMW,Eli Lilly,Janssen-Cilag

Intervention

Keyword: Alzheimer's Disease, PET, Subjective Cognitive Decline, Tau

Outcome measures

Primary outcome

The change of [18F]AV-1451 binding in time

Secondary outcome

1. Amyloid positivity, as measured by [18F]Florbetapir PET scan

2. Cognitive fucntioning in neuropsychological testing

3. Baseline grey matter atrophy on MRI

4. Baseline CSF measures of amyloid-beta 1-42, total tau, phosphorylated tau

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, Aβ 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 Aβ - 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.
Patients with subjective cognitive decline (SCD) are those who present with cognitive complaints, but perform normally after thorough investigation. Longitudinal studies show SCD is a risk factor for future cognitive decline. This means a cohort of patients with subjective complaints may be enriched for incipient AD. Therefore, these subjects form an ideal population to study the incidence and time course of changes in AD hallmark pathologies.
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. Studying tau pathology in a longitudinal fashion offers a new perspective on its prevalence, distribution and natural time course. This is relevant not only for a better understanding of AD pathogenesis, but [18F]AV-1451 has also potential as a surrogate outcome measure in clinical trials tailored to reduce tau burden.

Study objective

Primary objective:
To explore the natural time course of specific [18F]AV-1451 binding in patients with subjective cognitive decline after two and four year follow up
a. To compare rate of change in [18F]AV-1451 binding according to baseline amyloid status
b. To compare rate of change in [18F]AV-1451 binding according to clinical progression over time

Secondary objectives:
1. To investigate the relationship between tau pathology, as measured with [18F]AV-1451, and amyloid load, as measured with [18F]Florbetapir
2. To investigate the correlation between [18F]AV-1451 binding and neuropsychological performance
3. To investigate the correlation between [18F]AV-1451 binding and grey matter volume on MRI
4. To investigate the correlation between [18F]AV-1451 binding and CSF measures of amyloid-beta 1-42, total tau and phosphorylated tau

Study design

This is a prospective, longitudinal observational study

Study burden and risks

1. Radiation exposure
Subjects receive 5 PET-scans: on baseline 1 [18F]AV-1451 scan, after 2 and 4 year follow up [18F]AV-1451 and [18F]Florbetapir scan. Before every scan, a low dose CT scan is made. The radiation exposure is 13.6 mSv each year.
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 intravenous 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

- Clinically diagnosed with 'subjective cognitive decline' after the standardized dementia screening performed at the VUmc Alzheimer Center
- At least 50 years of age
- Enrollment in the FIAD cohort (protocol nr 13-256)
- Have received or will receive a [18F]Florbetapir PET scan 90 days before or after the [18F]AV-1451 PET scan

Exclusion criteria

- Has contraindications for MRI scanning and therefore has not received brain MRI

- Has evidence for structural abnormalities such as major stroke or mass on MRI that is likely to interfere with interpretation of PET scan
- Is a woman of childbearing potential who is not surgically sterile, not refraining from sexual activity or not using reliable methods for contraception. Women of childbearing potential must not be pregnant or breast feeding at screening.
- Has a relevant history of severe drug allergy or hypersensitivity. Relevant severe drug allergies should be determined by the Principal Investigator or Co-Prinicipal Investigator, and any questions about a subject's eligibility can be directed to Avid Radiopharmaceuticals Inc.;
- 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;
- Has been injected with a previously administered radiopharmaceutical within 6 terminal half-lives OR when total yearly radiation exposure exceeds 10 mSv
- Has a history of severe traumatic brain injury (TBI)

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-03-2016
Enrollment:	50
Type:	Actual

Medical products/devices used

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

Product type:	Medicine
Brand name:	AMYVID
Generic name:	Florbetapir

Ethics review

Approved WMO Date:	06-10-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-05-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-12-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-01-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-06-2018

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-12-2019
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:	07-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-01-2021
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	EUCTR2015-003705-42-NL
CCMO	NL54520.029.15