The clinical prognostic value of amyloid imaging with [18F]AV-45 in a subjects with subjective complaints

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neurological disorders NEC
Study type	Interventional

Summary

ID

NL-OMON47767

Source
ToetsingOnline

Brief title
Clinical prognostic value [18F]AV-45

Condition

- Neurological disorders NEC
- Dementia and amnestic conditions

Synonym
Alzheimer's Disease, dementia of the Alzheimer type

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Gieskes-Strijbis Fonds en AVID

Radiopharmaceuticals

Intervention

Keyword: 18F-Florbetapir (AV-45), Alzheimer's disease, □-amyloid, Positron Emission Tomography (PET)

Outcome measures

Primary outcome

The outcome measure, amyloid deposition (both visual and quantitative), acquired with [18F]AV-45 PET scans in a memory clinic patient cohort. Quantification is performed with optimized kinetic models acquired in another research Florbetapir protocol (kinetic modelling of 18 F labeled amyloid tracers).

Secondary outcome

Secondary study parameters are the concordance of [18F]AV-45 PET with MRI markers (MTA) and with CSF markers (A* 1-42, total tau and p-tau 181) will be assessed by binary rating (e.g. *normal* or *abnormal*) and amyloid tracer quantification for each of these measures. Furthermore, at baseline dementia severity and neuropsychological measures will be obtained to allow analysis of associations with continuous measures of cognitive impairment to determine the prognostic value of [18F]AV-45 PET.

Study description

Background summary

Neuropathologically, Alzheimer*s Disease (AD) is characterized by amyloid plaques and neurofibrillary tangles. Development of the positron emission tomography (PET) tracer [11C]Pittsburgh compound-B ([11C]PIB) has for the first

time enabled the visualization of amyloid-beta (A*) in vivo, and evidence shows high sensitivity and specificity in separating AD from controls. Despite encouraging results, the short half-life (20 minutes) of the 11C isotope limits the utility of 11C-PIB as a tool for community based diagnostic screening and therapeutic evaluation.
In contrast, [18F]AV-45 is a novel amyloid binding agent (Zhang et al. 2005; Zhang et al. 2006) labelled with 18F. Since 18F has a radioactive half-life of 110 minutes, regional preparation and shipping of doses is possible, thereby reducing the cost and increasing the number of potential imaging centers. In addition, [18F]AV-45 is one of the first tracers fulfilling FDA requirements of postmortem verification and correlation of the specific binding and as such will probably be the first tracer to be used in drug development programs.

Study objective

Determination of possible Alzheimer pathology in the brain and to follow-up participants over time (by means of another research protocol). In addition, its [18F]-label with a half-life of 110 minutes will enable use in hospitals without an on-site cyclotron, greatly enhancing its clinical applicability. The present study is designed to evaluate tracer kinetics of [18F]AV-45 and to investigate its clinical diagnostic and prognostic value in early cognitive and memory complaints.

Study design

The clinical prognostic study exists of one PET scan. This study includes 250 cognitively normal subjects. Subjects will undergo a PET-scan after intravenous administration of the [18F]AV-45 tracer twice, over the course of 2 years. Analysis will be perfomed to investigate whether there is significant amyloid deposition in the brain.

Intervention

Intervention with a diagnostic medicine.

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 an intra-venous and intra-arterial (only in kinetische modeling study including 15 AD patients and 15 controls) catheter; 4) discomfort during scanning, and 5) blood sampling.
1) Administration of 185 MBq [18F]Florbetapir will result in a whole body effective dose of 3.5 mSv according to the GE-067study (see IB Edition 6/ March 2012). For comparison, the natural background radiation dose in the Netherlands gives an annual dose of 2 - 2.5 mSv. Thus, the total radiation exposure of the

total PET procedure is within an acceptable range of a yearly (unnatural) radiation exposure with a maximum of 10 mSv. In case of previous exposure to radioactivity, subjects will be eligible if the yearly cumulative dose due to exposure to radiation remains below 10 mSv.
2) Idiosyncratic reaction to the tracer The injected mass of [18F]Flutemetamol PET used in this study is negligible. [18F]Flutemetamol PET is a radiotracer that have been used in humans. Side effects have never been reported at the tracer doses used in PET studies. A physician will be available during each injection of the radiotracer.
3) Intravenous cannulation There is a very small risk of infection and bleeding associated with intravenous catheters, which are prevented by proper techniques.
4) Discomfort during scanning It may be uncomfortable to lie motionless in the cameras (both PET and MRI) and it may cause some subjects to feel anxious. Subjects will be made acquainted with the surroundings beforehand. Our staff will be available to provide support, reduce anxiety, optimise the comfort of the subject and remove the subject from the scanner if requested.

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

- age >45
- Written informed consent
- Weight >50 kg , - Able to tolerate 70-minute scanning
- No objective cognitive impairment (i.e. no diagnosis of dementia, mild cognitive impairment, psychiatric or neurological disorder explaining cognitive complaints).
- MMSE ><= 18

Exclusion criteria

Patients who
1. Have a current a major psychiatric disorder, such as psychosis, schizophrenia, severe personality disorder or depression with vital signs, abuse of alcohol or other substances. Or patients who have a neurological disorder, such as Parkinson's disease, symptomatic stroke, mental retardation.
2. Are women of childbearing potential who are not surgically sterile, not refraining from sexual activity or not using reliable methods of contraception. Women of childbearing potential must not be pregnant (negative urine *-hCG at the time of screening and negative urine *-hCG on the day of imaging) or breast feeding at screening. Women must avoid becoming pregnant, and must agree to refrain from sexual activity or to use reliable contraceptive methods such as prescribed birth control or IUD for 24 hours following administration of florbetapir (18F);
3. Have 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. If a subject has a history of severe drug allergies, it may be dangerous for them to participate in a study with a novel compound);
4. Have ever participated in an experimental study with an amyloid targeting agent (e.g. anti-amyloid immunotherapy, *-secretase or *-secretase inhibitor) unless it can be documented that the subject received no investigational medication (yet) or only placebo during the course of the trial;
5. Have had a radiopharmaceutical imaging or treatment procedure within 7 days prior to the study imaging session.

Study design

Design

Study phase:	4
Study type:	Interventional
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):	24-11-2014
Enrollment:	280
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Amyvid (AV-45)
Generic name:	[18F]Florbetapir

Ethics review

Approved WMO Date:	11-02-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	04-03-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	23-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-05-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-06-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-07-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-11-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-04-2019
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	EUCTR2012-001599-12-NL
CCMO	NL39189.029.13