The Dutch CSF and PET Biomarker Concordance of Alzheimer*s Disease pathology study

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

Summary

ID

NL-OMON38876

Source
ToetsingOnline

Brief title
Dutch Study on CSF and PET Biomarker Concordance

Condition

- Neurological disorders NEC

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: Farmaceutisch bedrijf MERCK,MERCK

Intervention

Keyword: Alzheimer's Disease, amyloid-beta, cerebrospinal fluid (CSF), Positron Emission Tomography (PET)

Outcome measures

Primary outcome

The main outcome measures are the concordance (diagnostic agreement of reported brain amyloid status) between [18F]Flutemetamol PET and a range of CSF tau:abeta1-42 ratio values that meet independently-defined minimum criteria for a binary classifier of AD (sensitivity * 0.8, specificity >0.6). This range of CSF threshold values will be determined in a separate study currently underway, using additional independently collected CSF samples. Secondary outcome is the concordance between PET amyloid status and routine CSF abeta 1-42, total tau and p-tau 181 values.

Secondary outcome

Secondary outcome is the concordance between PET amyloid status and routine CSF abeta 1-42, total tau and p-tau 181 values.

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.
However, [11C]PIB-PET can only be used where an on-site cyclotron is available for production, hampering its widespread implementation. [18F]-tracers, which do not require on-site production are therefore more suitable to be used by many more centers and enable studying the discriminatory value in the clinical

setting.
In parallel to amyloid PET tracers, CSF-based biomarkers reflecting abnormalities of amyloid processing in AD brain have been developed and refined for clinical use. Both CSF and PET-based biomarkers are expected to prove useful in defining patient populations appropriate for treatment with amyloid-targeting disease modifying therapy. However, the degree of concordance between specific PET- and CSF-based amyloid diagnostic measurements as proxy for AD pathology is not well established.

Study objective

In the present study, we aim to estimate concordance between two biomarkers developed to interrogate the presence of brain amyloid deposition. This includes a new amyloid PET-tracer, [18F]Flutemetamol, and a CSF biomarker
The objective of the current study will be to compare [18F]Flutemetamol PET imaging measures of brain amyloid to protein measurements in CSF.

Study design

Prospective, observational study

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 catheter; 4) discomfort during scanning; 5) lumbar puncture procedure risk.

1) Administration of 185 MBq [18F]Flutemetamol will result in a whole body effective dose of 4.1 mSv. 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 PET camera 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.

5) LP is performed routinely during screening at VUmc Alzheimer Center, unless patient is not willing to undergo LP or any contra-indications exist. The withdrawal of an extra 2 ml for this protocol is deemed not to cause extra discomfort

Contacts

Public
Vrije Universiteit Medisch Centrum

De Boelelaan 1118
Amsterdam 1007 MB
NL
Scientific
Vrije Universiteit Medisch Centrum

De Boelelaan 1118
Amsterdam 1007 MB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Each subject :
- must be * 50 to * 85 years of age;
- is seen at the memory clinic of the VUmc Alzheimer Center upon referral of another clinician and follows the routine screening procedure;
- must have results of routine clinical laboratory tests including a complete blood count (CBC) a physical examination, vital signs within normal limits or clinically acceptable to the investigator within 60 days prior to enrollment;
- must have signed (the study specific)informed consent form, which covers the scope and nature of this agreement before screening assessments;
- must have given additional cerebrospinal fluid for this study and checked "Yes" to the following questions located on page 2 of the general informed consent form of the Alzheimer Center; 'I give my consent for the storage and use of my coded medical information' and 'I give my consent for the collection, storage and provision of coded samples of my cerebrospinal fluid to the Alzheimer*s Center Biobank and the String of Pearls Initiative Parelsnoer Initiatief for the purposes outlined in the information'.;- The maximum time frame between LP and PET scanning is 6 months

Exclusion criteria

Patients who
- are considered medically unstable;
- require additional laboratory tests or workup between enrolment and completion of the PET scan;
- have a clinically significant infectious disease, including Acquired Immunodeficiency Syndrome (AIDS) or Human Immunodeficiency Virus (HIV) infection;
- are receiving any investigational medications, or have participated in a trial with investigational medications within the last 30 days prior to the PET scan;
- 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 he subject received only placebo during the course of the trial;
- have had a radiopharmaceutical imaging or treatment procedure within 7 days prior to the PET scan;
- are females of childbearing potential who are not surgically sterile, not refraining from sexual activity or not using reliable methods of contraception. Females of childbearing potential must not be pregnant (negative serum *-hCG at the time of screening and negative urine *-hCG on the day of imaging) or breast feeding at screening. Females 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 [18F]Flutemetamol;
- are claustrophobic;
- have abnormalities on MRI other than white matter changes or an incidental small lacunar lesion which may can affect Flutemetamol PET scan reading.

- have donated blood within 3 months before the scan day;

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-11-2013
Enrollment:	90
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[18F]Flutemetamol Injection
Generic name:	[18F]Flutemetamol

Ethics review

Approved WMO Date:	24-10-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-11-2013
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	EUCTR2013-003733-15-NL
CCMO	NL46225.029.13