AMYPAD Prognostic and Natural History Study (PNHS), an open label, prospective, multicentre, cohort study in individuals without dementia to evaluate the additional value of quantitative amyloid imaging in determining Alzheimer*s Disease (AD) dementia risk

Published: 25-06-2018
Last updated: 12-04-2024

The aim of this study is to evaluate the additional value of quantitative amyloid imaging analysis for modelling and assessing Alzheimer*s Disease (AD) dementia risk in individuals without dementia, compared to a range of existing cognitive, imaging...

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

Summary

ID

NL-OMON55776

Source
ToetsingOnline

Brief title
AMYPAD Prognostic and Natural History Study

Condition

- Neurological disorders NEC
- Dementia and amnestic conditions

Synonym

Alzheimer's disease, amyloidosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum
Source(s) of monetary or material Support: GE Healthcare Ltd ,Innovative Medicines Initiative Joint Undertaking (IMI JU),Janssen-Cilag,Piramal Imaging Ltd

Intervention

Keyword: alzheimer's disease, amyloid, dementia risk, PET

Outcome measures

Primary outcome

Primary Variables

1. Composite Centiloid, SUVR and/or BPND values measured from [18F]flutemetamol

or [18F]florbetaben PET images

2. Change from baseline in measures of cognitive status, daily functioning,

and/or MRI measures of brain atrophy

Secondary outcome

Secondary Variables:

1. Change from baseline in measures of cognitive status (e.g. RBANS Total Scale

Index Score)

2. Change from baseline in MRI measures of brain atrophy

3. Change from baseline in measures of daily functioning

4. Regional SUVR and/or BPND values at baseline

5. Change from baseline in Centiloid, SUVR and BPND values (global and/or

regional)

6. Baseline R1 values from dynamic scans

7. Change from baseline in R1 values from dynamic scans

8. Threshold values of Centiloid, SUVR and/or BPND for negative/positive

amyloid status that produce the greatest agreement with visual interpretation

by a trained nuclear physician or radiologist

9. Threshold values of Centiloid, SUVR and/or BPND for

negative/positive/grey-zone amyloid status that produce the highest accuracy

with respect to predicting cognitive decline (and/or brain atrophy as measured

by MRI)

Study description

Background summary

The Amyloid Imaging to Prevent Alzheimer*s Disease (AMYPAD) Prognostic and Natural History Study (PNHS) is planned as an open label, prospective, multicentre, cohort study linked to the European Prevention of Alzheimer*s Dementia (EPAD) Longitudinal Cohort Study (LCS). For the purpose of phenotyping and disease modelling, the EPAD LCS employs the concept of an Alzheimer*s Disease (AD) risk probability spectrum that comprises three main dimensions - research participant clinical outcomes (e.g. cognition), disease biomarkers, and traditional risk factors (genetic and environmental). With the incorporation of longitudinal change scores as relevant, these dimensions are used to estimate an individual*s overall predicted probability of AD-related decline in terms of a variety of outcomes.

AMYPAD PNHS is a natural history study that will evaluate how amyloid imaging might help improve the understanding of the natural course of AD. The study will assess amyloid positron emission tomography (PET) imaging as an additional and potentially relevant AD biomarker to complement the phenotyping and disease modelling efforts of parent cohorts (PC) such as EPAD LCS. As measured from [18F]flutemetamol and [18F]florbetaben PET images, brain amyloid load will be quantified at baseline and mean change in amyloid load over at least 12 months will be estimated. The ability to accurately estimate in vivo amyloid load could lead to a better understanding of disease evolution, earlier detection of the disease, and enable researchers to objectively monitor change in amyloid load to measure the impact of novel therapies.

Study objective

The aim of this study is to evaluate the additional value of quantitative amyloid imaging analysis for modelling and assessing Alzheimer*s Disease (AD) dementia risk in individuals without dementia, compared to a range of existing cognitive, imaging, laboratory and genetic biomarkers. Risk modelling will be performed to determine the optimal combination of quantitative amyloid imaging and other biomarker measures to determine placement of individuals on an AD risk probability spectrum.

Study design

The AMYPAD PNHS study is an observational study where an invasive measurement is performed (i.e. amyloid PET scan) in a sub-population of the participants of different parent cohorts (e.g. EPAD LCS/PreclinAD/EMIF-AD 90+/AMYPAD DPMS etc).

Eligible Parent Cohorts (PCs):

The main PC for AMYPAD PNHS is the EPAD LCS. Additional PCs can be added at the discretion of the Sponsor, as long as they fulfill the following criteria:

1. The PC recruits or has recruited non-demented participants of at least 50 years of age;
2. Participants in the PC have information available on each of the domains of the AD risk probability spectrum (clinical outcomes (including but not limited to cognition), disease biomarkers (including but not limited to CSF or MRI measures), and traditional risk factors (genetic and environmental));

Participants of AMYPAD PNHS will undergo a baseline amyloid PET scan and around 50% of those will get invited for a second follow-up amyloid PET scan at least 12 months after baseline. In case PCs do not acquire essential variables for primary analyses, AMYPAD PNHS can request for additional data collection (i.e. RBANS, MMSE, CDR, 3D T1 MRI, medication and changes to medical history) following appropriate informed consent.

Study burden and risks

Risks associated with participation in this study are related to:
- radiation exposure
- idiosyncratic reaction to the radiotracer injection
- placement of the intra-venous catheter
- discomfort during the PET scan
- incidental findings

Contacts

Public
Selecteer

De Boelelaan 1117
Amsterdam 1081 HV
NL
Scientific
Selecteer

De Boelelaan 1117
Amsterdam 1081 HV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Participants from Sponsor-approved parent cohorts who fulfill the following criteria:, 1. Current or former participants of a Sponsor-approved PC, not demented, and older than 50 years of age will be eligible if they provide separate written informed consent to participate in the AMYPAD PNHS., 2. Participants with a suitable baseline biomarker, cognitive and risk factor profile, as determined by the Selection and Feasibility Committee, based on an adaptive selection algorithm that aims to provide optimal representation of the probability spectrum for AD risk; OR participants that have been randomly selected to maintain a non-disclosure policy., 3. Participants who are assessed by the recruiting investigator to be physically fit to undergo PET scanning and able to tolerate the PET scanning procedure for at least the duration of a

static scan (20 minutes).

Exclusion criteria

Exclusion Criteria:
1. Participants in whom PET scanning or magnetic resonance imaging (MRI) are contraindicated.
2. Participants who are not able to complete the study procedures as judged by the investigator.
3. Participants who have known hypersensitivities to the active ingredients of [18F]flutemetamol and [18F]florbetaben, or the excipients for both products (listed in section 6.1 of the respective Summary of Product Characteristics [SPC]).
4. Women of childbearing potential who are pregnant, planning to become pregnant, lactating, or do not follow the contraceptive methods recommended by the Clinical Trial Facilitation Group.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-10-2018
Enrollment:	300
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	NeuraCeq
Generic name:	[18F]florbetaben

Product type:	Medicine
Brand name:	Vizamyl
Generic name:	[18F]flutemetamol

Ethics review

Approved WMO Date:	25-06-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-09-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-12-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-03-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-08-2020

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-05-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-06-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-10-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-01-2022
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	EUCTR2018-002277-22-NL
CCMO	NL66389.029.18

Study results

Date completed: 23-06-2022

Actual enrolment: 314

Summary results
Trial is onging in other countries