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Depletion of serum Amyloid P Component in Alzheimer's Disease

Submission date	Recruitment status	[X] Prospectively registered
02/05/2017	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
24/05/2017	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
06/03/2026	Nervous System Diseases	[X] Record updated in last year

Plain English summary of protocol

Current plain English summary as of 04/08/2021:

Background and study aims:

Alzheimer's disease (AD) is the most common cause of dementia, affecting around 30 million individuals worldwide. It is caused by the abnormal build-up of various proteins in the brain to form what are known as amyloid plaques. The plaques are toxic to brain cells, and eventually cause their death, leading to the gradual decline in day-to-day memory and other mental functions. Serum amyloid P component (SAP) is a normal protein that occurs in everyone. It is produced in the liver and travels via the blood stream to reach other organs including the brain. Although only very small amounts of SAP enter the brain, it binds to the abnormal proteins in the brains of patients with AD. It forms part of the amyloid plaques and prevents them from breaking down. Therefore, preventing SAP from binding amyloid plaques may lead to faster breakdown of the amyloid plaques and so delay the progression of Alzheimer's disease. There is also evidence that SAP directly damages brain cells and may contribute to the development of Alzheimer's disease. Removal of SAP may reduce this damage to brain cells. A new drug has been developed, called miridesap, which eliminates SAP almost completely from the blood and thereby stops SAP from reaching the brain. miridesap may also remove the SAP already present in the brain. This may reduce the brain damage caused by the disease. The aim of this study is to explore the safety, tolerability and potential effectiveness of miridesap in patients with mild AD.

Who can participate?

Patients over the age of 50 who have been diagnosed with mild AD.

What does the study involve?

Participants are randomly allocated to one of two groups. Those in the first group receive three injections per day of miridesap into their tummy for 12 months. Those in the second group receive three injections per day of a placebo (dummy drug) into their tummy for 12 months. At the start of the study, over the 12 months of treatment, and one month later, participants in both groups undergo brain scanning to look at the effects of the treatment, as well as having blood and cerebrospinal fluid (the fluid found in the brain and spinal cord) samples taken for testing and completing assessments of their memory.

What are the possible benefits and risks of participating?
It is not known whether taking part in this study will benefit participants; however, those who receive the miridesap may benefit from a reduced amount of SAP in the blood and removal of SAP from the brain throughout the period of treatment. There are no anticipated risks; however, as this is a study looking at a new experimental drug there is a potential that patients may experience side effects.

Where is the study run from?
University College London (UK)

When is study starting and how long is it expected to run for?
August 2015 to December 2024

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Catherine Ryan, c-ryan@ucl.ac.uk, catherine.ryan15@nhs.net

Previous plain English summary:
Background and study aims:
Alzheimer's disease (AD) is the most common cause of dementia, affecting around 30 million individuals worldwide. It is caused by the abnormal build-up of various proteins in the brain to form what are known as amyloid plaques. The plaques are toxic to brain cells, and eventually cause their death, leading to the gradual decline in day-to-day memory and other mental functions. Serum amyloid P component (SAP) is a normal protein that occurs in everyone. It is produced in the liver and travels via the blood stream to reach other organs including the brain. Although only very small amounts of SAP enter the brain, it binds to the abnormal proteins in the brains of patients with AD. It forms part of the amyloid plaques and prevents them from breaking down. Therefore, preventing SAP from binding amyloid plaques may lead to faster breakdown of the amyloid plaques and so delay the progression of Alzheimer's disease. There is also evidence that SAP directly damages brain cells and may contribute to the development of Alzheimer's disease. Removal of SAP may reduce this damage to brain cells. A new drug has been developed, called CPHPC, which eliminates SAP almost completely from the blood and thereby stops SAP from reaching the brain. CPHPC may also remove the SAP already present in the brain. This may reduce the brain damage caused by the disease. The aim of this study is to explore the safety, tolerability and potential effectiveness of CPHPC in patients with mild AD.

Who can participate?
Patients aged 50-80 who have been diagnosed with mild AD.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group receive three injections per day of CPHPC into their tummy for 12 months. Those in the second group receive three injections per day of a placebo (dummy drug) into their tummy for 12 months. At the start of the study, over the 12 months of treatment, and one month later, participants in both groups undergo brain scanning to look at the effects of the treatment, as well as having blood and cerebrospinal fluid (the fluid found in the brain and spinal cord) samples taken for testing and completing assessments of their memory.

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Where is the study run from?
University College London (UK)

When is study starting and how long is it expected to run for?
August 2015 to March 2024

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Mr Chinaza Ezirim
c.ezirim@ucl.ac.uk

Contact information

Type(s)
Public

Contact name
Ms Catherine Ryan

Contact details
Clinical Trials Manager
Dementia Research Centre
UCL Queen Square Institute of Neurology
8-11 Queen Square
London
United Kingdom
WC1N 3AR
+44 (0)20 3448 3804
c-ryan@ucl.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2016-003284-19

Central Portfolio Management System (CPMS)
33953

Study information

Scientific Title
DESPIAD: A double-blind placebo controlled randomised phase IIb trial of SAP depletion by miridesap in mild Alzheimer’s disease

Acronym
DESPIAD

Study objectives
The aim of this study is to determine whether Serum Amyloid P component (SAP) reduction improves established clinical and other measures of Alzheimer's disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central – Berkshire B REC, 24/01/2017, ref: 16/SC/0590

Study design
Randomised; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Specialty: Dementias and neurodegeneration, Primary sub-specialty: Dementia; UKCRC code/ Disease: Neurological/ Demyelinating diseases of the central nervous system

Interventions
Current interventions as of 04/08/2021:
Participants will be randomly allocated 1:1 into 2 groups by minimisation/

Intervention group: Participants receive (R)-1-[6-[(R)-2-carboxy-pyrrolidin-1-yl]-6-oxo-hexanoyl] pyrrolidine-2-carboxylic acid, (miridesap) 60 mg (0.3 ml) t.d.s by subcutaneous (s.c.) injection three times daily for 12 months

Control group: Participants receive a placebo (0.3 ml t.d.s of water for injection adjusted to pH 5.0 with sodium hydroxide or hydrochloric acid by s.c. injection, with no active component or other additives, three times daily for 12 months

Participants are followed up at month 13 which involves a review of adverse events and concomitant medications, general physical and neurological examination, vital signs, ECG, bloods, urine tests and cognitive testing.

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Intervention Type
Other

Primary outcome(s)
Current primary outcome measure as of 04/08/2021:
Safety and tolerability of miridesap is assessed by MRI at baseline, 3 months and 12 months.

Previous primary outcome measure:
Safety and tolerability of CPHPC is assessed by MRI at baseline, 3 months and 12 months.

Key secondary outcome(s))
Current secondary outcome measures as of 04/08/2021:
1. Rates of whole brain and hippocampal atrophy is assessed using quantitative semi-automated analysis of volumetric MRI of brain scans obtained at baseline and 12 months
2. Cognition is assessed using a version of the Preclinical Alzheimer Cognitive Composite (PACC), comprising: Face Name Associative Memory Performance, Wechsler Logical Memory (paragraph recall), Mini Mental State Examination (MMSE) and Digit Symbol Substitution Test score from the Wechsler Adult Intelligence Scale–Revised; verbal fluency; an in-house computer-based reaction time task; Clinical Dementia Rating (CDR), and Neuropsychiatric Inventory (NPI). The tests will be performed at baseline, 6, 12, and 13 months.
3. Other qualitative and quantitative MRI parameters which provide high-resolution maps of grey and white matter microstructure, and so can serve as a biomarker of disease modification by miridesap are assessed by CSF fluid at baseline and 12 months
4. Amyloid PET-CT is assessed using florbetapir (18F) PET-CT by single intravenous dose and scanning at the Institute of Nuclear Medicine, UCLH at baseline (or within the previous 4 weeks), and 12 months.
5. Lumbar puncture is assessed by measuring CSF concentrations of SAP, miridesap, Aβ1-42, total and phosphorylated τ at baseline and 12 months
6. Plasma SAP concentration is assessed by blood test at baseline, 3, 6, 9, 12 and 13 months

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Completion date
06/12/2024

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 04/08/2021:
1. A clinical diagnosis of mild AD (MMSE 18-28 inclusive for all patients with unknown amyloid status or MMSE 18 or greater inclusive for patients with positive amyloid status from amyloid PET imaging or CSF total Tau and Abeta levels)
2. Male or female aged ≥50 years
3. Supportive evidence of AD pathology from all of the following:
3.1. MRI brain scan consistent with a diagnosis of AD
3.2. Amyloid PET imaging, using a commercially available amyloid PET ligand, consistent with a diagnosis of AD
3.3. CSF total Tau and Abeta levels consistent with a diagnosis of AD
4. Participant must live with a partner, relative, or carer who can both attend study visits and oversee the management of the dosing of medication by subcutaneous injection
5. Agree to undergo MRI and amyloid PET imaging
6. Ability to provide written informed consent
7. Women of child bearing potential (WOCBP) and males with partners that are of child bearing potential willing to use highly effective contraception for the duration and 30 days post completion of trial treatment
8. WOCBP must have a negative pregnancy test within 7 days prior to treatment initiation
9. In the opinion of the CI or delegate, adequate understanding of written and verbal information in English

Previous participant inclusion criteria:
1. A clinical diagnosis of mild AD (MMSE 20-28 inclusive)
2. Male or female between 50-80 years of age inclusive
3. Supportive evidence of AD pathology from:
3.1. MRI brain scan consistent with a diagnosis of AD
3.2. Florbetapir (18F) PET imaging consistent with a diagnosis of AD
4. Participant must live with a partner, relative or carer who can both attend study visits and oversee the management of the dosing of medication by s.c. injection
5. Agree to undergo MRI, PET imaging and lumbar puncture
6. Ability to provide written informed consent
7. Women of child bearing potential3 and males willing to use effective4 contraception for the duration and 30 days post completion of trial treatment
8. In the opinion of the CI or delegate, adequate understanding of written and verbal information in English

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
50 years

Upper age limit
100 years

Sex
All

Total final enrolment
46

Key exclusion criteria
Current participant exclusion criteria as of 04/08/2021:
1. Ongoing clinically significant depression, in the opinion of the PI likely to impede completion of the trial, or other diseases or drugs influencing cognition; anti-depressant medication stable for more than 3 months is acceptable
2. Significantly abnormal renal (eGFR <50mls/min/m2) or hepatic enzyme (alanine aminotransferase) values two fold or greater above the upper limit of the reference range
3. Current use of warfarin, rivaroxaban, apixaban and or dabigatran; low dose aspirin or clopidogrel are permitted
4. Current use of cholinesterase inhibitors or memantine unless maintained on a stable dose for at least 3 months prior to randomisation
5. Use of other experimental drugs within 3 months of randomisation
6. Pregnancy or lactation* (current, or planned in the next 13 months)
7. Any medical condition that could be expected to progress, recur, or change to an extent that it could bias the assessment of the clinical or mental status of the participant to a significant degree or put the participant at special risk in the opinion of the investigator
8. Any known hypersensitivity to the constituents or the vehicle of miridesap
9. Any known claustrophobia
10. Weight greater than 150 Kg

*The safety of miridesap in pregnancy is unknown. Teratogenicity risks for female partners of males being treated with miridesap are unknown.

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Date of first enrolment
01/08/2017

Date of final enrolment
31/10/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
UCLH/Leonard Wolfson Experimental Neurology Centre
National Hospital for Neurology & Neurosurgery
Queen Square
London
England
WC1N 3BG

Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type

Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	version V1	16/01/2017	24/05/2017	No	Yes
Participant information sheet	version V2	16/01/2017	24/05/2017	No	Yes