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A study of JNJ-64042056 in participants with preclinical Alzheimer's disease

Submission date	Recruitment status	[X] Prospectively registered
27/03/2024	Recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
17/05/2024	Ongoing	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
04/06/2024	Nervous System Diseases	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Alzheimer’s disease (AD) is a brain disorder that slowly destroys memory and thinking skills and, eventually, the ability to carry out the simplest tasks. Preclinical AD begins long before any symptoms are clearly visible.
JNJ-64042056 is a *liposomal active immunotherapy* that helps the body to generate specific antibodies against pathological forms of the tau protein causing Alzheimer’s Disease (an antibody is a protein made in the body in response to foreign, or in our case unwanted substance).
Liposomal active immunotherapy - Liposome is a closed, circular lipid bilayer, which can carry drug solutions. Active immunotherapy helps the body’s immune system to generate a specific immune response against a disease or infectious agent.
The primary purpose of the study is to see how effective JNJ-64042056 is compared to placebo on cognitive decline.

Who can participate?
This study will include participants of 55 to 75 years of age diagnosed with preclinical Alzheimer’s Disease.

What does the study involve?
This study will consist of:
- a pre-screening phase (approximately 4 weeks)
- a screening period (up to 13 weeks prior to randomization)
- a double-blind treatment period (approximately 48 months)
- a post-treatment follow-up period (2 weeks)
The participants will be assigned by chance to 1 of 2 treatment groups: JNJ-64042056 or placebo.
JNJ-64042056 or placebo will be administered from Week 0 up to Week 180 through injection into the muscle.
Study assessments will include questionaries, vital signs, electrocardiogram (ECG), blood and urine lab safety (including coagulation, thyroid function, vitamin B12, folic acid), antibody

assessments, biomarker assessments, magnetic resonance imaging (MRI), positron emission tomography (PET), physical and neurological examination.
Total study duration for each participant will be approximately 4 years.

What are the possible benefits and risks of participating?
There is no established benefit to participants of this study. Based on scientific theory, taking JNJ-64042056 may slow Alzheimer's Disease progression and delay symptom onset. However, this cannot be guaranteed because JNJ-64042056 is still under investigation as a treatment. Participation may help other people with preclinical AD in the future.
If participants are put into the placebo treatment group, they will not receive JNJ-64042056 and will only receive placebo during this study.
Participants may have side effects from the drugs or procedures (such as procedural pain during insertion of a needle) used in this study that may be mild to severe and even life-threatening, and they can vary from person to person. Since JNJ-64042056 has only been given to a relatively small number of people thus far, all possible side effects and risks related to JNJ-64042056 are not known. As of today, JNJ64042056 has been found safe and well tolerated in a small number of people. No pattern of adverse events considered related to JNJ-64042056 has emerged to date, other than mild and self-limiting injection site reactions after intramuscular (muscle of the upper arm) administration, consisting of pain, redness and/or swelling and/or pruritus (itching) and/or induration (thickening and/or hardening of the skin), on one or more occasion.
The participant information sheet and informed consent form, which will be signed by every participant agreeing to participate in the study, includes a detailed section outlining the known risks to participating in the study.
During the study, the sponsor may learn new information about JNJ-64042056. The study doctor will tell participants as soon as possible about any new information that might make them change their mind about being in the study, such as new risks.
To minimise the risk associated with taking part in the study, participants are frequently assessed for any side effects and other medical events. Participants are educated to report any such events to the study doctor who will provide appropriate medical care. Any serious side effects that are reported to the sponsor are thoroughly reviewed by a specialist drug safety team.

Where is the study run from?
Janssen-Cilag International NV (Netherlands)

When is the study starting and how long is it expected to run for?
April 2024 to July 2031

Who is funding the study?
Janssen Pharmaceutica (Belgium)

Who is the main contact?
JanssenUKRegistryQueries@its.jnj.com
medinfo@its.jnj.com

Contact information

Type(s)
Scientific

Contact name

Dr . Study Team

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1008651

ClinicalTrials.gov number
Nil known

Secondary identifying numbers

64042056ALZ2001, IRAS 1008651, CPMS 58779

Study information

Scientific Title
A multicenter, randomized, placebo-controlled, double-blind, parallel-group study, to assess efficacy, safety and immunogenicity of JNJ-64042056, a phosphorylated tau targeted active immunotherapy, in participants with preclinical Alzheimer's disease

Acronym
Retain

Study objectives
Primary objective:
To evaluate the effect of JNJ-64042056 in comparison with placebo on cognitive decline (gradual loss of thinking abilities) in participants with preclinical Alzheimer’s Disease (AD).

Secondary objectives:
1. To assess the effect of JNJ-64042056 in comparison with placebo on the spread and accumulation of tau pathology (Tau is a protein that helps stabilize the internal skeleton of nerve cells [neurons] in the brain), as measured by tau positron emission tomography (PET).
2. To investigate the effect of JNJ-64042056 in comparison with placebo on cognitive decline and clinical progression.
3. To evaluate changes in participants’ ability to perform daily activities when treated with JNJ-64042056 or placebo.
4. To investigate the effect of JNJ-64042056 in comparison with placebo on the behaviour of participants.
5. To evaluate changes in quality of life between participants treated with JNJ-64042056 or placebo.
6. To evaluate differences in healthcare resource utilization between participants treated with JNJ-64042056 or placebo.
7. To assess the immune (protective) response of JNJ-64042056 in serum.
8. To assess the overall safety and tolerability of JNJ-64042056 in comparison with placebo.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 09/05/2024, South Central - Berkshire B Research Ethics Committee (Level 3, Block B, Whitefriars, Lewins Mead, Avon, Bristol , BS1 2NT, United Kingdom; +44 (0)207 104 8253, +44 (0) 207 104 8276, +44 (0)207 104 8256; berkshireb.rec@hra.nhs.uk), ref: 24/SC/0126

Study design
Interventional double-blind randomized parallel-group placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Safety, Efficacy

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Preclinical Alzheimer’s Disease

Interventions
Participants will be assigned by chance to one of two treatment groups: JNJ-64042056 or placebo. Participants will be assigned randomly by a central randomisation process.

Participants will receive the study drug/treatment on Day 1, at 2 months, at 6 months and then 6 additional injections occurring every 6 months up to Week 180 (a total of 9 injections throughout the study period).

The study intervention will be administered at the study site via an intramuscular injection in the deltoid muscle (upper arm).

After the end of the study at Week 206, participants will have an option to participate in a separate open-label extension study (if eligible).

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacodynamic, Pharmacogenomic, Others (Biomarkers, imaging, immunogenicity)

Phase
Phase II

Drug/device/biological/vaccine name(s)
JNJ-64042056

Primary outcome measure
Change From Baseline in Preclinical Alzheimer's Disease Cognitive Composite 5 (PACC-5) Total Scores up to Week 206

Secondary outcome measures
Baseline up to Week 206 (unless noted otherwise):
1. Change From Baseline in Brain tau Burden as Measured by tau PET- Baseline and Weeks 102, 154 and 206
2. Change From Baseline in PACC-5 Individual Domain Scores
3. Time to Event of Clinical Progression as Measured by Clinical Dementia Rating-Global Score (CDR-GS)
4. Change From Baseline in Clinical Dementia Rating-Sum of Boxes (CDR-SB) Scores

5. Change from Baseline in Tau PET Standardized Uptake Value Ratio (SUVR) Biomarkers (tau Naiive Composite ROI and Other ROIs)
6. Change From Baseline in p217+tau
7. Change From Baseline in PACC-5 Total Score - Baseline up to Week 180
8. Change From Baseline in Brain Tau Burden as Measured by Tau PET in Other ROI
9. Change From Baseline in Alzheimer's Disease Cooperative Study - Activities of Daily Living - Prevention Instrument (ADCS-ADL-PI)
10. Change From Baseline in Mild Behavioral Impairment Checklist (MBI-C) Score
11. Change From Baseline in the Quality of Life- Alzheimer's Disease (QoL-AD)
12. Change From Baseline in European Quality of Life-5 Dimensions 5-Levels (EQ-5D-5L) Score
13. Change From Baseline in Resource Utilization in Dementia-Lite (RUD-Lite) Score
14. Levels of IgG Titers Against Enriched Paired Helical Filaments (ePHF), p-tau and tau in Serum
15. Number of Participants With Treatment-Emergent Adverse Events (TEAEs) - Up to Week 208
16. Number of Participants With Reactogenicity - Up to Week 182
17. Change from Baseline in Vital Signs
18. Change From Baseline in Clinical Laboratory Values
19. Change from Baseline in Electrocardiogram (ECG) Values
20. Change From Baseline in Columbia-Suicidality Severity Rating Scale (C-SSRS)
21. Change From Baseline in Magnetic Resonance Imaging (MRI) Findings

Overall study start date
09/04/2024

Completion date
17/07/2031

Eligibility

Key inclusion criteria
1. 55 to 75 years of age, inclusive, at randomisation visit.
2. Elevated brain tau pathology defined as Braak 3 ROI SUVR > 1.1 on a screening tau PET scan, reviewed centrally by a qualified reader.
3. CDR global score of 0 at screening and baseline.
4. MMSE ≥27 (with educational adjustment).
5. Able to read and write and with a minimum 5 years of formal education as reported by participant and study partner at screening.

Participant type(s)
Patient

Age group
Adult

Lower age limit
55 Years

Upper age limit
75 Years

Sex

Both

Target number of participants
498

Key exclusion criteria
1. MRI evidence of any brain disease or intracranial pathology other than potential very early signs of AD or typical age-related changes, which in the opinion of the investigator or the central imaging reader and/or the sponsor, may affect cognition.
2. History consistent with or known autosomal dominant AD.
3. Fulfills diagnostic criteria for Alzheimer's Dementia or non-Alzheimer's Dementia, including, but not limited to Frontotemporal Dementia (FTD), Diffuse Lewy Body Dementia (DLBD), Vascular Dementia (VAD), alcoholic dementia, Parkinson's dementia, Korsakov, Creutzfeldt-Jakob or other prion diseases, Posterior Cortical Atrophy.
4. Diagnosis ofMild Cognitive Impairment (MCI)
5. Presence of any neurological, psychiatric, or medical conditions associated with a longterm risk of significant cognitive impairment or dementia

Date of first enrolment
28/05/2024

Date of final enrolment
02/07/2027

Locations

Countries of recruitment
Australia

Belgium

England

France

Germany

Japan

Netherlands

Scotland

Spain

Sweden

United Kingdom

Study participating centre
Rice - the Research Institute for the Care of Older People
The RICE Centre
Royal United Hospital
Combe Park
Bath
United Kingdom
BA1 3NG

Study participating centre
Re:Cognition Health
centres based in Bristol, Birmingham, Winchester, Plymouth, London and Guildford
-
United Kingdom
-

Study participating centre
Kings College Hospital
Mapother House
De Crespigny Park
Denmark Hill
London
United Kingdom
SE5 8AB

Study participating centre
Moorgreen Hospital
Botley Road
West End
Southampton
United Kingdom
SO30 3JB

Study participating centre
Charing Cross Hospital
Fulham Palace Road
London
United Kingdom
W6 8RF

Study participating centre

Warneford Hospital
Warneford Lane
Headington
Oxford
United Kingdom
OX3 7JX

Study participating centre
Southampton
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Southmead Hospital
Southmead Road
Westbury-on-trym
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BS10 5NB

Study participating centre
Scottish Brain Sciences
Gyleview House, 3 Redheughs Rigg, South Gyle
Edinburgh
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EH12 9DQ

Sponsor information

Organisation
Janssen-Cilag International NV

Sponsor details
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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Janssen Pharmaceutica

Alternative Name(s)
Janssen Pharmaceutica NV, JANSSEN-CILAG NV, Janssen Belgium, Janssen, Janssen Pharmaceuticals

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Belgium

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Internal report
Conference presentation
Publication on website
Other publication
Submission to regulatory authorities

Study results will be available via publication in scientific journals, the EudraCT database & presentation at scientific meetings. Results will be made available to participants via a Plain Language Summary a year after the end of the study. The summary will describe the results regardless of study outcome in language that is understandable to the general public. It will not contain individual participant results or their personal information. A copy of the Summary will be provided to the REC.

Intention to publish date
17/07/2032

Individual participant data (IPD) sharing plan
The data sharing policy of the Janssen Pharmaceutical Companies of Johnson & Johnson is available at https://www.janssen.com/clinical-trials/transparency. As noted on this site, requests for access to the study data can be submitted through the Yale Open Data Access (YODA) Project site at yoda.yale.edu

IPD sharing plan summary
Available on request