

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

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		<input type="checkbox"/> Protocol
<b>Registration date</b> 17/05/2024	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 04/06/2024	<b>Condition category</b> Nervous System Diseases	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> 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 questionnaires, 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

**Contact details**

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United Kingdom

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**Type(s)**

Principal investigator

**Contact name**

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**Additional identifiers**

**Integrated Research Application System (IRAS)**

1008651

**Central Portfolio Management System (CPMS)**

58779

**Protocol serial number**

64042056ALZ2001

**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

## Study type(s)

Safety, Efficacy

## 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

## Phase

Phase II

## Drug/device/biological/vaccine name(s)

JNJ-64042056

## Primary outcome(s)

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

## Key secondary outcome(s)

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

**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  $\geq$ 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

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

55 years

**Upper age limit**

75 years

**Sex**

All

**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 of Mild 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**

United Kingdom

England

Scotland

Australia

Belgium

France

Germany

Japan

Netherlands

Spain

Sweden

**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

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United Kingdom

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**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  
Bristol  
United Kingdom  
BS10 5NB

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

## **Sponsor information**

**Organisation**  
Janssen-Cilag International NV

## **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

## **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](http://yoda.yale.edu)

## **IPD sharing plan summary**

Available on request