Clinical trial results:
Evaluating rapamycin treatment in Alzheimer’s disease using positron emission tomography (ERAP)

Summary

EudraCT number	2023-000127-36
Trial protocol	SE
Global end of trial date	11 December 2024

Results information

Result version number	v1 (current)
This version publication date	24 October 2025
First version publication date	24 October 2025

Trial information

Trial identification

Sponsor protocol code	KIH22001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT06022068
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Karolinska Institutet
Sponsor organisation address	Nobels väg 15a, Stockholm, Sweden, 17177
Public contact	Brain Molecular Imaging Centre, Karolinska Institutet, jonas.svensson@ki.se
Scientific contact	Brain Molecular Imaging Centre, Karolinska Institutet, 46 702753831, jonas.svensson@ki.se

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 August 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 December 2024
Global end of trial reached?	Yes
Global end of trial date	11 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of sirolimus in patients suffering from MCI or early-stage AD.

Protection of trial subjects:

The study was approved by the Swedish Medical Products Agency (5.120238283) and the Swedish Ethical Review Authority (20230307502 and 20230061101). Written informed consent was obtained from all participants and their designated study partners before any study procedures were initiated.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2023
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	12
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from the Memory Clinic patient population. Some patients had previously consented to be contacted about clinical trial opportunities, while others expressed interest after being informed about the trial by their treating physician.

Pre-assignment

Screening details:

Inclusion criteria: amyloid-positivity, age between 50 and 89 years of age, has amyloid-positivity with a clinical diagnosis of mild cognitive impairment (MCI) or mild dementia of Alzheimer's type according to the NIA-AA 2018 criteria.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Arm title	Rapamycin

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Rapamycin
Investigational medicinal product code	
Other name	Rapamune
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The first dose was 3 mg, which was increased to the target dose of 7 mg/week from the second week onward if well tolerated.

Number of subjects in period 1	Rapamycin
Started	14
Completed	13
Not completed	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	14	14	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	60.9		
standard deviation	± 4.2	-	
Gender categorical Units: Subjects			
Female	8	8	
Male	6	6	

End points

End points reporting groups	
Reporting group title	Rapamycin
Reporting group description: -	
Subject analysis set title	Baseline
Subject analysis set type	Full analysis
Subject analysis set description: 15 days prior to first dose of rapamycin	
Subject analysis set title	Follow-up
Subject analysis set type	Full analysis
Subject analysis set description: 14 days post last dose of rapamycin	

Primary: Change in brain FDG-PET uptake	
End point title	Change in brain FDG-PET uptake
End point description: % change from baseline in FDG SUVR (temporoparietal lobe)	
End point type	Primary
End point timeframe: Pre and post treatment	

End point values	Baseline	Follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	13		
Units: unitless ratio				
arithmetic mean (standard deviation)	1.04 (± 0.10)	1.04 (± 0.11)		

Statistical analyses

Statistical analysis title	Change in brain FDG-PET uptake
Comparison groups	Baseline v Follow-up
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.991
Method	t-test, 2-sided

Notes:
[1] - mean comparison

Secondary: Change in CSF markers - Ab42	
End point title	Change in CSF markers - Ab42
End point description: Ab42 at baseline and at follow-up	

End point type	Secondary

End point timeframe:
pre and post treatment

End point values	Baseline	Follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: pg/mL				
arithmetic mean (standard deviation)	614 (± 191)	653 (± 135)		

Statistical analyses

Statistical analysis title	Change in CSF markers protein concentration levels
Comparison groups	Baseline v Follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.18
Method	t-test, 2-sided

Notes:
[2] - mean comparison

Secondary: Change in CSF markers - p-tau

End point title	Change in CSF markers - p-tau

End point description:
p-tau at baseline and at follow-up

End point type	Secondary

End point timeframe:
pre and post treatment

End point values	Baseline	Follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: pg/mL				
arithmetic mean (standard deviation)	107.10 (± 34.37)	110.10 (± 33.30)		

Statistical analyses

Statistical analysis title	Change in CSF markers protein concentration levels
Comparison groups	Baseline v Follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.59
Method	t-test, 2-sided

Notes:
[3] - mean comparison

Secondary: Change in CSF markers - total-tau	
End point title	Change in CSF markers - total-tau
End point description: Total-tau at baseline and at follow-up	
End point type	Secondary
End point timeframe: pre and post treatment	

End point values	Baseline	Follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: pg/mL				
arithmetic mean (standard deviation)	616 (± 150)	751 (± 206)		

Statistical analyses

Statistical analysis title	Change in CSF markers protein concentration levels
Comparison groups	Baseline v Follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.003
Method	t-test, 2-sided

Notes:
[4] - mean comparison

Secondary: Change in cognition	
End point title	Change in cognition
End point description: Total Montreal Cognitive Assessment (MoCA) score at baseline and at follow-up	
End point type	Secondary
End point timeframe: pre and post treatment	

End point values	Baseline	Follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	12		
Units: MoCA sum score				
arithmetic mean (standard deviation)	24.33 (± 2.93)	24.75 (± 4.61)		

Statistical analyses

Statistical analysis title	change in total MoCA score
Comparison groups	Baseline v Follow-up
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.54
Method	t-test, 2-sided

Notes:

[5] - mean comparison

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 1st Sep 2023 - 11th Dec 2024	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	NA
Dictionary version	NA
Reporting groups	
Reporting group title	Overall study

Reporting group description: -

Serious adverse events	Overall study		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Overall study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 14 (85.71%)		
Injury, poisoning and procedural complications			
Wisdom teeth removal			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Erythrocyte sedimentation rate increased	Additional description: increased erythrocyte sedimentation rate (ESR)		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
creatine kinase increased			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Nervous system disorders			

Vertigo			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Paraesthesia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Restless legs syndrome	Additional description: crawling / tingling feeling in legs		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Tinnitus	Additional description: worsening of pre-existing tinnitus		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Hearing disability	Additional description: Trouble hearing		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	6		
mouth sore			
subjects affected / exposed	4 / 14 (28.57%)		
occurrences (all)	9		
Dysgeusia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Flatulence			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
stomach pain			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough	Additional description: Dry cough		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Throat irritation	Additional description: sore throat		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Hair growth abnormal	Additional description: Regrowth of scalp hair		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Rash	Additional description: skin rash		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Skin tightness	Additional description: reduced facial wrinkles		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Psychiatric disorders			
feeling low			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Endocrine disorders			
Glucose tolerance impaired	Additional description: increased fasting glucose		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Hot flush			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Thyroid hormones decreased	Additional description: Increased levotyroxin dose		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Skin discolouration	Additional description: swelling / discoloration of hand		

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Swelling	Additional description: swelling of legs		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Infections and infestations			
Bacterial infection			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Upper respiratory tract infection	Additional description: viral infections		
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
increased serum lipids			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 June 2023	Added magnetic resonance tomography measurements procedures as exploratory outcomes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported