



Clinical trial results:

A Phase 2a, Proof-of-Concept, Open-Label Study to Evaluate the Pharmacodynamics, Pharmacokinetics, and Safety of Obicetrapib in Patients with Early Alzheimer's Disease (Hetero/Homozygote APOE4 Carriers)

Summary

EudraCT number	2021-002687-41
Trial protocol	NL
Global end of trial date	01 June 2023

Results information

Result version number	v1 (current)
This version publication date	06 April 2025
First version publication date	06 April 2025

Trial information

Trial identification

Sponsor protocol code	TA-8995-AD-1
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05161715
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	NewAmsterdam Pharma BV
Sponsor organisation address	Gooimeer 2-35, DC Naarden, Netherlands, 1411
Public contact	Study Director, NewAmsterdam Pharma BV, 31 352062971, study.director@newamsterdampharma.com
Scientific contact	Study Director, NewAmsterdam Pharma BV, +31 352062971, study.director@newamsterdampharma.com

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	24 August 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 May 2023
Global end of trial reached?	Yes
Global end of trial date	01 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the pharmacodynamics (PD) (apolipoproteins/lipid particles and cholesterol efflux) of obicetrapib in cerebrospinal fluid (CSF) and plasma (apolipoproteins/lipid particles) in patients with early Alzheimer's Disease (AD) (hetero/homozygote APOE4 carriers).

The exploratory objectives of this study are to evaluate:

- other PD markers of obicetrapib (additional lipoproteins, neurodegeneration, and inflammation) in patients with early AD.
- the cognitive effects of obicetrapib in patients with early AD.
- the pharmacokinetics (PK) of obicetrapib in patients with early AD.

The safety objective of this study is to evaluate the safety and tolerability of obicetrapib in patients with early AD.

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and with all applicable laws and regulations of the locale and country where the study was conducted, and in compliance with Good Clinical Practice Guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 January 2022
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	Netherlands: 13
Worldwide total number of subjects	13
EEA total number of subjects	13

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)	8
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

13 participants were randomized

Pre-assignment

Screening details:

18 participants were screened

Period 1

Period 1 title	Overall Study
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Obicetrapib
Arm description: Obicetrapib (10 mg)	
Arm type	Experimental
Investigational medicinal product name	Obicetrapib 5 mg tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Once daily 2 x 5 mg obicetrapib tablet

Number of subjects in period 1	Obicetrapib
Started	13
Completed	13

Period 2

Period 2 title	Overall Study
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Obicetrapib
Arm description: Obicetrapib (10 mg)	
Arm type	Experimental
Investigational medicinal product name	Obicetrapib 5 mg tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Once daily 2 x 5 mg obicetrapib tablet

Number of subjects in period 2	Obicetrapib
Started	13
Completed	13

Baseline characteristics

Reporting groups

Reporting group title	Obicetrapib
Reporting group description: Obicetrapib (10 mg)	

Reporting group values	Obicetrapib	Total	
Number of subjects	13	13	
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			
Baseline Population is defined as all participants who received at least one dose of study drug.			
Units: years			
arithmetic mean	64.5		
standard deviation	± 6.2	-	
Gender categorical			
Baseline Population is defined as all participants who received at least one dose of study drug.			
Units: Subjects			
Female	12	12	
Male	1	1	

End points

End points reporting groups

Reporting group title	Obicetrapib
Reporting group description:	
Obicetrapib (10 mg)	
Reporting group title	Obicetrapib
Reporting group description:	
Obicetrapib (10 mg)	
Subject analysis set title	Baseline Population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Baseline Population is defined as all participants who received at least one dose of study drug.	

Primary: 1. Mean Percent Change in Apolipoprotein A-I (ApoA-I) In Cerebrospinal Fluid (CSF)

End point title	1. Mean Percent Change in Apolipoprotein A-I (ApoA-I) In Cerebrospinal Fluid (CSF)
End point description:	
Mean percent change from screening (V1) to end of treatment (V6) in ApoA-I in CSF	
End point type	Primary
End point timeframe:	
24 weeks	

End point values	Obicetrapib	Obicetrapib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[1]	12 ^[2]		
Units: Percentage Change from Screening Visit				
arithmetic mean (standard deviation)	-8.4 (± 13.6)	-8.4 (± 13.6)		

Notes:

[1] - Lumbar puncture was not possible for 1 patient at EOT (Day 168, Visit 6); hence n=12 for CSF

[2] - Lumbar puncture was not possible for 1 patient at EOT (Day 168, Visit 6); hence n=12 for CSF

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Obicetrapib v Obicetrapib
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.425 ^[3]
Method	Wilcoxon (Mann-Whitney)

Notes:

[3] - No multiple testing correction was performed

Primary: 2. Mean Percent Change in Apolipoprotein A-I (ApoA-I) in Plasma

End point title	2. Mean Percent Change in Apolipoprotein A-I (ApoA-I) in
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End point description:

Mean percent change in ApoA-I in plasma from baseline (V2) to week 24 (V6)

End point type

Primary

End point timeframe:

24 weeks

End point values	Obicetrapib	Obicetrapib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13 ^[4]	13		
Units: Percent Change from Baseline				
arithmetic mean (standard deviation)	37.5 (± 25.2)	37.5 (± 25.2)		

Notes:

[4] - For the PD endpoints in plasma, analyses were conducted on all 13 patients.

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Obicetrapib v Obicetrapib
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority ^[5]
P-value	= 0.0002
Method	Wilcoxon (Mann-Whitney)

Notes:

[5] - No multiple testing correction was performed

Primary: 3. Mean Percent Change in Apolipoprotein-E (ApoE) in Cerebrospinal Fluid (CSF)

End point title	3. Mean Percent Change in Apolipoprotein-E (ApoE) in Cerebrospinal Fluid (CSF)
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End point description:

Mean percent change from screening (V1) to end of treatment (V6) in ApoE

End point type

Primary

End point timeframe:

24 weeks

End point values	Obicetrapib	Obicetrapib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[6]	12 ^[7]		
Units: Percent Change from Baseline				
arithmetic mean (standard deviation)	3.9 (± 10.3)	3.9 (± 10.3)		

Notes:

[6] - Lumbar puncture was not possible for 1 patient at EOT (Day 168, Visit 6); hence n=12 for CSF

[7] - Lumbar puncture was not possible for 1 patient at EOT (Day 168, Visit 6); hence n=12 for CSF

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Obicetrapib v Obicetrapib
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0424 [8]
Method	Wilcoxon (Mann-Whitney)

Notes:

[8] - No multiple testing correction was performed

Primary: 4. Mean Percent Change in Apolipoprotein-E (ApoE) in Plasma

End point title	4. Mean Percent Change in Apolipoprotein-E (ApoE) in Plasma
End point description:	Mean percent change from baseline (V2) to week 24 (V6) in plasma in ApoE
End point type	Primary
End point timeframe:	24 weeks

End point values	Obicetrapib	Obicetrapib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13 ^[9]	13		
Units: Percent Change from Baseline				
arithmetic mean (standard deviation)	47.8 (± 46.9)	47.8 (± 46.9)		

Notes:

[9] - For the PD endpoints in plasma, analyses were conducted on all 13 patients.

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Obicetrapib v Obicetrapib
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [10]
Method	Wilcoxon (Mann-Whitney)

Notes:

[10] - No multiple testing correction was performed

Primary: 5. Small HDL (s-HDL) Particle Concentration in Cerebrospinal Fluid (CSF) at Baseline

End point title	5. Small HDL (s-HDL) Particle Concentration in Cerebrospinal Fluid (CSF) at Baseline ^[11]
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End point description:

Small high-density lipoprotein (s-HDL) particle concentration in cerebrospinal fluid (CSF) measured by Ion Mobility Assay (<https://doi.org/10.1002/alz.12649>)

End point type	Primary
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End point timeframe:

At Baseline

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Average relative abundance was reported and statistical analysis was not performed. Small high-density lipoprotein (s-HDL) particle concentration in CSF measured by Ion Mobility Assay (<https://doi.org/10.1002/alz.12649>)

End point values	Obicetrapib			
Subject group type	Reporting group			
Number of subjects analysed	12 ^[12]			
Units: Average relative abundance				
arithmetic mean (standard deviation)	0.542 (± 0.138)			

Notes:

[12] - Lumbar puncture was not possible for 1 patient at EOT (Day 168, Visit 6); hence n=12 for CSF

Statistical analyses

No statistical analyses for this end point

Primary: 6. Small HDL (s-HDL) Particle Concentration in Cerebrospinal Fluid (CSF) at Week 24

End point title	6. Small HDL (s-HDL) Particle Concentration in Cerebrospinal Fluid (CSF) at Week 24 ^[13]
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End point description:

Small high-density lipoprotein (s-HDL) particle concentration in CSF measured by Ion Mobility Assay (<https://doi.org/10.1002/alz.12649>)

End point type	Primary
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End point timeframe:

At Week 24

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Average relative abundance was reported and statistical analysis was not performed. Small high-density lipoprotein (s-HDL) particle concentration in CSF measured by Ion Mobility Assay (<https://doi.org/10.1002/alz.12649>)

End point values	Obicetrapib			
Subject group type	Reporting group			
Number of subjects analysed	12 ^[14]			
Units: Average Relative Abundance				
arithmetic mean (standard deviation)	0.542 (± 0.106)			

Notes:

[14] - Lumbar puncture was not possible for 1 patient at EOT (Day 168, Visit 6); hence n=12 for CSF

Statistical analyses

No statistical analyses for this end point

Primary: 7. Small HDL (s-HDL) Particle Concentration in Plasma at Baseline

End point title	7. Small HDL (s-HDL) Particle Concentration in Plasma at Baseline ^[15]
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End point description:

Small high-density lipoprotein (s-HDL) particle concentration plasma measured by Ion Mobility Assay.

For more information on the measurement used please refer to this article:

<https://doi.org/10.1002/alz.12649>

End point type	Primary
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End point timeframe:

At Baseline

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Due to a non-optimal sample preparation procedure, a number of the samples allocated for the small HDL-C particle analysis were lost and therefore no samples were assessed for this measure.

End point values	Obicetrapib			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[16]			
Units: Average Relative Abundance				
arithmetic mean (standard deviation)	()			

Notes:

[16] - Due to a non-optimal sample prep, samples were not able to be assessed for this measure.

Statistical analyses

No statistical analyses for this end point

Primary: 8. Small HDL (s-HDL) Particle Concentration in Plasma at Week 24

End point title	8. Small HDL (s-HDL) Particle Concentration in Plasma at Week 24 ^[17]
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End point description:

Small high-density lipoprotein (s-HDL) particle concentration in plasma measured by Ion Mobility Assay at Week 24

For more information on the measurement used please refer to this article:

<https://doi.org/10.1002/alz.12649>

End point type	Primary
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End point timeframe:

At Week 24

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Due to a non-optimal sample preparation procedure, a number of the samples allocated for the small HDL-C particle analysis were lost and therefore no samples were assessed for this measure.

End point values	Obicetrapib			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[18]			
Units: Average Relative Abundance				
arithmetic mean (standard deviation)	()			

Notes:

[18] - Due to a non-optimal sample prep, samples were not able to be assessed for this measure.

Statistical analyses

No statistical analyses for this end point

Primary: 9. Mean Percent Change in Cholesterol Efflux Capacity in Cerebrospinal Fluid (CSF)

End point title	9. Mean Percent Change in Cholesterol Efflux Capacity in Cerebrospinal Fluid (CSF)
End point description:	Mean percent change in cholesterol efflux capacity in CSF from screening (V1) to week 24 (V6)
End point type	Primary
End point timeframe:	24 Weeks

End point values	Obicetrapib	Obicetrapib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[19]	12 ^[20]		
Units: Percent Change from Screening				
arithmetic mean (standard deviation)	1.9 (± 24.1)	1.9 (± 24.1)		

Notes:

[19] - Lumbar puncture was not possible for 1 patient at EOT (Day 168, Visit 6); hence n=12 for CSF

[20] - Lumbar puncture was not possible for 1 patient at EOT (Day 168, Visit 6); hence n=12 for CSF

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Obicetrapib v Obicetrapib
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.556 ^[21]
Method	Wilcoxon (Mann-Whitney)

Notes:

[21] - No multiple testing correction was performed

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug through Week 24.5

Adverse event reporting additional description:

Safety Population included all participants who received at least 1 dose of any study drug.

Assessment type Systematic

Dictionary used

Dictionary name MedDRA

Dictionary version 26.0

Reporting groups

Reporting group title Obicetrapib

Reporting group description:

Obicetrapib (10 mg)

Serious adverse events	Obicetrapib		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Obicetrapib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 13 (69.23%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
basal cell carcinoma face			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
General disorders and administration site conditions			
unilateral leg swelling			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			

Productive cough subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Investigations weight loss subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all) Lumbar puncture headache subjects affected / exposed occurrences (all) rib contusion subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1 1 / 13 (7.69%) 1 1 / 13 (7.69%) 1		
Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Nervous system disorders headache subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2		
Blood and lymphatic system disorders Normocytic anaemia subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Ear and labyrinth disorders benign paroxysmal positional vertigo subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) loose stool	1 / 13 (7.69%) 1		

<p>subjects affected / exposed occurrences (all)</p> <p>obstipation subjects affected / exposed occurrences (all)</p> <p>reflux esophagitis subjects affected / exposed occurrences (all)</p>	<p>1 / 13 (7.69%) 1</p> <p>1 / 13 (7.69%) 1</p> <p>1 / 13 (7.69%) 1</p>		
<p>Skin and subcutaneous tissue disorders hair loss subjects affected / exposed occurrences (all)</p>	<p>1 / 13 (7.69%) 1</p>		
<p>Musculoskeletal and connective tissue disorders hand arthritis subjects affected / exposed occurrences (all)</p> <p>Lateral epicondylitis subjects affected / exposed occurrences (all)</p> <p>low back pain subjects affected / exposed occurrences (all)</p> <p>lumbago subjects affected / exposed occurrences (all)</p>	<p>1 / 13 (7.69%) 1</p> <p>1 / 13 (7.69%) 1</p> <p>1 / 13 (7.69%) 1</p> <p>1 / 13 (7.69%) 1</p>		
<p>Infections and infestations COVID-19 subjects affected / exposed occurrences (all)</p> <p>Gastroenteritis subjects affected / exposed occurrences (all)</p> <p>Herpes zoster subjects affected / exposed occurrences (all)</p> <p>Laryngitis</p>	<p>1 / 13 (7.69%) 1</p> <p>1 / 13 (7.69%) 1</p> <p>1 / 13 (7.69%) 1</p>		

subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Metabolism and nutrition disorders Hyponatraemia subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported