Clinical trial results:
A Phase II Double-Blind, Randomized, Placebo-Controlled, Adaptive Design Study to Assess the Safety, Tolerability, Immunogenicity and Target Engagement of ACI-24 Formulations in Patients with Mild Alzheimer's Disease

Summary

EudraCT number	2018-000445-39
Trial protocol	FI SE GB
Global end of trial date	12 March 2021

Results information

Result version number	v1 (current)
This version publication date	25 March 2022
First version publication date	25 March 2022

Trial information

Trial identification

Sponsor protocol code	ACI-24-1801

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AC Immune SA
Sponsor organisation address	EPFL Innocation Park, Building B, Lausanne, Switzerland, 1015
Public contact	Clinical Trial Information, AC Immune SA, +41 213459121, clinicaltrials@acimmune.com
Scientific contact	Clinical Trial Information, AC Immune SA, +41 213459121, clinicaltrials@acimmune.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	19 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 March 2021
Global end of trial reached?	Yes
Global end of trial date	12 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Study Objective:
To assess the safety and tolerability of the ACI-24 in patients with mild Alzheimer's disease (AD).
To assess the effects of ACI-24 on induction of anti-Aβ antibody responses in serum.
To assess the effects of ACI-24 on brain amyloid load in patients with mild Alzheimer's disease, assessed by florbetaben-PET imaging at 52 weeks (12 months) and 76 weeks (18 months).
Secondary Study Objective:
To explore the effects of ACI-24 on putative biomarkers of the progression of AD as Aβ 1-40 and Aβ 1-42 levels in CSF.

Protection of trial subjects:

Before undertaking any study-related procedures with subjects, the purpose and nature of the study as well as possible adverse effects were explained to the subject and their caregiver, if appropriate, in understandable terms, and written informed consent was obtained from each study subject. Each informed consent form was appropriately signed and dated by the subject/caregiver and the person obtaining consent.
Subject safety in general was to be monitored by the independent Data and Safety Monitoring Board (DSMB) of the study. The DSMB consisted of specific experts in the field, who met on a regular basis to review the safety data of the subjects. Details of responsibilities and activities were described in a charter. The outcome of the DSMB meeting was registered in minutes and included a recommendation as to whether to continue the study as planned or to modify or stop the study.
For individual trial subjects and in addition to continous safety checks by the investigator, subjects were asked to stay on days when the study drug is administered in the clinic for at least one hour after the dose for safety reasons. For subjects, who withdraw from the study, a final safety check at the trial site was recommended.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 9
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	United Kingdom: 9
Worldwide total number of subjects	21
EEA total number of subjects	12

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)	5
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was performed in UK, Finland, Poland and Sweden. Fifty-four subjects were screened for the study; 33 subjects did not meet the eligibility criteria; 2 subjects were re-screened and qualified to participate.

Pre-assignment

Screening details:

Subjects between 50 and 85 years at screening and providing a written informed consent with a positive Florbetaben-PET scan at Screening consistent with the presence of amyloid pathology and fulfilling all further inclusion criteria could enter the clinical trial.

Period 1

Period 1 title	Phase 2 - treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Blinding implementation details:

The study was blinded to subjects, caregivers, Sponsor, and site personnel. The Principal Investigator (PI) was provided with the site specific unblinded list after data lock. Database lock was performed at a dose-cohort level. It was the PIs' responsibility to decide if this information should or should not be shared with the subjects.
In order to remain blinded, raters who performed the cognitive tests did not have access to any clinical assessment data (eg, clinical rating scales, AEs).

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment

Arm description:

Subjects receiving 8 doses of ACI-24 (week 0, 4, 8, 12, 24, 36, 48 and 74)

Arm type	Experimental
Investigational medicinal product name	ACI-24
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intramuscular use

Dosage and administration details:

8 doses of ACI-24 at 1000 µg/dose were tested using the Intramuscular route of administration at weeks 0, 4, 8, 12, 24, 36, 48 and 74.

Arm title	Placebo

Arm description:

Subjects receiving 8 doses of Placebo (week 0, 4, 8, 12, 24, 36, 48 and 74).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intramuscular use

Dosage and administration details:

Placebo consisted of a suspension of empty ACI-24 liposomes. Placebo was administered by the intramuscular route (week 0, 4, 8, 12, 24, 36, 48 and 74).

Number of subjects in period 1	Treatment	Placebo
Started	14	7
Completed	11	5
Not completed	3	2
Consent withdrawn by subject	2	1
Adverse event, non-fatal	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Treatment
Reporting group description:	
Subjects receiving 8 doses of ACI-24 (week 0, 4, 8, 12, 24, 36, 48 and 74)	
Reporting group title	Placebo
Reporting group description:	
Subjects receiving 8 doses of Placebo (week 0, 4, 8, 12, 24, 36, 48 and 74).	

Reporting group values	Treatment	Placebo	Total
Number of subjects	14	7	21
Age categorical			
Age greater than or equal to 50 and less than or equal to 85 years.			
Units: Subjects			
Adults (18-64 years)	3	2	5
From 65-84 years	11	5	16
Gender categorical Units: Subjects			
Female	6	5	11
Male	8	2	10

Subject analysis sets	
Subject analysis set title	Randomized Set
Subject analysis set type	Full analysis
Subject analysis set description:	
The Randomized Set was used to describe all randomized subjects whether or not they received study drug	
Subject analysis set title	Intention-to-Treat (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The ITT Set was defined as all randomized subjects who received at least 1 dose of the study drug.	
Subject analysis set title	Per-Protocol Analysis Set (PPS)
Subject analysis set type	Per protocol
Subject analysis set description:	
The PPS was a subset of the ITT that included subjects who completed Week 76 and did not have any major protocol deviation, ie, deviations that would affect the evaluation of the primary objectives of the study.	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Analysis Set included all randomized subjects who received at least 1 dose of the drug during the study. The Safety Analysis Set, used for analysis of safety data, was identical to the ITT Analysis Set.	

Reporting group values	Randomized Set	Intention-to-Treat (ITT)	Per-Protocol Analysis Set (PPS)
Number of subjects	21	21	14
Age categorical			
Age greater than or equal to 50 and less than or equal to 85 years.			
Units: Subjects			
Adults (18-64 years)	5	5	3
From 65-84 years	16	16	11
Gender categorical Units: Subjects			
Female	11	11	8
Male	10	10	6

Reporting group values	Safety Analysis Set		
Number of subjects	21		
Age categorical			
Age greater than or equal to 50 and less than or equal to 85 years.			
Units: Subjects			
Adults (18-64 years)	5		
From 65-84 years	16		
Gender categorical Units: Subjects			
Female	11		
Male	10		

End points

End points reporting groups

Reporting group title	Treatment
Reporting group description: Subjects receiving 8 doses of ACI-24 (week 0, 4, 8, 12, 24, 36, 48 and 74)	
Reporting group title	Placebo
Reporting group description: Subjects receiving 8 doses of Placebo (week 0, 4, 8, 12, 24, 36, 48 and 74).	
Subject analysis set title	Randomized Set
Subject analysis set type	Full analysis
Subject analysis set description: The Randomized Set was used to describe all randomized subjects whether or not they received study drug	
Subject analysis set title	Intention-to-Treat (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description: The ITT Set was defined as all randomized subjects who received at least 1 dose of the study drug.	
Subject analysis set title	Per-Protocol Analysis Set (PPS)
Subject analysis set type	Per protocol
Subject analysis set description: The PPS was a subset of the ITT that included subjects who completed Week 76 and did not have any major protocol deviation, ie, deviations that would affect the evaluation of the primary objectives of the study.	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description: The Safety Analysis Set included all randomized subjects who received at least 1 dose of the drug during the study. The Safety Analysis Set, used for analysis of safety data, was identical to the ITT Analysis Set.	

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[1]
End point description: For Intention-to-treat (ITT) analysis set: MSD Free Anti-Abeta1-42 IgG, Serum (AU/mL) - change from baseline at week 52	
End point type	Primary
End point timeframe: Baseline - Week 52	

Notes:

[1] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	3		
Units: AU/ml				
arithmetic mean (standard deviation)	-17.25 (± 54.681)	-22.17 (± 38.394)		

Statistical analyses

No statistical analyses for this end point

Primary: Overview of Adverse Events, Safety analyses set

End point title	Overview of Adverse Events, Safety analyses set[2]

End point description:

Safety analyses set: All AEs and AEs related to global assessment of tolerability; physical and neurological examination results; vital signs; suicidal ideation/behavior; MRI results; electrocardiogram (ECG); routine hematology and biochemistry evaluation in blood and urine; inflammatory markers in blood and CSF.
The table shows number of subjects, who were affected by the respective adverse events.

End point type	Primary

End point timeframe:

Visit 1 until end of study participation of each individual subject

Notes:

[2] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	7		
Units: number of respective results				
Any AE	14	7		
Any treatment-related AE	4	1		
Any severe AE	1	0		
Any serious AE	3	2		
Any AE leading to study drug discontinuation	1	1		
Any AE leading to early termination	1	1		
Any serious treatment-related AE	0	0		
Any treat.-rel. AE lead. to study drug disc.	0	0		
Any treat.-rel. AE lead. to early termination	0	0		
Any AE leading to death	0	0		

Attachments (see zip file)	ACI-24-1801_CSR_Table_14.3.1.1.pdf ACI-24-1801_CSR_Tables_14.3.1.2-4.pdf

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[3]

End point description:

For Intention-to-treat (ITT) analysis set: MSD Free Anti-Abeta1-42 IgG, Serum (AU/mL) - change from baseline at week 2

End point type	Primary

End point timeframe:

Baseline - Week 2

Notes:

[3] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	7		
Units: AU/ml				
arithmetic mean (standard deviation)	-13.5 (± 45.698)	36.86 (± 93.698)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[4]

End point description:

For Intention-to-treat (ITT) analysis set: MSD Free Anti-Abeta1-42 IgG, Serum (AU/mL); change from baseline at week 4

End point type	Primary

End point timeframe:

Baseline - Week 4

Notes:

[4] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	6		
Units: AU/ml				
arithmetic mean (standard deviation)	-4.79 (± 40.794)	9.83 (± 40.881)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[5]

End point description:

For Intention-to-treat (ITT) analysis set: MSD Free Anti-Abeta1-42 IgG, Serum (AU/mL); change week 6 - baseline

End point type	Primary

End point timeframe:

Baseline - week 6

Notes:

[5] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	6		
Units: AU/ml				
arithmetic mean (standard deviation)	-15.36 (± 41.715)	-4.33 (± 22.520)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 induction of anti-Aβ antibody responses in serum[6]

End point description:

For Intention-to-treat (ITT) analysis set: MSD Free Anti-Abeta1-42 IgG, Serum (AU/mL); change from baseline at week 8

End point type	Primary

End point timeframe:

Baseline - week 8

Notes:

[6] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	6		
Units: AU/ml				
arithmetic mean (standard deviation)	-12.43 (± 28.149)	7.0 (± 24.538)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[7]

End point description:

For Intention-to-treat (ITT) analysis set: MSD Free Anti-Abeta1-42 IgG, Serum (AU/mL); change from baseline at week 10

End point type	Primary

End point timeframe:

Baseline - Week 10

Notes:

[7] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	5		
Units: AU/ml				
arithmetic mean (standard deviation)	0.93 (± 46.425)	-9.00 (± 15.807)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[8]

End point description:

For Intention-to-treat (ITT) analysis set: MSD Free Anti-Abeta1-42 IgG, Serum (AU/mL); change from baseline at week 12

End point type	Primary

End point timeframe:

Baseline - Week 12

Notes:

[8] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	6		
Units: AU/ml				
arithmetic mean (standard deviation)	-9.29 (± 25.150)	-10.00 (± 76.389)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[9]

End point description:

For Intention-to-treat (ITT) analysis set: MSD Free Anti-Abeta1-42 IgG, Serum (AU/mL); change from baseline at week 14

End point type	Primary

End point timeframe:

Baseline - Week 14

Notes:

[9] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	5		
Units: AU/ml				
arithmetic mean (standard deviation)	10.58 (± 38.195)	-2.10 (± 15.299)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[10]

End point description:

For Intention-to-treat (ITT) analysis set: MSD free Anti-Abeta1-42 IgG, Serum (AU/mL); change from baseline at week 24

End point type	Primary

End point timeframe:

Baseline - Week 24

Notes:

[10] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	5		
Units: AU/ml				
arithmetic mean (standard deviation)	-13.77 (± 44.965)	20.30 (± 40.724)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[11]

End point description:

For Intention-to-treat (ITT) analysis set: MSD Free Anti-Abeta1-42 IgG, Serum (AU/mL); change from baseline at week 26

End point type	Primary

End point timeframe:

Baseline - Week 26

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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	5		
Units: AU/ml				
arithmetic mean (standard deviation)	-12.31 (± 28.724)	6.50 (± 51.118)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[12]

End point description:

For Intention-to-treat (ITT) analysis set: MSD Free Anti-Abeta1-42 IgG, Serum (AU/mL); change from baseline at week 36

End point type	Primary

End point timeframe:

Baseline - Week 36

Notes:

[12] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	5		
Units: AU/ml				
arithmetic mean (standard deviation)	-24.46 (± 37.852)	-5.90 (± 24.527)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[13]

End point description:

For Intention-to-treat (ITT) analysis set: MSD Free Anti-Abeta1-42 IgG, Serum (AU/mL); change from baseline at week 38

End point type	Primary

End point timeframe:

Baseline - Week 38

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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	5		
Units: AU/ml				
arithmetic mean (standard deviation)	-27.62 (± 45.864)	-1.50 (± 11.325)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[14]

End point description:

For Intention-to-treat (ITT) analysis set: MSD Free Anti-Abeta1-42 IgG, Serum (AU/mL); change from baseline at week 48

End point type	Primary

End point timeframe:

Basline - Week 48

Notes:

[14] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	5		
Units: AU/ml				
arithmetic mean (standard deviation)	-29.42 (± 42.708)	-7.90 (± 25.560)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[15]

End point description:

For Intention-to-treat (ITT) analysis set: MSD Free Anti-Abeta1-42 IgG, Serum (AU/mL); change from baseline at week 74

End point type	Primary

End point timeframe:

Baseline - Week 74

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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	5		
Units: AU/ml				
arithmetic mean (standard deviation)	-35.41 (± 62.756)	-18.10 (± 67.802)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[16]

End point description:

For Intention-to-treat (ITT) analysis set: MSD Free Anti-Abeta1-42 IgG, Serum (AU/mL); change from baseline at week 76

End point type	Primary

End point timeframe:

Baseline - Week 76

Notes:

[16] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	5		
Units: AU/ml				
arithmetic mean (standard deviation)	-23.32 (± 32.709)	-9.10 (± 34.667)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[17]

End point description:

For Intention-to-treat (ITT) analysis set: MSD Free Anti-Abeta1-42 IgG, Serum (AU/mL); change from baseline at week 87

End point type	Primary

End point timeframe:

Baseline - Week 87

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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	5		
Units: AU/ml				
arithmetic mean (standard deviation)	-13.45 (± 27.343)	7.70 (± 60.151)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[18]

End point description:

For Intention-to-treat (ITT) analysis set: MSD Free Anti-Abeta1-42 IgG, Serum (AU/mL); change from baseline at week 100

End point type	Primary

End point timeframe:

Baseline - Week 100

Notes:

[18] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	3		
Units: AU/ml				
arithmetic mean (standard deviation)	16.93 (± 114.113)	-23.50 (± 40.703)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[19]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 2

End point type	Primary

End point timeframe:

Baseline - Week 2

Notes:

[19] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	7		
Units: AU/ml				
arithmetic mean (standard deviation)	1.701 (± 3.359)	0.429 (± 0.847)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[20]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 4

End point type	Primary

End point timeframe:

Baseline - Week 4

Notes:

[20] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	6		
Units: AU/ml				
arithmetic mean (standard deviation)	0.761 (± 1.575)	-0.144 (± 0.318)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[21]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 6

End point type	Primary

End point timeframe:

Baseline - Week 6

Notes:

[21] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	6		
Units: AU/ml				
arithmetic mean (standard deviation)	0.477 (± 0.946)	-0.284 (± 0.530)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[22]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 8

End point type	Primary

End point timeframe:

Baseline - Week 8

Notes:

[22] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	6		
Units: AU/ml				
arithmetic mean (standard deviation)	0.391 (± 0.671)	0.136 (± 0.289)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[23]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 10

End point type	Primary

End point timeframe:

Baseline - Week 10

Notes:

[23] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	5		
Units: AU/ml				
arithmetic mean (standard deviation)	0.531 (± 1.057)	-0.099 (± 0.589)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[24]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 12

End point type	Primary

End point timeframe:

Baseline - Week 12

Notes:

[24] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	6		
Units: AU/ml				
arithmetic mean (standard deviation)	-0.050 (± 0.732)	-0.147 (± 0.341)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[25]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 14

End point type	Primary

End point timeframe:

Baseline - Week 14

Notes:

[25] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	5		
Units: AU/ml				
arithmetic mean (standard deviation)	0.179 (± 0.481)	0.105 (± 0.146)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[26]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 24

End point type	Primary

End point timeframe:

Baseline - Week 24

Notes:

[26] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	5		
Units: AU/ml				
arithmetic mean (standard deviation)	0.804 (± 2.542)	0.239 (± 0.558)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[27]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 26

End point type	Primary

End point timeframe:

Baseline - Week 26

Notes:

[27] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	5		
Units: AU/ml				
arithmetic mean (standard deviation)	1.596 (± 3.459)	0.089 (± 0.681)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[28]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 36

End point type	Primary

End point timeframe:

Baseline - week 36

Notes:

[28] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	5		
Units: AU/ml				
arithmetic mean (standard deviation)	-0.338 (± 0.787)	-0.500 (± 0.254)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[29]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 38

End point type	Primary

End point timeframe:

Baseline - Week 38

Notes:

[29] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	5		
Units: AU/ml				
arithmetic mean (standard deviation)	-0.117 (± 1.161)	-0.636 (± 0.486)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[30]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 48

End point type	Primary

End point timeframe:

Baseline - Week 48

Notes:

[30] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	5		
Units: AU/ml				
arithmetic mean (standard deviation)	-0.625 (± 0.581)	-0.590 (± 0.409)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[31]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 52

End point type	Primary

End point timeframe:

Baseline- Week 52

Notes:

[31] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	3		
Units: AU/ml				
arithmetic mean (standard deviation)	-0.517 (± 0.730)	-0.711 (± 0.775)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[32]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 74

End point type	Primary

End point timeframe:

Baseline - Week 74

Notes:

[32] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	5		
Units: AU/ml				
arithmetic mean (standard deviation)	-0.760 (± 0.606)	-1.198 (± 1.461)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[33]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 76

End point type	Primary

End point timeframe:

Baseline - Week 76

Notes:

[33] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	5		
Units: AU/ml				
arithmetic mean (standard deviation)	0.309 (± 3.090)	-1.142 (± 1.410)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[34]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 87

End point type	Primary

End point timeframe:

Baseline - Week 87

Notes:

[34] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	5		
Units: AU/ml				
arithmetic mean (standard deviation)	-0.626 (± 0.657)	-0.763 (± 0.937)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects of ACI-24 on induction of anti-Aβ antibody responses in serum

End point title	Effects of ACI-24 on induction of anti-Aβ antibody responses in serum[35]

End point description:

For Intention-to-treat (ITT) analysis set: Anti-Abeta1-42 IgM, Serum (AU/mL); change from baseline at week 100

End point type	Primary

End point timeframe:

Baseline - Week 100

Notes:

[35] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	5		
Units: AU/ml				
arithmetic mean (standard deviation)	-0.741 (± 0.451)	-0.795 (± 0.715)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects on Mean Composite SUVR: Brain Amyloid Beta Load Assessed by PET Amyloid at baseline, 52 Weeks (12 months) and 76 Weeks (18 months)

End point title	Effects on Mean Composite SUVR: Brain Amyloid Beta Load Assessed by PET Amyloid at baseline, 52 Weeks (12 months) and 76 Weeks (18 months)[36]

End point description:

For Intention-to-treat (ITT) analysis set: Mean Composite SUVR - Actual values at baseline

End point type	Primary

End point timeframe:

Baseline

Notes:

[36] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	7		
Units: SUVR				
arithmetic mean (standard deviation)	1.834 (± 0.227)	1.881 (± 0.296)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects on Mean Composite SUVR: Brain Amyloid Beta Load Assessed by PET Amyloid at baseline, 52 Weeks (12 months) and 76 Weeks (18 months)

End point title	Effects on Mean Composite SUVR: Brain Amyloid Beta Load Assessed by PET Amyloid at baseline, 52 Weeks (12 months) and 76 Weeks (18 months)[37]

End point description:

For Intention-to-treat (ITT) analysis set: Mean Composite SUVR - Actual values at week 52

End point type	Primary

End point timeframe:

Week 52

Notes:

[37] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	3		
Units: SUVR				
arithmetic mean (standard deviation)	1.860 (± 0.290)	1.833 (± 0.199)		

Statistical analyses

No statistical analyses for this end point

Primary: Effects on Mean Composite SUVR: Brain Amyloid Beta Load Assessed by PET Amyloid at baseline, 52 Weeks (12 months) and 76 Weeks (18 months)

End point title	Effects on Mean Composite SUVR: Brain Amyloid Beta Load Assessed by PET Amyloid at baseline, 52 Weeks (12 months) and 76 Weeks (18 months)[38]

End point description:

For Intention-to-treat (ITT) analysis set: Mean Composite SUVR - Actual values at week 76

End point type	Primary

End point timeframe:

Week 76

Notes:

[38] - 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: Only descriptive analysis were performed with no specific hypothesis

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	5		
Units: SUVR				
arithmetic mean (standard deviation)	1.848 (± 0.203)	1.926 (± 0.237)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline of Amyloid Beta 1-40 levels in CSF

End point title	Change from Baseline of Amyloid Beta 1-40 levels in CSF
End point description:	
For Intention-to-treat (ITT) analysis set: Amyloid Beta levels 1-40 - change from baseline at week 52	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	3		
Units: ng/L				
arithmetic mean (standard deviation)	377.2 (± 442.2)	-189.7 (± 361.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline of Amyloid Beta 1-40 levels in CSF

End point title	Change from Baseline of Amyloid Beta 1-40 levels in CSF
End point description:	
For Intention-to-treat (ITT) analysis set: Amyloid Beta levels 1-40 - change from baseline at week 76	
End point type	Secondary
End point timeframe:	
Week 76	

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	4		
Units: ng/L				
arithmetic mean (standard deviation)	530.4 (± 885.5)	-418.8 (± 1049.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline of Amyloid Beta 1-42 levels in CSF

End point title	Change from Baseline of Amyloid Beta 1-42 levels in CSF
End point description:	
For Intention-to-treat (ITT) analysis set: Amyloid Beta levels 1-42 - change from baseline at week 52	
End point type	Secondary
End point timeframe:	
Baseline - Week 52	

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	3		
Units: ng/L				
arithmetic mean (standard deviation)	35.7 (± 33.2)	-12.3 (± 47.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline of Amyloid Beta 1-42 levels in CSF

End point title	Change from Baseline of Amyloid Beta 1-42 levels in CSF
End point description:	
For Intention-to-treat (ITT) analysis set: Amyloid Beta levels 1-42 - change from baseline at week 76	
End point type	Secondary
End point timeframe:	
Baseline - Week 76	

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	4		
Units: ng/L				
arithmetic mean (standard deviation)	35.9 (± 44.2)	-29.0 (± 71.9)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For the purpose of safety reporting, the study period for all AEs occuring was defined as the interval between the signature of the informed consent by the subject and the end of the follow-up period (or last visit/assessment in case of early termination)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	All subjects
Reporting group description: -	
Reporting group title	Active
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	All subjects	Active	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 21 (23.81%)	3 / 14 (21.43%)	2 / 7 (28.57%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Transient ischemic attack			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19 infection			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	All subjects	Active	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 21 (100.00%)	14 / 14 (100.00%)	7 / 7 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Phlebitis superficial			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Fatigue			
subjects affected / exposed	2 / 21 (9.52%)	1 / 14 (7.14%)	1 / 7 (14.29%)
occurrences (all)	2	1	1
Feeling abnormal			

subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Gait disturbance			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Hernia			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Injection site pain			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Cough			
subjects affected / exposed	2 / 21 (9.52%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	2	2	0
Epistaxis			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Oropharyngeal pain			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	3	3	0
Pulmonary fibrosis			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Rhinitis allergic			

subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Aggression			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Agitation			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Alcohol use disorder			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Depression			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Depressive symptom			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Insomnia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Post-traumatic amnestic disorder			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Sleep disorder			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Blood creatinine increased			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	2	2	0
C-reactive protein increased			

subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Mean cell volume increased			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Platelet count increased			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Face injury			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Fall			
subjects affected / exposed	3 / 21 (14.29%)	2 / 14 (14.29%)	1 / 7 (14.29%)
occurrences (all)	7	6	1
Hand fracture			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Head injury			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Joint dislocation			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Joint injury			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	2	2	0
Procedural pain			

subjects affected / exposed	2 / 21 (9.52%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	2	2	0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Atrioventricular block			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Atrioventricular block second degree			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Cerebral microhaemorrhage			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Dementia Alzheimer's type			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Dizziness			
subjects affected / exposed	2 / 21 (9.52%)	1 / 14 (7.14%)	1 / 7 (14.29%)
occurrences (all)	3	1	2
Headache			
subjects affected / exposed	4 / 21 (19.05%)	2 / 14 (14.29%)	2 / 7 (28.57%)
occurrences (all)	4	2	2
Hypoaesthesia			
subjects affected / exposed	2 / 21 (9.52%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	3	3	0
Memory impairment			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Paraesthesia			

subjects affected / exposed	2 / 21 (9.52%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	4	4	0
Presyncope			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Sciatica			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Eye disorders			
Eye pain			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	2	2	0
Dry eye			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	2	2	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Abdominal discomfort			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	6	6	0
Colitis microscopic			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Dyspepsia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	0
Mouth ulceration			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	2
Periodontal disease			

subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	3 / 21 (14.29%)	1 / 14 (7.14%)	2 / 7 (28.57%)
occurrences (all)	4	2	2
Abdominal pain upper			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	2	2	0
Vomiting			
subjects affected / exposed	3 / 21 (14.29%)	2 / 14 (14.29%)	1 / 7 (14.29%)
occurrences (all)	3	2	1
Toothache			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Hepatobiliary disorders			
Gallbladder polyp			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	2
Hyperhidrosis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Psoriasis			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Rash			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Skin lesion			

subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Haematuria			
subjects affected / exposed	2 / 21 (9.52%)	1 / 14 (7.14%)	1 / 7 (14.29%)
occurrences (all)	3	2	1
Urinary incontinence			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 21 (19.05%)	4 / 14 (28.57%)	0 / 7 (0.00%)
occurrences (all)	4	4	0
Back pain			
subjects affected / exposed	2 / 21 (9.52%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	2	2	0
Groin pain			
subjects affected / exposed	2 / 21 (9.52%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	2	2	0
Limb mass			
subjects affected / exposed	2 / 21 (9.52%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	2	2	0
Muscle spasms			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Musculoskeletal chest pain			
subjects affected / exposed	3 / 21 (14.29%)	2 / 14 (14.29%)	1 / 7 (14.29%)
occurrences (all)	4	3	1
Musculoskeletal pain			

subjects affected / exposed	5 / 21 (23.81%)	3 / 14 (21.43%)	2 / 7 (28.57%)
occurrences (all)	6	4	2
Myalgia			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	3	3	0
Neck pain			
subjects affected / exposed	2 / 21 (9.52%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	3	3	0
Osteoarthritis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Pain in extremity			
subjects affected / exposed	3 / 21 (14.29%)	3 / 14 (21.43%)	0 / 7 (0.00%)
occurrences (all)	11	11	0
Pain in jaw			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Conjunctivitis			
subjects affected / exposed	2 / 21 (9.52%)	1 / 14 (7.14%)	1 / 7 (14.29%)
occurrences (all)	2	1	1
Gastroenteritis			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Nasopharyngitis			
subjects affected / exposed	4 / 21 (19.05%)	3 / 14 (21.43%)	1 / 7 (14.29%)
occurrences (all)	4	3	1
Oral herpes			
subjects affected / exposed	3 / 21 (14.29%)	3 / 14 (21.43%)	0 / 7 (0.00%)
occurrences (all)	5	5	0
Pneumonia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1

Rhinitis			
subjects affected / exposed	2 / 21 (9.52%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	4	4	0
Sinusitis			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Tooth infection			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	4 / 21 (19.05%)	4 / 14 (28.57%)	0 / 7 (0.00%)
occurrences (all)	5	5	0
Urinary tract infection			
subjects affected / exposed	2 / 21 (9.52%)	1 / 14 (7.14%)	1 / 7 (14.29%)
occurrences (all)	3	1	2
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Folate deficiency			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Hyperlipidaemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Hyperuricaemia			
subjects affected / exposed	1 / 21 (4.76%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 July 2018	Version 2.0: Based on Swedish Medicinal Products Agency (MPA) questions. A more suitable observation time following dose administration was added. SUSARS will be communicated to all investigators taking part in this multi-center trial in addition to the Competent Authority and Ethics Committee. End of trial, clearly defined in the protocol as 'last patient last visit'. The investigator will be required to provide a written statement to confirm that he/she has carefully assessed that the patient is able to give written informed consent.
23 August 2018	Version 3.0: The change consists of stating the types of IUDs that would be considered acceptable for use in the ACI -24-1801 clinical trial in exclusion criteria
24 October 2019	Version 4.0: The decision on expansion to 45 patients will be based on the antibody responders from the interim analysis at 12 months, including target engagement data. Modification of the eligibility criteria following the request from the Polish MoH to outline the contraceptive measures for male patients. Update of the status of ACI-24-0701 phase I study as per latest available information. Change of the instructions for Drug administration to favor the injection into the deltoid muscle of the arm. Update of the temperature conditions for Drug preparation and administration. Update of drug inventory using drug destruction on site after Sponsor's approval. Update of the vital signs measures to be aligned with the eCRF design and data capture. Use of patient diary to report adverse events and medications taken between patient-visits. Clarification on restriction of use of certain prior/concomitant medications. Extension of the screening period taking into consideration sites' feedback on the difficulty to adhere to screening window.
05 May 2020	Version 5.0 On-site visit 14 (week 52) could not be performed in 6 patients. Instead, safety assessments of V14 are replaced by a telephone interview. Where possible, the assessments skipped at V14 including Lumbar Puncture, MRI and PET scan will be performed at a later date during an unscheduled visit. As a consequence, the second interim analysis planned in patients having reached 52 weeks will be conducted in less subjects than planned. In case the results at this time point are non-conclusive, the decision to expand cohort 1 to 45 patients may be deferred to the interim analysis of 18 months at week 76. Handling of potentially delayed visits 15 to 18 is described.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to pandemic COVID-19 limitations, some post-treatment subject visits at 1 year (week 52) were not performed. Therefore, some amyloid PET scans , lumbar punctures and blood sampling were not performed.

Notes: