



Clinical trial results:

A Phase 2 Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of AL002 in Participants with Early Alzheimer's Disease

Summary

EudraCT number	2019-001476-11
Trial protocol	NL PL DE IT FR
Global end of trial date	12 September 2024

Results information

Result version number	v1
This version publication date	13 June 2025
First version publication date	13 June 2025

Trial information

Trial identification

Sponsor protocol code	AL002-2
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05744401
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 136758

Notes:

Sponsors

Sponsor organisation name	Alector Inc.
Sponsor organisation address	131 Oyster Point Boulevard, Suite 600, South San Francisco, United States, CA 94080
Public contact	Alector Medical Information, Alector Inc., +1 650-826-2454, medinfo@alector.com
Scientific contact	Alector Medical Information, Alector Inc., +1 650-826-2454, medinfo@alector.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	15 April 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 September 2024
Global end of trial reached?	Yes
Global end of trial date	12 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of AL002 in participants with Early Alzheimer's Disease (AD) in delaying disease progression compared to placebo.

Protection of trial subjects:

This trial was designed and monitored in accordance with Alector procedures, which comply with the ethical principles of Good Clinical Practice (GCP) and the International Council for Harmonisation (ICH) as required by the major regulatory authorities, and in accordance with the ethical principles that have their origins in the Declaration of Helsinki.

Background therapy:

During the study, participants continued the use of accepted prescribed medications identified during the screening procedures, in accordance with study inclusion and exclusion criteria. Any concomitant medication deemed necessary for the welfare of the participant during the study was given at the discretion of the Investigator.

Evidence for comparator:

This study is placebo-controlled and Placebo is used for comparator.

Actual start date of recruitment	07 June 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 5
Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	United States: 70
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Poland: 22
Country: Number of subjects enrolled	Spain: 54
Country: Number of subjects enrolled	United Kingdom: 55
Country: Number of subjects enrolled	France: 30
Country: Number of subjects enrolled	Germany: 31
Country: Number of subjects enrolled	Italy: 67
Worldwide total number of subjects	356
EEA total number of subjects	208

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)	78
From 65 to 84 years	278
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Approximately 328 participants were planned to be enrolled: Part 1: Approximately 40 participants were to be randomized in a 1:1:1:1 ratio to receive either 15 mg/kg AL002, 40 mg/kg AL002, 60 mg/kg AL002, or placebo. Part 2: Approximately 288 participants were to be enrolled with the same allocation ratio (1:1:1:1) used in Part 1.

Pre-assignment

Screening details:

Screening period of up to 8 weeks prior to the optional Predose Baseline Visit or to Day 1 visit.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description: -

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

Dosage and administration details:

Placebo was administered as IV infusion every 4 weeks throughout the treatment period (for at least 48 weeks (up to a total of 13 doses) and up to 96 weeks (up to a total of 25 doses).

Arm title	AL002 15 mg/kg
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	AL002
Investigational medicinal product code	
Other name	recombinant humanized agonistic TREM2 monoclonal antibody
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

15 mg/kg AL002 administered as IV infusion every 4 weeks throughout the treatment period (for at least 48 weeks (up to a total of 13 doses) and up to 96 weeks (up to a total of 25 doses).

Arm title	AL002 40 mg/kg
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	AL002
Investigational medicinal product code	
Other name	recombinant humanized agonistic TREM2 monoclonal antibody
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 mg/kg AL002 administered as IV infusion every 4 weeks throughout the treatment period (for at least 48 weeks (up to a total of 13 doses) and up to 96 weeks (up to a total of 25 doses).

Arm title	AL002 60 mg/kg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	AL002
Investigational medicinal product code	
Other name	recombinant humanized agonistic TREM2 monoclonal antibody
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

60 mg/kg AL002 administered as IV infusion every 4 weeks throughout the treatment period (for at least 48 weeks (up to a total of 13 doses) and up to 96 weeks (up to a total of 25 doses).

Number of subjects in period 1	Placebo	AL002 15 mg/kg	AL002 40 mg/kg
Started	88	97	94
Completed	72	51	53
Not completed	16	46	41
Adverse event, serious fatal	1	1	1
Adverse event, non-fatal	4	28	25
Other	2	3	1
INV Choice	1	-	2
Withdrawal	7	11	10
Use conmeds	-	1	1
Noncompliant	1	1	1
Lost follow up	-	1	-

Number of subjects in period 1	AL002 60 mg/kg
Started	77
Completed	50
Not completed	27
Adverse event, serious fatal	1
Adverse event, non-fatal	15
Other	1
INV Choice	1
Withdrawal	8
Use conmeds	-
Noncompliant	1
Lost follow up	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	AL002 15 mg/kg
Reporting group description: -	
Reporting group title	AL002 40 mg/kg
Reporting group description: -	
Reporting group title	AL002 60 mg/kg
Reporting group description: -	

Reporting group values	Placebo	AL002 15 mg/kg	AL002 40 mg/kg
Number of subjects	88	97	94
Age categorical Units: Subjects			
Adults (18-64 years)	15	24	24
From 65-84 years	73	73	70
Age continuous Units: years			
median	72.5	70.0	70.0
full range (min-max)	51 to 85	51 to 85	51 to 83
Gender categorical Units: Subjects			
Female	44	45	52
Male	44	52	42

Reporting group values	AL002 60 mg/kg	Total	
Number of subjects	77	356	
Age categorical Units: Subjects			
Adults (18-64 years)	15	78	
From 65-84 years	62	278	
Age continuous Units: years			
median	71.0	-	
full range (min-max)	51 to 85	-	
Gender categorical Units: Subjects			
Female	39	180	
Male	38	176	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	AL002 15 mg/kg
Reporting group description: -	
Reporting group title	AL002 40 mg/kg
Reporting group description: -	
Reporting group title	AL002 60 mg/kg
Reporting group description: -	
Subject analysis set title	Non-e4/e4 Set
Subject analysis set type	Intention-to-treat
Subject analysis set description: Defined as all participants who received any study treatment and were non-e4/e4 (non apolipoprotein E (APOE) epsilon 4 (e4)-homozygous (e4/e4) participants). All analyses using the Non-e4/e4 Set grouped participants according to the actual treatment received and followed the same rules as described above for the As-Treated Set.	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description: Defined as all participants who were randomized, received any amount of study drug, and were non-e4/e4. All analyses using the FAS grouped participants according to the assigned treatment. When change (or percent change) from baseline was assessed, participants were included in the analysis only if the participant had both a baseline and a post-baseline measure.	
Subject analysis set title	Per-Protocol Set (PPS)
Subject analysis set type	Per protocol
Subject analysis set description: Defined as all participants in the FAS excluding participants who met either of the following criterion: • Did not receive at least 3 doses of study drug (ie, total doses of study drug <3) • Had a major protocol deviation due to inclusion/exclusion criteria All analyses using the PPS grouped participants according to the assigned treatment. This analysis set was used for supplementary analyses of the primary efficacy endpoint.	
Subject analysis set title	Pharmacokinetic (PK) Set
Subject analysis set type	Sub-group analysis
Subject analysis set description: Defined as all participants in the As-Treated Set that received AL002, had at least 1 post-dose measurable concentration, and were non-e4/e4. The PK Set was only used for AL002 concentration descriptive summaries. All analyses using the PK Set grouped participants according to the actual treatment received and followed the same rules as described above for the As-Treated Set.	

Primary: Change from baseline in Clinical Dementia Rating-Sum of Boxes (CDR-SB) score to Weeks 24, 48, 72, and 96

End point title	Change from baseline in Clinical Dementia Rating-Sum of Boxes (CDR-SB) score to Weeks 24, 48, 72, and 96
End point description:	
End point type	Primary
End point timeframe: Up to 96 weeks	

End point values	Placebo	AL002 15 mg/kg	AL002 40 mg/kg	AL002 60 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	97	94	77
Units: percent				
arithmetic mean (standard deviation)				
Week 24	38.50 (± 50.995)	36.91 (± 55.933)	31.28 (± 55.166)	38.43 (± 64.533)
Week 48	45.58 (± 51.065)	58.49 (± 69.643)	49.24 (± 49.454)	71.88 (± 92.600)
Week 72	61.85 (± 65.893)	80.33 (± 80.625)	105.12 (± 99.989)	77.23 (± 90.706)
Week 96	102.18 (± 85.865)	97.04 (± 93.621)	88.69 (± 66.055)	80.82 (± 73.224)

Statistical analyses

Statistical analysis title	Week 24 - AL002 15 mg/kg vs. Placebo
Comparison groups	Placebo v AL002 15 mg/kg
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6282
Method	pMMRM = proportional mixed-effects model
Parameter estimate	LSM Difference
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	0.39
Variability estimate	Standard error of the mean
Dispersion value	0.266

Statistical analysis title	Week 24 - AL002 40 mg/kg vs. Placebo
Comparison groups	Placebo v AL002 40 mg/kg
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1756
Method	pMMRM = proportional mixed-effects model
Parameter estimate	LSM Difference
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.87
upper limit	0.16

Variability estimate	Standard error of the mean
Dispersion value	0.26

Statistical analysis title	Week 24 - AL002 60 mg/kg vs. Placebo
Comparison groups	Placebo v AL002 60 mg/kg
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7521
Method	pMMRM = proportional mixed-effects model
Parameter estimate	LSM Difference
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.44
Variability estimate	Standard error of the mean
Dispersion value	0.264

Statistical analysis title	Week 48 - AL002 15 mg/kg vs. Placebo
Comparison groups	Placebo v AL002 15 mg/kg
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9862
Method	pMMRM = proportional mixed-effects model
Parameter estimate	LSM Difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	0.68
Variability estimate	Standard error of the mean
Dispersion value	0.347

Statistical analysis title	Week 48 - AL002 40 mg/kg vs. Placebo
Comparison groups	Placebo v AL002 40 mg/kg

Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8407
Method	pMMRM = proportional mixed-effects model
Parameter estimate	LSM Difference
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	0.61
Variability estimate	Standard error of the mean
Dispersion value	0.347

Statistical analysis title	Week 48 - AL002 60 mg/kg vs. Placebo
Comparison groups	Placebo v AL002 60 mg/kg
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4416
Method	pMMRM = proportional mixed-effects model
Parameter estimate	LSM Difference
Point estimate	0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	0.96
Variability estimate	Standard error of the mean
Dispersion value	0.349

Statistical analysis title	Week 72 - AL002 15 mg/kg vs. Placebo
Comparison groups	Placebo v AL002 15 mg/kg
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.472
Method	pMMRM = proportional mixed-effects model
Parameter estimate	LSM Difference
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	1.32

Variability estimate	Standard error of the mean
Dispersion value	0.488

Statistical analysis title	Week 72 - AL002 40 mg/kg vs. Placebo
Comparison groups	Placebo v AL002 40 mg/kg
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1615
Method	pMMRM = proportional mixed-effects model
Parameter estimate	LSM Difference
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	1.63
Variability estimate	Standard error of the mean
Dispersion value	0.482

Statistical analysis title	Week 72 - AL002 60 mg/kg vs. Placebo
Comparison groups	Placebo v AL002 60 mg/kg
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7877
Method	pMMRM = proportional mixed-effects model
Parameter estimate	LSM Difference
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.11
upper limit	0.84
Variability estimate	Standard error of the mean
Dispersion value	0.492

Statistical analysis title	Week 96 - AL002 15 mg/kg vs. Placebo
Comparison groups	Placebo v AL002 60 mg/kg

Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6341
Method	pMMRM = proportional mixed-effects model
Parameter estimate	LSM Difference
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.61
upper limit	0.98
Variability estimate	Standard error of the mean
Dispersion value	0.653

Statistical analysis title	Week 96 - AL002 40 mg/kg vs. Placebo
Comparison groups	Placebo v AL002 40 mg/kg
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8489
Method	pMMRM = proportional mixed-effects model
Parameter estimate	LSM Difference
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.18
upper limit	1.43
Variability estimate	Standard error of the mean
Dispersion value	0.66

Statistical analysis title	Week 96 - AL002 60 mg/kg vs. Placebo
Comparison groups	Placebo v AL002 60 mg/kg
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7975
Method	pMMRM = proportional mixed-effects model
Parameter estimate	LSM Difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	1.15

Variability estimate	Standard error of the mean
Dispersion value	0.666

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs have been reported from the screening up to the end of study.

Safety findings related to AL002 treatment in this study included ARIA-E, ARIA-H, and infusion-related reactions.

Adverse event reporting additional description:

A total of 236 participants in the AL002 groups had at least 1 TEAE during the study compared to 71 participants in the placebo group. The incidence of ARIA was higher in the AL002 groups compared with the placebo group. The incidence of infusion-related reactions was also higher in the AL002 groups and increased with increasing dose of AL002.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.1
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Reporting groups

Reporting group title	Placebo
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Reporting group description: -

Reporting group title	AL002 15 mg/kg
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Reporting group description: -

Reporting group title	AL002 40 mg/kg
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Reporting group description: -

Reporting group title	AL002 60 mg/kg
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Reporting group description: -

Serious adverse events	Placebo	AL002 15 mg/kg	AL002 40 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 88 (7.95%)	14 / 97 (14.43%)	12 / 94 (12.77%)
number of deaths (all causes)	1	1	1
number of deaths resulting from adverse events	1	1	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast neoplasm			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal stromal tumour			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Hodgkin's lymphoma			

subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma	Additional description: The death was due to TEAE (treatment-emergent adverse event) and it wasn't considered related to study treatment by the investigator.		
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Diffuse large B-cell lymphoma	Additional description: The death was due to TEAE (treatment-emergent adverse event) and it wasn't considered related to study treatment by the investigator.		
subjects affected / exposed	1 / 88 (1.14%)	0 / 97 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 88 (0.00%)	2 / 97 (2.06%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 88 (1.14%)	0 / 97 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aggression			

subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Joint injury			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb traumatic amputation			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin wound			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 88 (1.14%)	0 / 97 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	1 / 88 (1.14%)	0 / 97 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Atrial fibrillation			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphasia			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			

subjects affected / exposed	1 / 88 (1.14%)	1 / 97 (1.03%)	0 / 94 (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
Dementia Alzheimer's type	Additional description: The death was due to TEAE (treatment-emergent adverse event) and it wasn't considered related to study treatment by the investigator.		
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diverticular perforation	Additional description: The death was due to TEAE (treatment-emergent adverse event) and it wasn't considered related to study treatment by the investigator.		
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Inguinal hernia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 97 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary obstruction			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			

subjects affected / exposed	1 / 88 (1.14%)	1 / 97 (1.03%)	0 / 94 (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			
Colonic abscess			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parotitis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 88 (1.14%)	0 / 97 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			

subjects affected / exposed	1 / 88 (1.14%)	0 / 97 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	AL002 60 mg/kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 77 (12.99%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast neoplasm			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal stromal tumour			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatic carcinoma	Additional description: The death was due to TEAE (treatment-emergent adverse event) and it wasn't considered related to study treatment by the investigator.		

subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diffuse large B-cell lymphoma	Additional description: The death was due to TEAE (treatment-emergent adverse event) and it wasn't considered related to study treatment by the investigator.		
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aggression			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Joint injury			

subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Limb traumatic amputation			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pelvic fracture			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Radius fracture			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin wound			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			

subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aphasia			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dementia Alzheimer's type	Additional description: The death was due to TEAE (treatment-emergent adverse event) and it wasn't considered related to study treatment by the investigator.		

subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Epilepsy			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Loss of consciousness			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Polyneuropathy			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diverticular perforation	Additional description: The death was due to TEAE (treatment-emergent adverse event) and it wasn't considered related to study treatment by the investigator.		
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Rectal haemorrhage			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Biliary obstruction			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Jaundice			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Colonic abscess			

subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Parotitis			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Escherichia bacteraemia			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	AL002 15 mg/kg	AL002 40 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 88 (72.73%)	66 / 97 (68.04%)	75 / 94 (79.79%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	11 / 88 (12.50%)	5 / 97 (5.15%)	19 / 94 (20.21%)
occurrences (all)	11	5	19
Infusion related reaction			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	9 / 94 (9.57%)
occurrences (all)	0	0	9
Radius fracture			
subjects affected / exposed	0 / 88 (0.00%)	0 / 97 (0.00%)	4 / 94 (4.26%)
occurrences (all)	0	0	4
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 88 (6.82%)	0 / 97 (0.00%)	6 / 94 (6.38%)
occurrences (all)	6	0	6
Nervous system disorders			
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
subjects affected / exposed	0 / 88 (0.00%)	28 / 97 (28.87%)	28 / 94 (29.79%)
occurrences (all)	0	28	28
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	0 / 88 (0.00%)	21 / 97 (21.65%)	22 / 94 (23.40%)
occurrences (all)	0	21	22

Headache subjects affected / exposed occurrences (all)	10 / 88 (11.36%) 10	10 / 97 (10.31%) 10	13 / 94 (13.83%) 13
Dizziness subjects affected / exposed occurrences (all)	10 / 88 (11.36%) 10	10 / 97 (10.31%) 10	14 / 94 (14.89%) 14
Syncope subjects affected / exposed occurrences (all)	6 / 88 (6.82%) 6	1 / 97 (1.03%) 1	2 / 94 (2.13%) 2
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0	0 / 97 (0.00%) 0	0 / 94 (0.00%) 0
Eye disorders Cataract subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0	7 / 97 (7.22%) 7	6 / 94 (6.38%) 6
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0	6 / 97 (6.19%) 6	8 / 94 (8.51%) 8
Nausea subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0	5 / 97 (5.15%) 5	6 / 94 (6.38%) 6
Diarrhoea subjects affected / exposed occurrences (all)	7 / 88 (7.95%) 7	8 / 97 (8.25%) 8	0 / 94 (0.00%) 0
Psychiatric disorders Confusional state subjects affected / exposed occurrences (all)	5 / 88 (5.68%) 5	1 / 97 (1.03%) 1	3 / 94 (3.19%) 3
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0	5 / 97 (5.15%) 5	0 / 94 (0.00%) 0
Arthralgia			

subjects affected / exposed occurrences (all)	6 / 88 (6.82%) 6	0 / 97 (0.00%) 0	0 / 94 (0.00%) 0
Infections and infestations			
COVID-19			
subjects affected / exposed	19 / 88 (21.59%)	11 / 97 (11.34%)	12 / 94 (12.77%)
occurrences (all)	19	11	12
Nasopharyngitis			
subjects affected / exposed	0 / 88 (0.00%)	6 / 97 (6.19%)	0 / 94 (0.00%)
occurrences (all)	0	6	0
Upper respiratory tract infection			
subjects affected / exposed	7 / 88 (7.95%)	0 / 97 (0.00%)	5 / 94 (5.32%)
occurrences (all)	7	0	5
Urinary tract infection			
subjects affected / exposed	5 / 88 (5.68%)	5 / 97 (5.15%)	0 / 94 (0.00%)
occurrences (all)	5	5	0

Non-serious adverse events	AL002 60 mg/kg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	59 / 77 (76.62%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	7 / 77 (9.09%)		
occurrences (all)	7		
Infusion related reaction			
subjects affected / exposed	10 / 77 (12.99%)		
occurrences (all)	10		
Radius fracture			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 77 (9.09%)		
occurrences (all)	7		
Nervous system disorders			
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			

subjects affected / exposed occurrences (all) Amyloid related imaging abnormality-oedema/effusion subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Syncope subjects affected / exposed occurrences (all)	21 / 77 (27.27%) 21 17 / 77 (22.08%) 17 4 / 77 (5.19%) 4 4 / 77 (5.19%) 4 1 / 77 (1.30%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	4 / 77 (5.19%) 4		
Eye disorders Cataract subjects affected / exposed occurrences (all)	7 / 77 (9.09%) 7		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	7 / 77 (9.09%) 7 9 / 77 (11.69%) 9 0 / 77 (0.00%) 0		
Psychiatric disorders Confusional state subjects affected / exposed occurrences (all)	0 / 77 (0.00%) 0		

Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all)	 0 / 77 (0.00%) 0 0 / 77 (0.00%) 0		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 13 / 77 (16.88%) 13 5 / 77 (6.49%) 5 5 / 77 (6.49%) 5 0 / 77 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 March 2021	Protocol Version 3.0 Removed the potential to drop a dose between Part 1 and Part 2; thus, the study included 3 AL002 dose arms compared to placebo. Updated the statistical methodology such that proportional mixed-effect models for repeated measures (MMRM) is the primary analysis method, and reestimated the sample size. Updated such that interim analyses were not mandatory. Specified the management of ARIA.
16 August 2021	Protocol Version 4.0 A titration period was incorporated such that newly enrolled participants randomized to 40 or 60 mg/kg would be titrated to their assigned dose over 2 or 3 doses, respectively. Additional MRI scans were added for participants in Part 1 which were to be conducted after the first dose, on Study Day 15, and before the second dose. An additional MRI scan was added for participants in Part 2 which was to be conducted after the third dose and before the fourth dose. Additional monitoring guidelines were added for participants with any evidence of ARIA, including recommendations for administration of steroids, as applicable. The option to collect an additional PET and/or LP after an occurrence of ARIA was added. The status of Study AL002-1 and study results were updated. Collection of additional optional blood samples for PK from approximately 24 Part 2 participants added; to be collected at 1 of the following timepoints: Week 25, 37 or 49. Central reads for triplicate electrocardiograms from Day 1 and Weeks 25 or 49 in approximately 100 participants added. Inclusion of criteria for administration of rescue medication for participants who experienced rapid cognitive decline. Statistical methodology updated to be consistent with the latest version of the Statistical Analysis Plan.

23 August 2022	Protocol Version 5.0 Additional information added related to ARIA risks and descriptions. Participants with the APOE e4/e4 genotype were no longer eligible for this study; added due to emerging ARIA seen in this patient population. Option for additional unscheduled MRI scans to be requested by the Sponsor for the detection and follow-up of ARIA added. Inclusion/Exclusion criteria updated for clarity, safety, and to facilitate recruitment (specific details are available in the protocol). Statistical methods updated to enhance precision of statistical analyses with revised estimands and associated analytical methods including revisions to sample size calculations, analysis sets, analyses of the primary efficacy endpoint, secondary efficacy endpoints, and interim analysis. Updated to allow participants who consented to the optional Winterlight Labs Speech Assessment (WLSA) to complete the baseline measurement either at the Predose Baseline Visit or prior to dosing on Day 1. Additional optional blood samples for PK to be collected from approximately 64 participants (previously 24) in Part 2 at 4, 8 and 24 (or 48) hours after the end of infusion at Week 25 or 37, or 49. Additional safety surveillance activities added: AEs and special situations related to Neuraceq® to be reported within 24 hours of awareness. In the event of treatment-emergent ARIA, post-randomization MRIs required and study drug dosing to be managed. Clarified that MRIs will be read by a Central Imaging Reader.
21 September 2022	Protocol Version 6.0 Exclusion criterion updated for safety (specific details are available in the protocol). Restriction on use of anticoagulant medications updated for safety. For participants who temporarily stop study drug due to ARIA-E/ARIA-H, requirement for MRI after restarting study drug (prior to second postresumption dose) added.
20 June 2023	Protocol Version 7.0 Detailed, specific content related to early ARIA cases removed and crossreference to the Investigator's Brochure maintained to ensure the most recent data are available to investigators. Estimand description for the primary efficacy endpoint updated to include change from baseline in Clinical Dementia Rating-Sum of Boxes (CDR-SB) from Weeks 24, 48, 72, and 96 to Weeks 25, 49, 73, and 97. Number of participants enrolled updated from 264 to 328 and sample size calculations updated to account for the increase. Number of sites updated to 'approximately 90 sites'. Description related to potential study drug administration in a home setting removed. Clarified that extensions to the screening period may be permitted with approval by the Sponsor for reasons other than Coronavirus disease 2019 (COVID-19) and imaging study-related delays. Inclusion/Exclusion criteria updated for clarity, safety, and to facilitate recruitment (specific details are available in the protocol). Requirement to repeat a positive PrecivityAD™-Aβ blood assessment on rescreening removed. Updated to indicate that signs and symptoms indicative of uveitis should be recorded as adverse events and followed by ophthalmology until they have resolved or uveitis ruled out. Content and references for ARIA-related symptoms and signs added for investigator awareness.

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.

None reported.

Notes: