Clinical trial results:
A Phase 3b/4 Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Verify the Clinical Benefit of Aducanumab (BIIB037) in Participants With Alzheimer's Disease

Summary

EudraCT number	2022-001671-14
Trial protocol	DE ES FI PT BE IT PL
Global end of trial date	12 August 2024

Results information

Result version number	v1 (current)
This version publication date	16 March 2025
First version publication date	16 March 2025

Trial information

Trial identification

Sponsor protocol code	221AD305

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05310071
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	225 Binney Street, Cambridge, Massachusetts, United States, 02142
Public contact	Biogen Study Medical Director, Biogen, clinicaltrials@biogen.com
Scientific contact	Biogen Study Medical Director, Biogen, clinicaltrials@biogen.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	12 August 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 August 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to verify the clinical benefit of monthly doses of aducanumab in slowing cognitive and functional impairment as measured by changes in the Clinical Dementia Rating Scale Sum of Boxes (CDR-SB) score as compared with placebo in participants with early Alzheimer's disease.

Protection of trial subjects:

Written informed consent was obtained from each subject's legally authorized representative or (e.g., legal guardian), as applicable prior to evaluations being performed for eligibility. Subjects or the subject's legally authorized representative were given adequate time to review the information in the informed consent/assent and were allowed to ask, and have answered questions concerning all portions of the conduct of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 June 2022
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	Australia: 21
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Brazil: 2
Country: Number of subjects enrolled	Canada: 53
Country: Number of subjects enrolled	Finland: 17
Country: Number of subjects enrolled	France: 74
Country: Number of subjects enrolled	Germany: 59
Country: Number of subjects enrolled	Italy: 65
Country: Number of subjects enrolled	Japan: 86
Country: Number of subjects enrolled	Korea, Republic of: 19
Country: Number of subjects enrolled	Mexico: 5
Country: Number of subjects enrolled	Poland: 110
Country: Number of subjects enrolled	Spain: 133
Country: Number of subjects enrolled	Sweden: 8
Country: Number of subjects enrolled	United Kingdom: 40
Country: Number of subjects enrolled	United States: 327

Worldwide total number of subjects	1024
EEA total number of subjects	471

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)	124
From 65 to 84 years	894
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at the investigative sites in Australia, Belgium, Brazil, Canada, Finland, France, Germany, Italy, Japan, Mexico, Poland, South Korea, Spain, Sweden, United Kingdom, and United States from 02 Jun 2022 to 12 Aug 2024.

Pre-assignment

Screening details:

A total of 1027 participants with Alzheimer's Disease (AD) were enrolled and randomised in this study. Of these, 1024 participants were dosed to receive placebo or aducanumab. None of the participants completed the study due to early termination of the study. [Change in Treatment (CIT)].

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo, once every four weeks (Q4W), administered as an intravenous (IV) infusion.

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

Dosage and administration details:

Administered as specified in the treatment arm.

Arm title	Aducanumab

Arm description:

Participants received aducanumab, up to 10 milligrams per kilogram (mg/kg) of body weight, Q4W, administered as an IV infusion.

Arm type	Experimental
Investigational medicinal product name	Aducanumab
Investigational medicinal product code	BIIB037
Other name	ADUHELM
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered as specified in the treatment arm.

Number of subjects in period 1	Placebo	Aducanumab
Started	344	680
Completed	0	0
Not completed	344	680
Adverse event, serious fatal	-	3
Reason Not Specified	1	3
Withdrawal by Participant - Relocation	1	3
Site Terminated by Sponsor	-	2
Study Terminated by Sponsor	282	559
Failure to Meet Continuation Criteria	2	-
Adverse event, non-fatal	4	31
Failure to Meet Randomization Criteria	1	2
Lack of Efficacy - Based on Participant Perception	-	2
Withdrawal by Participant - Other	25	30
Randomised by Mistake	-	1
Withdrawal by Participant - Concern About Study	2	6
Lost to follow-up	2	4
Withdrawal by Participant - Scheduling Conflicts	14	17
Withdrawal by Participant - Desire for CIT	8	17
Protocol deviation	2	-

Baseline characteristics

Subject analysis sets	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received placebo, once every four weeks (Q4W), administered as an intravenous (IV) infusion.

Subject analysis set title	Aducanumab
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received aducanumab, up to 10 milligrams per kilogram (mg/kg) of body weight, Q4W, administered as an IV infusion.

Reporting group values	Placebo	Aducanumab	
Number of subjects	344	680	
Age Categorical Units: Subjects			
Age continuous			
Full Analysis Set (FAS) included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo).			
Units: years			
arithmetic mean	72.4	72.2	
standard deviation	± 6.18	± 5.81	
Gender categorical Units: Subjects			
Male	157	327	
Female	187	353	
Race Units: Subjects			
American Indian or Alaska Native	1	0	
Asian	39	73	
Black or African American	3	9	
Native Hawaiian or Other Pacific Islander	1	0	
White	273	533	
Not Reported Due to Confidentiality Regulations	26	57	
Other	0	3	
American Indian or Alaska Native and White	0	1	
Unknown	1	4	
Ethnicity Units: Subjects			
Hispanic or Latino	27	51	
Not Hispanic or Latino	293	585	
Not Reported Due to Confidentiality Regulations	24	43	

Unknown	0	1	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo, once every four weeks (Q4W), administered as an intravenous (IV) infusion.	
Reporting group title	Aducanumab
Reporting group description:	
Participants received aducanumab, up to 10 milligrams per kilogram (mg/kg) of body weight, Q4W, administered as an IV infusion.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants received placebo, once every four weeks (Q4W), administered as an intravenous (IV) infusion.	

Subject analysis set title	Aducanumab
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants received aducanumab, up to 10 milligrams per kilogram (mg/kg) of body weight, Q4W, administered as an IV infusion.	

Primary: Change From Baseline in Clinical Dementia Rating Scale - Sum of Boxes (CDR-SB) Score at Week 78

End point title	Change From Baseline in Clinical Dementia Rating Scale - Sum of Boxes (CDR-SB) Score at Week 78[1]
End point description:	
The Clinical Dementia Rating Scale integrates assessments from 3 domains of cognition (memory, orientation, judgment/problem-solving) and 3 domains of function (community affairs, home/hobbies, personal care). Following the caregiver interview and systematic participant examination, the rater assigns a score describing the participant's current performance level in each of these domains of life functioning. The "Sum of boxes" scoring methodology sums the score for each of the 6 domains and provides a value ranging from 0 to 18. Higher scores indicate greater impairment. A positive change from baseline indicates greater impairment. FAS included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). Here, 'overall number of participants analysed' signifies the number of participants available for outcome measure analysis.	
End point type	Primary
End point timeframe:	
Baseline, Week 78	

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 statistical data were planned for this endpoint.

End point values	Placebo	Aducanumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	8		
Units: score on a scale				
arithmetic mean (standard deviation)	0.67 (± 0.408)	1.56 (± 1.635)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Integrated Alzheimer's Disease Rating Scale (iADRS) Score at Week 78

End point title	Change From Baseline in Integrated Alzheimer's Disease Rating Scale (iADRS) Score at Week 78

End point description:

The iADRS composite captures a decline in both cognition and daily function. It is a simple linear combination of Alzheimer's disease assessment scale, cognitive subscale (ADAS-Cog13), and Alzheimer's disease cooperative study scale for activities of daily living in mild cognitive impairment (ADCS-ADL-MCI). ADAS-Cog13 scale ranges from 0 to 85 (higher scores indicate worse performance) and ADCS-ADL-MCI scale ranges from 0 to 53 (higher scores indicate greater independent, healthy functioning). Total score for iADRS scale ranges from 0 to 138, where higher scores indicate better performance. A negative change from baseline indicates worse performance. FAS. Here, 'overall number of participants analysed' signifies number of participants available for outcome measure analysis. Assessment was also planned for Week 106 for this outcome measure, but no assessments were conducted at Week 106 due to early termination.

End point type	Secondary

End point timeframe:

Baseline, Week 78

End point values	Placebo	Aducanumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	5		
Units: score on a scale				
arithmetic mean (standard deviation)	-14.667 (± 4.4869)	-7.796 (± 6.7805)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Alzheimer's Disease Cooperative Study for Activities of Daily Living in Mild Cognitive Impairment (ADCS-ADL-MCI) Scale Score at Weeks 78

End point title	Change From Baseline in Alzheimer's Disease Cooperative Study for Activities of Daily Living in Mild Cognitive Impairment (ADCS-ADL-MCI) Scale Score at Weeks 78

End point description:

The ADCS-ADL-MCI scale consists of 17 instrumental items (e.g., shopping, preparing meals, using household appliances.etc.) and 1 basic item (getting dressed). Ratings reflect caregiver observations about the participant's actual functioning over the previous month and provide an assessment of change in the functional state of the participant over time. The total score ranges from 0 to 53. Higher scores indicate greater independent, healthy functioning. A positive change from baseline indicates healthy functioning while a negative change from baseline indicates a decline in independent functioning. FAS included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). Here 'overall number of participants analysed' signifies the number of participants available for outcome measure analysis. Assessment was also planned for Week 106 for this outcome measure, but no assessments were conducted at Week 106 due to early termination.

End point type	Secondary

End point timeframe:
Baseline, Week 78

End point values	Placebo	Aducanumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	5		
Units: score on a scale				
arithmetic mean (standard deviation)	-5.0 (± 3.61)	-0.4 (± 7.60)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Alzheimer's Disease Assessment Scale, Cognitive Subscale (ADAS-Cog13) at Week 78

End point title	Change From Baseline in Alzheimer's Disease Assessment Scale, Cognitive Subscale (ADAS-Cog13) at Week 78

End point description:

ADAS-Cog13 comprises both cognitive tasks and clinical ratings of cognitive performance. The cognitive subscale items capture word recall, ability to follow commands, the ability to correctly copy or draw an image, naming, the ability to interact with everyday objects, orientation, word recognition, memory, comprehension of spoken language, word-finding, and language ability, with a measure for delayed word recall and concentration/distractibility. The total score ranges from 0 to 85. Higher scores indicate worse performance. A positive change from baseline indicates decline in cognitive performance. FAS included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). Here, 'overall number of participants analysed' signifies the number of participants available for outcome measure analysis. Assessment was also planned for Week 106 for this outcome measure, but no assessments were conducted at Week 106 due to early termination.

End point type	Secondary

End point timeframe:
Baseline, Week 78

End point values	Placebo	Aducanumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	5		
Units: score on a scale				
arithmetic mean (standard deviation)	9.667 (± 0.8844)	7.396 (± 2.3262)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mini-Mental State Examination (MMSE) Scale

Score at Week 78

End point title	Change From Baseline in Mini-Mental State Examination (MMSE) Scale Score at Week 78

End point description:

The MMSE scale is a performance-based test of global cognitive status. It consists of 11 tasks that assess orientation, word recall, attention and calculation, language abilities, and visuospatial functions. The scores from the 11 tests are combined to obtain the total score, which ranges from 0 to 30. Higher scores indicate better performance. A negative change from baseline indicates decline in cognitive performance. FAS included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). Here, 'overall number of participants analysed' signifies the number of participants available for outcome measure analysis. Assessment was also planned for Week 106 for this outcome measure, but no assessments were conducted at Week 106 due to early termination.

End point type	Secondary

End point timeframe:

Baseline, Week 78

End point values	Placebo	Aducanumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	5		
Units: score on a scale				
arithmetic mean (standard deviation)	-6.0 (± 1.00)	-1.2 (± 1.48)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Tau PET Signal at Weeks 38

End point title	Change From Baseline in Tau PET Signal at Weeks 38

End point description:

The cerebral tau level was measured by tau PET imaging. Tau PET imaging was conducted using radiotracer. SUVR is a ratio of PET uptake measured in brain region of interest and a disease-free reference region. A higher SUVR is an indication of increased PET radiotracer uptake and worsening disease. FAS included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). 9999 indicates that standard deviation was not estimable as there was only 1 participant analysed. Here, ‘overall number of participants analysed’ signifies the number of participants available for outcome measure analysis. Assessment was planned for Weeks 78 and 104 for this outcome measure but was not performed due to early termination (ET). The analysis was performed at week 38, hence data for week 38 is reported here.

End point type	Secondary

End point timeframe:

Baseline, Week 38

End point values	Placebo	Aducanumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0[2]		
Units: SUVR				
arithmetic mean (standard deviation)				
Total Anterior Cingulate Cortex:Early Termination	1.130 (± 9999)	()		
Total Braak 1 and 2: Early Termination	1.320 (± 9999)	()		
Total Braak 3 and 4: Early Termination	1.270 (± 9999)	()		
Total Braak 5 and 6: Early Termination	1.150 (± 9999)	()		
Total Frontal Cortex: Early Termination	1.190 (± 9999)	()		
Total Inferior Temporal Cortex:Early Termination	1.420 (± 9999)	()		
Total Lateral Temporal Cortex: Early Termination	1.320 (± 9999)	()		
Total Medial Temporal Lobe Gray Matter: ET	1.480 (± 9999)	()		
Total Occipital Cortex: Early Termination	1.220 (± 9999)	()		
Total Parietal Cortex: Early Termination	1.110 (± 9999)	()		
Total Post Cingulate Cortex: Early Termination	1.100 (± 9999)	()		
Total Temporal Cortex: Early Termination	1.360 (± 9999)	()		

Notes:

[2] - 'Overall number of participants analysed' = number of participants available for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Neuropsychiatric Inventory-10 (NPI-10) Score at Week 78

End point title	Change From Baseline in Neuropsychiatric Inventory-10 (NPI-10) Score at Week 78

End point description:

The NPI-10 is a questionnaire administered to the informant, designed to obtain information on the presence of neuropsychiatric symptoms and behaviors in a participant with Alzheimer's disease. Ten areas are assessed: delusions, hallucinations, agitation/aggression, depression, anxiety, elation/euphoria, apathy/indifference, disinhibition, irritability and aberrant motor behavior. The NPI total score ranges from 0 to 120. Higher scores indicate greater impairment. A negative change from baseline indicates improvement (symptom reduction). FAS included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). Here, 'overall number of participants analysed' signifies the number of participants available for outcome measure analysis. Assessment was also planned for Week 106 for this outcome measure, but no assessments were conducted at Week 106 due to early termination.

End point type	Secondary

End point timeframe:

Baseline, Week 78

End point values	Placebo	Aducanumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	5		
Units: score on a scale				
arithmetic mean (standard deviation)	-8.3 (± 16.20)	-1.8 (± 6.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Amyloid Positron Emission Tomography (PET) Signal at Week 78

End point title	Change From Baseline in Amyloid Positron Emission Tomography (PET) Signal at Week 78

End point description:

Amyloid PET scan assesses cerebral amyloid load using radiotracers which is standardized into centiloids. Centiloid values on centiloid scale is based on mean composite standardized uptake value ratio (SUVR). FAS included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). 9999 indicates that standard deviation was not estimable as there was only 1 participant analysed. Here, 'overall number of participants analysed' signifies the number of participants available for outcome measure analysis. Assessment was also planned for Week 104 for this outcome measure, but no assessments were conducted at Week 104 due to early termination.

End point type	Secondary

End point timeframe:

Baseline, Week 78

End point values	Placebo	Aducanumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[3]	1		
Units: SUVR				
arithmetic mean (standard deviation)	()	-2.360 (± 9999)		

Notes:

[3] - ‘Overall number of participants analysed’ = number of participants available for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CDR-SB Score at Week 106

End point title	Change From Baseline in CDR-SB Score at Week 106

End point description:

The CDR integrates assessments from 3 domains of cognition (memory, orientation, judgment/problem-solving) and 3 domains of function (community affairs, home/hobbies, personal care). Following caregiver interview and systematic participant examination, the rater assigns a score describing the participant’s current performance level in each of these domains of life functioning. The CDR-SB sums the score for each of the 6 domains and provides a value ranging from 0 to 18. Higher scores indicate greater impairment. Positive change from baseline indicates greater impairment. Assessment was planned for Week 106 for this outcome measure, but no assessments were conducted at Week 106 due

to early termination.

End point type	Secondary

End point timeframe:

Baseline, Week 106

End point values	Placebo	Aducanumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[4] - Data is not reported for week 106 as no assessments were conducted due to the ET of the study.

[5] - Data is not reported for week 106 as no assessments were conducted due to the ET of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Global Statistical Test (GST) Composite Z-Score at Week 78

End point title	Change From Baseline in Global Statistical Test (GST) Composite Z-Score at Week 78

End point description:

GST is composite z-score defined as average of standardized z-scores of CDR-SB,ADASCog13,and ADCS-ADL-MCI.CDR-SB assess 3 cognitive (memory,orientation,judgment/problem-solving)and 3 functional(community affairs,home/hobbies,personal care)domains,with scores based on caregiver interviews and participant exams.“SB”method combines scores across 6 domains,ranging from 0-18(Higher score=greater impairment).ADAS-Cog13 evaluates cognitive tasks like word recall,naming,orientation,and memory,with a total score from 0-85(Higher score=worse performance).ADCS-ADL-MCI rates 17 instrumental tasks(e.g,shopping,preparing meal)and 1 basic task(dressing),with scores from 0-53(Higher score=greater independent,healthy functioning).A positive change from baseline indicates improvement.FAS.Overall number of participants analysed=number of participants available for outcome measure analysis.Assessment was also planned for Week 106, but no assessments were conducted due to early termination.

End point type	Secondary

End point timeframe:

Baseline, Week 78

End point values	Placebo	Aducanumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	4		
Units: z-score				
arithmetic mean (standard deviation)	0.88 (± 0.116)	0.48 (± 0.515)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to last follow-up visit (up to approximately 2 years 2 months)

Adverse event reporting additional description:

Safety analysis set included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). One participant in the placebo arm received drug. This participant was considered in Aducanumab group for safety analysis.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Aducanumab

Reporting group description:

Participants received aducanumab, up to 10 mg/kg of body weight, Q4W, administered as IV infusion.

Reporting group title	Placebo

Reporting group description:

Participants received placebo, Q4W, administered as IV infusion.

Serious adverse events	Aducanumab	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	59 / 681 (8.66%)	23 / 343 (6.71%)	
number of deaths (all causes)	3	0	
number of deaths resulting from adverse events	3	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer stage i			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal proliferative breast lesion			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Non-small cell lung cancer			
subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural mesothelioma malignant			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertensive emergency			
subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	2 / 681 (0.29%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fatigue			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			

subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Procedural pneumothorax			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	7 / 681 (1.03%)	3 / 343 (0.87%)	
occurrences causally related to treatment / all	0 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fractured sacrum			
subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			

subjects affected / exposed	2 / 681 (0.29%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Poisoning			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Bradycardia			

subjects affected / exposed	1 / 681 (0.15%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 681 (0.00%)	2 / 343 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			

subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
subjects affected / exposed	2 / 681 (0.29%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	3 / 681 (0.44%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normal pressure hydrocephalus			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological symptom			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar stroke			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic cerebral infarction			

subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 681 (0.15%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphasia			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	7 / 681 (1.03%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	7 / 7	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	2 / 681 (0.29%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			

subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	6 / 681 (0.88%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superficial siderosis of central nervous system			
subjects affected / exposed	2 / 681 (0.29%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			
subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	3 / 681 (0.44%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Covid-19			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Urinary tract infection			
subjects affected / exposed	1 / 681 (0.15%)	2 / 343 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 681 (0.15%)	0 / 343 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 681 (0.00%)	1 / 343 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Aducanumab	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	359 / 681 (52.72%)	127 / 343 (37.03%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	55 / 681 (8.08%)	32 / 343 (9.33%)	
occurrences (all)	66	36	
Nervous system disorders			
Superficial siderosis of central nervous system			
subjects affected / exposed	69 / 681 (10.13%)	5 / 343 (1.46%)	
occurrences (all)	87	5	
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	159 / 681 (23.35%)	8 / 343 (2.33%)	
occurrences (all)	228	8	
Dizziness			
subjects affected / exposed	42 / 681 (6.17%)	17 / 343 (4.96%)	
occurrences (all)	59	19	
Headache			

subjects affected / exposed	81 / 681 (11.89%)	33 / 343 (9.62%)	
occurrences (all)	123	48	
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
subjects affected / exposed	167 / 681 (24.52%)	34 / 343 (9.91%)	
occurrences (all)	238	40	
Infections and infestations			
Covid-19			
subjects affected / exposed	49 / 681 (7.20%)	19 / 343 (5.54%)	
occurrences (all)	50	21	
Nasopharyngitis			
subjects affected / exposed	42 / 681 (6.17%)	26 / 343 (7.58%)	
occurrences (all)	45	27	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 April 2022	Typographical errors were corrected in the Schedule of Assessment.

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.

The study was terminated prematurely based on the sponsor's decision.

Notes: