Clinical trial results:
Assessment of Safety, Tolerability, and Efficacy of Donanemab in Early Symptomatic Alzheimer's Disease

Summary

EudraCT number	2020-000077-25
Trial protocol	PL NL CZ
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	27 April 2024
First version publication date	27 April 2024

Trial information

Trial identification

Sponsor protocol code	I5T-MC-AACI

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04437511
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 17737

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

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	Interim
Date of interim/final analysis	14 April 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 April 2023
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The reason for this study is to see how safe and effective the study drug donanemab is in participants with early Alzheimer's disease. Additional participants will be enrolled to an addendum safety cohort. The participants will be administered open-label donanemab.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 June 2020
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: 17
Country: Number of subjects enrolled	Canada: 137
Country: Number of subjects enrolled	Czechia: 22
Country: Number of subjects enrolled	Japan: 88
Country: Number of subjects enrolled	Netherlands: 22
Country: Number of subjects enrolled	Poland: 159
Country: Number of subjects enrolled	United Kingdom: 39
Country: Number of subjects enrolled	United States: 1252
Worldwide total number of subjects	1736
EEA total number of subjects	203

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)	176
From 65 to 84 years	1531
85 years and over	29

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Not Applicable

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	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Donanemab

Arm description:

Participants received 700 milligram (mg) Donanemab every 4 weeks (Q4W) x 3 doses, then 1400 mg Q4W given intravenously (IV) for up to 72 weeks

Arm type	Experimental
Investigational medicinal product name	Donanemab
Investigational medicinal product code	
Other name	LY3002813
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 700 mg Donanemab Q4W x 3 doses, then 1400 mg Q4W given IV for up to 72 weeks.

Arm title	Placebo

Arm description:

Participants received placebo given IV.

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

Dosage and administration details:

Participants received placebo given IV.

Number of subjects in period 1	Donanemab	Placebo
Started	860	876
Received at Least One Dose of Drug	853	874
Completed	622	698
Not completed	238	178
Adverse event, serious fatal	15	10
Consent withdrawn by subject	111	94
Physician decision	19	10
Adverse event, non-fatal	50	21
Progressive Disease	4	7
Withdrawal due to Caregiver Circumstances	21	20
Lost to follow-up	11	11
Continuing Study	7	5

Baseline characteristics

Reporting groups	
Reporting group title	Donanemab
Reporting group description:	
Participants received 700 milligram (mg) Donanemab every 4 weeks (Q4W) x 3 doses, then 1400 mg Q4W given intravenously (IV) for up to 72 weeks	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo given IV.	

Reporting group values	Donanemab	Placebo	Total
Number of subjects	860	876	1736
Age categorical			
Units: Subjects			
Age continuous			
All randomized participants.			
Units: years			
arithmetic mean	72.98	73.04	
standard deviation	± 6.16	± 6.20	-
Gender categorical			
All randomized participants.			
Units: Subjects			
Female	493	503	996
Male	367	373	740
Ethnicity (NIH/OMB)			
All randomized participants.			
Units: Subjects			
Hispanic or Latino	35	36	71
Not Hispanic or Latino	583	594	1177
Unknown or Not Reported	242	246	488
Race (NIH/OMB)			
All randomized participants.			
Units: Subjects			
American Indian or Alaska Native	2	0	2
Asian	57	47	104
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	19	21	40
White	781	807	1588
More than one race	0	1	1
Unknown or Not Reported	1	0	1
Region of Enrollment			
All randomized participants.			
Units: Subjects			
Australia	13	4	17
Canada	64	73	137
Czechia	12	10	22

Japan	45	43	88
Netherlands	13	9	22
Poland	77	82	159
United Kingdom	16	23	39
United States	620	632	1252
Screening Tau Category			
All randomized participants who have only evaluable Screening Tau category data. Intermediate tau (Low-medium): All participants with baseline composite tau PET standardized uptake value ratio (SUVr) <= 1.46 and a topographic deposition pattern consistent with advanced AD (AD++) or 1.10 <= SUVr <= 1.46 and a topographic deposition pattern consistent with moderate AD (AD+). High tau: All participants with SUVr >1.46 and a topographic deposition pattern consistent with either moderate (AD+) or advanced AD (AD++).			
Units: Subjects			
Intermediate (Low-medium)	588	594	1182
High	271	281	552
Missing	1	1	2
Integrated Alzheimer's Disease Rating Scale (iADRS)			
Integrated Alzheimer's Disease Rating Scale is used to assess whether donanemab slows down the clinical decline associated with AD compared with placebo. iADRS is an integrated assessment of cognition and daily function comprised of items from the Alzheimer's disease assessment scale-cognitive subscale (ADAS-Cog13) and the Alzheimer's disease cooperative study-instrumental activities of daily living scale (ADCS-iADL). The scale ranges from 0 to 144, where lower scores indicate worse performance and higher score indicates better performance.			
Units: Score on a scale			
arithmetic mean	104.10	103.60	
standard deviation	± 14.30	± 14.02	-

End points

End points reporting groups

Reporting group title	Donanemab
Reporting group description:	
Participants received 700 milligram (mg) Donanemab every 4 weeks (Q4W) x 3 doses, then 1400 mg Q4W given intravenously (IV) for up to 72 weeks	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo given IV.	

Primary: Change from Baseline on the integrated Alzheimer’s Disease Rating Scale (iADRS) (Overall population)

End point title	Change from Baseline on the integrated Alzheimer’s Disease Rating Scale (iADRS) (Overall population)
End point description:	
Integrated Alzheimer's Disease Rating Scale is used to assess whether donanemab slows down the clinical decline associated with AD compared with placebo. iADRS is an integrated assessment of cognition and daily function comprised of items from the Alzheimer's disease assessment scale-cognitive subscale (ADAS-Cog13) and the Alzheimer's disease cooperative study-instrumental activities of daily living scale (ADCS-iADL). The scale ranges from 0 to 144, where lower scores indicate worse performance and higher score indicates better performance. Least Squares (LS) Mean value was adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction, and covariates for age at baseline, pooled investigator, baseline tau level, and baseline acetylcholinesterase inhibitor (AchI)/Memantine use. Analysis population description (APD) included all randomized participants with a baseline and at least one postbaseline iADRS data point.	
End point type	Primary
End point timeframe:	
Baseline, Week 76	

End point values	Donanemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	775	824		
Units: score on a scale				
least squares mean (standard error)	-10.19 (± 0.53)	-13.11 (± 0.50)		

Statistical analyses

Statistical analysis title	Change from Baseline on iADRS
Statistical analysis description:	
Overall population	
Comparison groups	Donanemab v Placebo

Number of subjects included in analysis	1599
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean change difference (Final Values)
Point estimate	2.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.508
upper limit	4.331
Variability estimate	Standard error of the mean
Dispersion value	0.72

Primary: Change from Baseline on the integrated Alzheimer’s Disease Rating Scale (iADRS) (Intermediate (Low-medium) Tau Population)

End point title	Change from Baseline on the integrated Alzheimer’s Disease Rating Scale (iADRS) (Intermediate (Low-medium) Tau Population)

End point description:

Integrated Alzheimer's Disease Rating Scale is used to assess whether donanemab slows down the clinical decline associated with AD compared with placebo. iADRS is an integrated assessment of cognition and daily function comprised of items from the Alzheimer's disease assessment scale-cognitive subscale (ADAS-Cog13) and the Alzheimer's disease cooperative study-instrumental activities of daily living scale (ADCS-iADL). The scale ranges from 0 to 144, where lower scores indicate worse performance and higher score indicates better performance. LS Mean value was adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction, and covariates for age at baseline, pooled investigator, and baseline AchI/Memantine use. APD included all randomized participants with baseline Intermediate Tau level and with baseline and at least one postbaseline iADRS data point.

End point type	Primary

End point timeframe:

Baseline, Week 76

End point values	Donanemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	533	560		
Units: score on a scale				
least squares mean (standard error)	-6.02 (± 0.50)	-9.27 (± 0.49)		

Statistical analyses

Statistical analysis title	Change from Baseline on iADRS

Statistical analysis description:

Intermediate (Low-medium) Tau Population

Comparison groups	Donanemab v Placebo

Number of subjects included in analysis	1093
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean change difference (Final Values)
Point estimate	3.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.883
upper limit	4.618
Variability estimate	Standard error of the mean
Dispersion value	0.7

Secondary: Change from Baseline on the Mini Mental State Examination (MMSE) Score (Overall Population)

End point title	Change from Baseline on the Mini Mental State Examination (MMSE) Score (Overall Population)

End point description:

MMSE is an instrument used to assess cognitive function (orientation, memory, attention, ability to name objects, follow verbal/written commands, write a sentence, and copy figures). Total score ranges from 0 to 30; lower score indicates greater disease severity. LS Mean value was adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction, and covariates for age at baseline, pooled investigator, baseline tau level, and baseline AchI/Memantine use. APD included all randomized participants with a baseline and at least one postbaseline MMSE data point.

End point type	Secondary

End point timeframe:

Baseline, Week 76

End point values	Donanemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	796	841		
Units: score on a scale				
least squares mean (standard error)	-2.47 (± 0.14)	-2.94 (± 0.13)		

Statistical analyses

Statistical analysis title	Change from Baseline on MMSE Score

Statistical analysis description:

Overall Population

Comparison groups	Donanemab v Placebo

Number of subjects included in analysis	1637
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	Mixed models analysis
Parameter estimate	LS Mean change difference (Final Values)
Point estimate	0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.104
upper limit	0.841
Variability estimate	Standard error of the mean
Dispersion value	0.19

Secondary: Change from Baseline on the Mini Mental State Examination (MMSE) Score (Intermediate (Low-medium) Tau Population)

End point title	Change from Baseline on the Mini Mental State Examination (MMSE) Score (Intermediate (Low-medium) Tau Population)

End point description:

MMSE is an instrument used to assess cognitive function (orientation, memory, attention, ability to name objects, follow verbal/written commands, write a sentence, and copy figures). Total score ranges from 0 to 30; lower score indicates greater disease severity. LS Mean value was adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction, and covariates for age at baseline, pooled investigator, and baseline AchI/Memantine use. APD included all randomized participants with baseline Intermediate Tau level and with baseline and at least one postbaseline MMSE data point.

End point type	Secondary

End point timeframe:

Baseline, Week 76

End point values	Donanemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	549	573		
Units: score on a scale				
least squares mean (standard error)	-1.61 (± 0.14)	-2.09 (± 0.14)		

Statistical analyses

Statistical analysis title	Change from Baseline on MMSE Score

Statistical analysis description:

Intermediate (Low-medium) Tau Population

Comparison groups	Donanemab v Placebo

Number of subjects included in analysis	1122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.016
Method	Mixed models analysis
Parameter estimate	LS Mean change difference (Final Values)
Point estimate	0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.089
upper limit	0.868
Variability estimate	Standard error of the mean
Dispersion value	0.2

Secondary: Change from Baseline on the Alzheimer's Disease Assessment Scale – Cognitive Subscale (ADAS-Cog13) (Overall Population)

End point title	Change from Baseline on the Alzheimer's Disease Assessment Scale – Cognitive Subscale (ADAS-Cog13) (Overall Population)

End point description:

The ADAS is a rater administered instrument that was designed to assess the severity of the dysfunction in the cognitive and noncognitive behaviors characteristic of persons with AD. The cognitive subscale of the ADAS-cog consists of 13 items assessing areas of cognitive function most typically impaired in AD: orientation, verbal memory, language, praxis, delayed free recall, digit cancellation. The ADAS-Cog13 scale ranges from 0 to 85. Higher scores indicate greater disease severity. LS Mean value was adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction, and covariates for age at baseline, pooled investigator, baseline tau level, and baseline AchI/Memantine use. APD included all randomized participants with a baseline and at least one postbaseline ADAS-Cog13 data point.

End point type	Secondary

End point timeframe:

Baseline, Week 76

End point values	Donanemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	797	841		
Units: score on a scale				
least squares mean (standard error)	5.46 (± 0.28)	6.79 (± 0.27)		

Statistical analyses

Statistical analysis title	Change from Baseline on ADAS-Cog13

Statistical analysis description:

Overall Population

Comparison groups	Donanemab v Placebo

Number of subjects included in analysis	1638
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006
Method	Mixed models analysis
Parameter estimate	LS Mean change difference (Final Values)
Point estimate	-1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.086
upper limit	-0.565
Variability estimate	Standard error of the mean
Dispersion value	0.39

Secondary: Change from Baseline on the Clinical Dementia Rating Scale-Sum of Boxes (CDR-SB) (Overall Population)

End point title	Change from Baseline on the Clinical Dementia Rating Scale-Sum of Boxes (CDR-SB) (Overall Population)

End point description:

CDR-SB is a semi-structured interview of participants and their caregivers. Participant's cognitive status is rated across 6 domains of functioning, including memory, orientation, judgment/problem solving, community affairs, home/hobbies, and personal care. Severity score assigned for each of 6 domains; Total score (SB) ranges from 0 to 18. Higher scores indicate greater disease severity. LS Mean value was adjusted for treatment, visit, treatment-by-visit interaction, and covariates for baseline score, baseline score-by-visit interaction, age at baseline, baseline tau category, pooled investigator, and baseline AchI/Memantine use. APD included all randomized participants with a baseline and at least one postbaseline CDR-SB data point.

End point type	Secondary

End point timeframe:

Baseline, Week 76

End point values	Donanemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	794	838		
Units: score on a scale				
least squares mean (standard error)	1.72 (± 0.096)	2.42 (± 0.092)		

Statistical analyses

Statistical analysis title	Change from Baseline on CDR-SB

Statistical analysis description:

Overall Population

Comparison groups	Donanemab v Placebo

Number of subjects included in analysis	1632
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean change difference (Final Values)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.95
upper limit	-0.45
Variability estimate	Standard error of the mean
Dispersion value	0.127

Secondary: Change from Baseline on the Alzheimer's Disease Assessment Scale – Cognitive Subscale (ADAS-Cog13) (Intermediate (Low-medium) Tau Population)

End point title	Change from Baseline on the Alzheimer's Disease Assessment Scale – Cognitive Subscale (ADAS-Cog13) (Intermediate (Low-medium) Tau Population)

End point description:

The ADAS-Cog13 is a rater administered instrument that was designed to assess the severity of the dysfunction in the cognitive and noncognitive behaviors characteristic of persons with AD. The cognitive subscale of the ADAS-Cog13 consists of 13 items assessing areas of cognitive function most typically impaired in AD: orientation, verbal memory, language, praxis, delayed free recall, digit cancellation. The ADAS-Cog13 scale ranges from 0 to 85. Higher scores indicate greater disease severity. LS Mean value was adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction, and covariates for age at baseline, pooled investigator, and baseline AchI/Memantine use. APD included all randomized participants with baseline Intermediate Tau level and with baseline and at least one postbaseline ADAS-Cog13 data point.

End point type	Secondary

End point timeframe:

Baseline, Week 76

End point values	Donanemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	550	570		
Units: score on a scale				
least squares mean (standard error)	3.17 (± 0.27)	4.69 (± 0.26)		

Statistical analyses

Statistical analysis title	Change from Baseline on ADAS-Cog13

Statistical analysis description:

Intermediate (Low-medium) Tau Population

Comparison groups	Donanemab v Placebo

Number of subjects included in analysis	1120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean change difference (Final Values)
Point estimate	-1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.25
upper limit	-0.794
Variability estimate	Standard error of the mean
Dispersion value	0.37

Secondary: Change from Baseline on the Clinical Dementia Rating Scale-Sum of Boxes (CDR-SB) (Intermediate (Low-medium) Tau Population)

End point title	Change from Baseline on the Clinical Dementia Rating Scale-Sum of Boxes (CDR-SB) (Intermediate (Low-medium) Tau Population)

End point description:

CDR-SB is a semi-structured interview of participants and their caregivers. Participant's cognitive status is rated across 6 domains of functioning, including memory, orientation, judgment/problem solving, community affairs, home/hobbies, and personal care. Severity score assigned for each of 6 domains; Total score (SB) ranges from 0 to 18. Higher scores indicate greater disease severity. LS Mean value was adjusted for treatment, visit, treatment-by-visit interaction, and covariates for baseline score, baseline score-by-visit interaction, age at baseline, pooled investigator, and baseline AchI/Memantine use. APD included all randomized participants with baseline Intermediate Tau level and with baseline and at least one postbaseline CDR-SB data point.

End point type	Secondary

End point timeframe:

Baseline, Week 76

End point values	Donanemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	546	569		
Units: score on a scale				
least squares mean (standard error)	1.20 (± 0.105)	1.88 (± 0.102)		

Statistical analyses

Statistical analysis title	Change from Baseline on CDR-SB

Statistical analysis description:

Intermediate (Low-medium) Tau Population

Comparison groups	Donanemab v Placebo

Number of subjects included in analysis	1115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean change difference (Final Values)
Point estimate	-0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.95
upper limit	-0.4
Variability estimate	Standard error of the mean
Dispersion value	0.141

Secondary: Change from Baseline on the Alzheimer's Disease Cooperative Study – instrumental Activities of Daily Living (ADCS-iADL) Score (Overall Population)

End point title	Change from Baseline on the Alzheimer's Disease Cooperative Study – instrumental Activities of Daily Living (ADCS-iADL) Score (Overall Population)

End point description:

The ADCS-ADL is a 23-item inventory developed as a rater-administered questionnaire answered by the participant's caregiver. The ADCS-ADL measures both basic and instrumental activities (instrumental activity items 6a, 7-23) of daily living by participants. The range for the ADCS-iADL is 0-59 with higher scores reflecting better performance. LS Mean value was adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction, and covariates for age at baseline, pooled investigator, baseline tau level, and baseline AchI/Memantine use. APD included all randomized participants with a baseline and at least one postbaseline ADCS-iADL data point.

End point type	Secondary

End point timeframe:

Baseline, Week 76

End point values	Donanemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	780	826		
Units: score on a scale				
least squares mean (standard error)	-4.42 (± 0.32)	-6.13 (± 0.30)		

Statistical analyses

Statistical analysis title	Change from Baseline on ADCS-iADL Score

Statistical analysis description:

Overall Population

Comparison groups	Donanemab v Placebo

Number of subjects included in analysis	1606
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean change difference (Final Values)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	2.566
Variability estimate	Standard error of the mean
Dispersion value	0.44

Secondary: Change from Baseline in Brain Amyloid Plaque Deposition as Measured by Amyloid Positron Emission Tomography (PET) Scan

End point title	Change from Baseline in Brain Amyloid Plaque Deposition as Measured by Amyloid Positron Emission Tomography (PET) Scan

End point description:

Florbetapir or florbetaben PET imaging was used as a quantitative amyloid biomarker. Amyloid PET scans at baseline and at 76 weeks after the first treatment were used to quantitatively estimate change in amyloid plaques. Quantitative amyloid burden was first formalized as the average Standardized Uptake Value Ratio (SUVR) in six predetermined cortical brain regions relative to the cerebellum as a reference region. Larger SUVR reflects the larger cortical amyloid burden relative to cerebellum. SUVR values were further calibrated to a centiloid (CL) scale. The Centiloid scale anchor points are 0 and 100, where 0 represents a high-certainty amyloid negative scan and 100 represents the amount of global amyloid deposition found in a typical AD scan. LS Mean value was adjusted for treatment, visit, treatment-by-visit interaction, and covariates for baseline score, baseline score-by-visit interaction, baseline tau category, and age at baseline.

End point type	Secondary

End point timeframe:

Baseline, Week 76
APD included all randomized participants with a baseline and at least one postbaseline amyloid PET scan data point.

End point values	Donanemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	765	812		
Units: centiloids				
least squares mean (standard error)	-87.03 (± 0.950)	-0.67 (± 0.909)		

Statistical analyses

Statistical analysis title	Change from Baseline in Brain Amyloid Plaque
Comparison groups	Donanemab v Placebo
Number of subjects included in analysis	1577
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean change difference (Final Values)
Point estimate	-86.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-88.87
upper limit	-83.87
Variability estimate	Standard error of the mean
Dispersion value	1.275

Secondary: Change from Baseline in Brain Tau Deposition as Measured by Flortaucipir F18 PET Scan

End point title	Change from Baseline in Brain Tau Deposition as Measured by Flortaucipir F18 PET Scan

End point description:

Flortaucipir PET imaging was used as a quantitative tau biomarker. Tau PET scans at baseline and at 76 weeks after the first treatment were used to quantitatively estimate change in aggregated tau neurofibrillary tangles (NFTs). Quantitative tau burden was formalized using Standardized Uptake Value Ratio (SUVR) in frontal lobe relative to the cerebellum gray as a reference region. Larger SUVR reflects larger tau burden in the frontal lobe relative to cerebellum gray. LS Mean value was adjusted for baseline score, screening tau category, age and treatment (Type III sum of squares). APD included all randomized participants with a baseline and post-baseline tau PET scan.

End point type	Secondary

End point timeframe:

Baseline, Week 76

End point values	Donanemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	578	654		
Units: standardized uptake value ratio (SUVR)				
least squares mean (standard error)	0.0401 (± 0.00398)	0.0442 (± 0.00374)		

Statistical analyses

Statistical analysis title	Change from Baseline in Brain Tau Deposition
Comparison groups	Donanemab v Placebo

Number of subjects included in analysis	1232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4522
Method	ANCOVA
Parameter estimate	LS Mean change difference (Final Values)
Point estimate	-0.0041
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0148
upper limit	0.0066

Secondary: Change from Baseline in Brain Volume as Measured by volumetric Magnetic Resonance Imaging (vMRI)

End point title	Change from Baseline in Brain Volume as Measured by volumetric Magnetic Resonance Imaging (vMRI)

End point description:

MRI scans at baseline and at 76 weeks after the first treatment were used to quantitatively estimate change in brain volume. Volumetric MRI parameters were measured in bilateral hippocampus, bilateral whole brain, and bilateral ventricles. LS Mean value was adjusted for treatment, visit, treatment-by-visit interaction, and covariates for baseline score, baseline tau category, and age at baseline. APD included all randomized participants with a baseline and at least one postbaseline vMRI data point

End point type	Secondary

End point timeframe:

Baseline, Week 76

End point values	Donanemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	786	831		
Units: cubic centimeter (cm^3)				
least squares mean (standard error)				
Bilateral Hippocampus	-0.20 (± 0.005)	-0.22 (± 0.005)		
Bilateral Whole Brain	-27.46 (± 0.409)	-20.79 (± 0.392)		
Bilateral Ventricles	10.07 (± 0.185)	7.05 (± 0.178)		

Statistical analyses

Statistical analysis title	Change from Baseline in Brain Volume by vMRI

Statistical analysis description:

Bilateral Hippocampus

Comparison groups	Donanemab v Placebo

Number of subjects included in analysis	1617
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	LS Mean change difference (Final Values)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.007

Statistical analysis title	Change from Baseline in Brain Volume by vMRI
Statistical analysis description: Bilateral Whole Brain	
Comparison groups	Donanemab v Placebo
Number of subjects included in analysis	1617
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean change difference (Final Values)
Point estimate	-6.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.76
upper limit	-5.56
Variability estimate	Standard error of the mean
Dispersion value	0.561

Statistical analysis title	Change from Baseline in Brain Volume by vMRI
Statistical analysis description: Bilateral Ventricles	
Comparison groups	Donanemab v Placebo
Number of subjects included in analysis	1617
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean change difference (Final Values)
Point estimate	3.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.52
upper limit	3.52
Variability estimate	Standard error of the mean
Dispersion value	0.256

Secondary: Change From Baseline on the Alzheimer's Disease Cooperative Study – Instrumental Activities of Daily Living (ADCS-iADL) Score (Intermediate (Low-medium) Tau Population)

End point title	Change From Baseline on the Alzheimer's Disease Cooperative Study – Instrumental Activities of Daily Living (ADCS-iADL) Score (Intermediate (Low-medium) Tau Population)

End point description:

The ADCS-ADL is a 23-item inventory developed as a rater-administered questionnaire answered by the participant's caregiver. The ADCS-ADL measures both basic and instrumental activities (instrumental activity items 6a, 7-23) of daily living by participants. The range for the ADCS-iADL is 0-59 with higher scores reflecting better performance. LS Mean value was adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction, and covariates for age at baseline, pooled investigator, and baseline AchI/Memantine use. APD included all randomized participants with a baseline Intermediate Tau level and with baseline and at least one postbaseline ADCS-iADL data point.

End point type	Secondary

End point timeframe:

Baseline, Week 76

End point values	Donanemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	535	562		
Units: score on a scale				
least squares mean (standard error)	-2.76 (± 0.34)	-4.59 (± 0.32)		

Statistical analyses

Statistical analysis title	Change from Baseline on ADAS-iADL Score

Statistical analysis description:

Intermediate (Low-medium) Tau Population

Comparison groups	Donanemab v Placebo
Number of subjects included in analysis	1097
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean change difference (Final Values)
Point estimate	1.83

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.913
upper limit	2.748
Variability estimate	Standard error of the mean
Dispersion value	0.47

Secondary: Pharmacokinetics (PK): Average Serum Concentration at Steady State of Donanemab

End point title	Pharmacokinetics (PK): Average Serum Concentration at Steady State of Donanemab[1]

End point description:

The average serum concentration at steady state, calculated as Cav = AUCtau/tau, where tau is the dosing interval (4 weeks). APD included all randomized participants who received at least one dose of study drug and had evaluable PK data.

End point type	Secondary

End point timeframe:

Predose: Week 4, 8, 12, 16, 24, 36, 52, 64; Postdose: Week 0, 12, 24, 52 and random at week 76

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK endpoint is evaluated only for Donanemab.

End point values	Donanemab			
Subject group type	Reporting group			
Number of subjects analysed	853			
Units: micrograms per milliliter (µg/mL)				
geometric mean (geometric coefficient of variation)	63 (± 32)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number or Participants with Anti-Donanemab Antibodies

End point title	Number or Participants with Anti-Donanemab Antibodies

End point description:

Number of participants with treatment-emergent positive Anti-Donanemab antibodies was summarized by treatment group. APD included all randomized participants who received at least one dose of study drug and had evaluable anti-drug antibody measurement.

End point type	Secondary

End point timeframe:

Baseline through Week 76

End point values	Donanemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	793	821		
Units: participants	693	48		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline Up To 76 Weeks plus 57 Days (Follow-up period)
Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly.

Adverse event reporting additional description:

Safety population included all randomized participants who received at least one dose of study drug. There were 25 deaths reported in subject disposition and 26 deaths in All-cause mortality, because 1 participant death occurred in the plus 57-day follow-up period was considered as completer in the study disposition period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Donanemab

Reporting group description:

Participants received 700 mg Donanemab Q4W x 3 doses, then 1400 mg Q4W given IV for up to 72 weeks.

Reporting group title	Placebo

Reporting group description:

Participants received placebo given IV.

Serious adverse events	Donanemab	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	148 / 853 (17.35%)	138 / 874 (15.79%)	
number of deaths (all causes)	16	10	
number of deaths resulting from adverse events		0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
adenocarcinoma pancreas			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
bladder cancer			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

bladder papilloma			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
breast cancer stage i			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cervix carcinoma			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed[1]	0 / 488 (0.00%)	1 / 501 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
choroid melanoma			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
diffuse large b-cell lymphoma			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
endometrial adenocarcinoma			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed[2]	1 / 488 (0.20%)	0 / 501 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
invasive ductal breast carcinoma			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
invasive lobular breast carcinoma			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
lung neoplasm malignant			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
lung adenocarcinoma stage iv			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
lymphoproliferative disorder			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
metaplastic breast carcinoma			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed[3]	0 / 488 (0.00%)	1 / 501 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
mucinous breast carcinoma			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

non-hodgkin's lymphoma			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pancreatic carcinoma			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
plasma cell myeloma			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 853 (0.23%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
prostate cancer			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed[4]	2 / 365 (0.55%)	1 / 373 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
rectal cancer			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	2 / 874 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
schwannoma			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
aortic stenosis			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
arteriosclerosis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
circulatory collapse			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
essential hypertension			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypertensive emergency			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypotension			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
labile hypertension			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

orthostatic hypotension			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	2 / 874 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
subclavian steal syndrome			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
chest pain			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
chest discomfort			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
death			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	3 / 853 (0.35%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	1 / 3	0 / 1	
medical device site pain			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
non-cardiac chest pain			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 853 (0.23%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
infusion related hypersensitivity reaction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
benign prostatic hyperplasia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed[5]	2 / 365 (0.55%)	0 / 373 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
priapism			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed[6]	1 / 365 (0.27%)	0 / 373 (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			
acute respiratory failure			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
dyspnoea			
alternative dictionary used:			

MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
haemoptysis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoxia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonitis aspiration			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumothorax			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	3 / 853 (0.35%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary embolism			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	4 / 853 (0.47%)	2 / 874 (0.23%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 0	
respiratory distress			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
respiratory arrest			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
respiratory failure			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
sleep apnoea syndrome			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
agitation			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	4 / 853 (0.47%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
alcohol abuse			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
anxiety			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
behaviour disorder			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
completed suicide			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 853 (0.23%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
confusional state			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	2 / 874 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
delirium			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	3 / 853 (0.35%)	3 / 874 (0.34%)	
occurrences causally related to treatment / all	1 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
hallucination, visual			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
mental status changes			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 853 (0.23%)	3 / 874 (0.34%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

mental disorder			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
suicide attempt			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
electrocardiogram qt prolonged			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
troponin increased			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
accidental overdose			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
anaesthetic complication			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
carbon monoxide poisoning			

alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
contusion			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
fall			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	5 / 853 (0.59%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
femur fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 853 (0.23%)	2 / 874 (0.23%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
femoral neck fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	2 / 874 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
forearm fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
head injury			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hip fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
infusion related reaction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
lower limb fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
lumbar vertebral fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
multiple fractures			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
periprosthetic fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

pelvic fracture alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
pneumothorax traumatic alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
post procedural haemorrhage alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
radius fracture alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
respiratory fume inhalation disorder alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 1		
rib fracture alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
road traffic accident alternative dictionary used: MedDRA 25.1				

subjects affected / exposed	1 / 853 (0.12%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
skin laceration			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
spinal compression fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
spinal fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
stress fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
sternal fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
subdural haematoma			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	3 / 853 (0.35%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

thoracic vertebral fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 853 (0.23%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
wrist fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	5 / 853 (0.59%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
angina pectoris			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 853 (0.23%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
atrioventricular block complete			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
atrial fibrillation			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	4 / 874 (0.46%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
bradycardia			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	1 / 853 (0.12%)	2 / 874 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiac arrest			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (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			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	2 / 874 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
myocardial infarction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
sinus bradycardia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
sinus node dysfunction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ventricular fibrillation			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
amnesia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
amyloid related imaging abnormality-oedema/effusion			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	13 / 853 (1.52%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	13 / 13	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	4 / 853 (0.47%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
balance disorder			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cerebellar infarction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cerebrovascular accident			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cervical radiculopathy			

alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dementia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dementia alzheimer's type			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 853 (0.23%)	2 / 874 (0.23%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
dizziness			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dysarthria			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
embolic stroke			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
haemorrhagic stroke			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	1 / 853 (0.12%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ischaemic cerebral infarction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ischaemic stroke			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
loss of consciousness			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
neurological symptom			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
presyncope			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	2 / 874 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
seizure			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	3 / 853 (0.35%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

subarachnoid haemorrhage			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 853 (0.23%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
syncope			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	9 / 853 (1.06%)	13 / 874 (1.49%)	
occurrences causally related to treatment / all	1 / 9	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
transient ischaemic attack			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	3 / 874 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
visual impairment			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
abdominal discomfort			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
abdominal wall haematoma			

alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
colitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
diarrhoea			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
duodenitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
enterovesical fistula			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
femoral hernia strangulated			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastric ulcer perforation			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastric antral vascular ectasia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastritis erosive			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
intestinal obstruction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
inguinal hernia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 853 (0.23%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
intestinal perforation			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

large intestine perforation			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
large intestine polyp			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
lower gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
oesophagitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
obstruction gastric			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
obstructive pancreatitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pancreatitis acute			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	2 / 853 (0.23%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pancreatitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
rectal prolapse			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
retroperitoneal haemorrhage			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
small intestinal obstruction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	3 / 853 (0.35%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
small intestinal perforation			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
upper gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatobiliary disorders			
bile duct stone			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cholecystitis acute			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cholelithiasis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
erythema			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
urticaria			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	4 / 853 (0.47%)	2 / 874 (0.23%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
chronic kidney disease			

alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
haematuria			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
nephrolithiasis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	2 / 874 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary bladder haemorrhage			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary retention			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary tract obstruction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
arthritis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
musculoskeletal chest pain			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
osteoporotic fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
rotator cuff syndrome			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	2 / 874 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
spinal stenosis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
abscess limb			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
appendicitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	2 / 874 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
appendicitis perforated			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
bacterial sepsis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
covid-19			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	9 / 853 (1.06%)	4 / 874 (0.46%)	
occurrences causally related to treatment / all	0 / 9	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
covid-19 pneumonia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	3 / 874 (0.34%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
cellulitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

cystitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
diverticulitis intestinal perforated			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
diverticulitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
enterococcal bacteraemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
escherichia sepsis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
influenza			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	2 / 874 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
pelvic abscess			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	5 / 853 (0.59%)	5 / 874 (0.57%)	
occurrences causally related to treatment / all	1 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 2	
pneumonia aspiration			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia legionella			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pyelonephritis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
sepsis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 853 (0.23%)	3 / 874 (0.34%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
staphylococcal bacteraemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

staphylococcal infection			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary tract infection			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	3 / 853 (0.35%)	4 / 874 (0.46%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary tract infection pseudomonal			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
urosepsis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (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			
decreased appetite			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dehydration			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	3 / 853 (0.35%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
diabetes mellitus inadequate control			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
diabetic ketoacidosis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypokalaemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 853 (0.12%)	0 / 874 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hyponatraemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 853 (0.23%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypovolaemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 853 (0.00%)	1 / 874 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly.
[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly.
[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly.
[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly.

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

Non-serious adverse events	Donanemab	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	567 / 853 (66.47%)	425 / 874 (48.63%)	
Injury, poisoning and procedural complications			
infusion related reaction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	73 / 853 (8.56%)	4 / 874 (0.46%)	
occurrences (all)	166	7	
fall			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	111 / 853 (13.01%)	109 / 874 (12.47%)	
occurrences (all)	149	141	
Nervous system disorders			
amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	166 / 853 (19.46%)	65 / 874 (7.44%)	
occurrences (all)	225	77	
amyloid related imaging abnormality-oedema/effusion			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	200 / 853 (23.45%)	17 / 874 (1.95%)	
occurrences (all)	270	17	
dizziness			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	52 / 853 (6.10%)	48 / 874 (5.49%)	
occurrences (all)	59	60	
headache			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	119 / 853 (13.95%)	86 / 874 (9.84%)	
occurrences (all)	188	105	
superficial siderosis of central nervous system			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	58 / 853 (6.80%)	10 / 874 (1.14%)	
occurrences (all)	84	12	
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	42 / 853 (4.92%)	45 / 874 (5.15%)	
occurrences (all)	43	68	
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	43 / 853 (5.04%)	50 / 874 (5.72%)	
occurrences (all)	51	56	
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	49 / 853 (5.74%)	41 / 874 (4.69%)	
occurrences (all)	55	44	
Infections and infestations			
covid-19			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	130 / 853 (15.24%)	150 / 874 (17.16%)	
occurrences (all)	135	157	
urinary tract infection			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	42 / 853 (4.92%)	56 / 874 (6.41%)	
occurrences (all)	52	65	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 December 2020	- Added titration period of 700 mg for first 3 doses; - Added instructions for when a participant does not complete the titration phase; - Added instructions for when a participant develops amyloid-related imaging abnormalities (ARIA).
17 February 2021	- Updated study to Phase 3; - Updated screening window and follow up and clarified notes in schedule of activities; - Clarification for scientific rationale for study design, justification for dose, Inclusion criteria, study interventions, efficacy and Clinical Safety laboratory assessments, Pharmacokinetics, Statistical considerations; - Modified language describing interim analyses, data monitoring committee (DMC) members description, -safety profile of flortaucipir.
03 September 2021	- Modified Number of Participants; - Added description of blinding for Cohorts 1 and 2; - Added and defined Cohorts 1 and 2; - Added details related to the Cohort 1 statistical analysis plan (SAP) and Study SAP; - Added "Interim analyses of Cohort 1 will be conducted by Lilly. Specified that other interim analyses involving Cohort 2 will be executed through the external data monitoring committee (DMC).
05 October 2021	- Clarification on schedule of Activities; - Modified description of primary endpoint. Added rationale and design details for long-term extension period; -Modified Inclusion Criteria; -Added recommendation of data monitoring committee (DMC); - Clarification on text regarding magnetic resonance imaging; - Clarification on time period and frequency for collecting AE and SAE Information; - Added clarifying text regarding Sample size determination; - Added details related to the Primary, secondary and tertiary/exploratory endpoint(s).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported