Clinical trial results:
A Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Efficacy and Safety Study of Gantenerumab in Patients With Early (Prodromal to Mild) Alzheimer's Disease

Summary

EudraCT number	2017-001364-38
Trial protocol	ES BE LT DE HU DK IT
Global end of trial date	17 February 2023

Results information

Result version number	v1 (current)
This version publication date	06 March 2024
First version publication date	06 March 2024

Trial information

Trial identification

Sponsor protocol code	WN29922

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03444870
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, + 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, + 41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 February 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 February 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the efficacy and safety of gantenerumab administered by subcutaneous (SC) injection compared with placebo.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form (ICF).

Background therapy:

Participants were allowed to take standard of care symptomatic treatment throughout the study i.e., cholinesterase inhibitors and/or memantine.

Evidence for comparator: -

Actual start date of recruitment	06 June 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Brazil: 30
Country: Number of subjects enrolled	Australia: 61
Country: Number of subjects enrolled	Canada: 64
Country: Number of subjects enrolled	China: 70
Country: Number of subjects enrolled	Germany: 112
Country: Number of subjects enrolled	Spain: 146
Country: Number of subjects enrolled	France: 47
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Italy: 89
Country: Number of subjects enrolled	Japan: 68
Country: Number of subjects enrolled	Lithuania: 21
Country: Number of subjects enrolled	Peru: 35
Country: Number of subjects enrolled	Russian Federation: 77
Country: Number of subjects enrolled	Taiwan: 27
Country: Number of subjects enrolled	United States: 202
Worldwide total number of subjects	1052
EEA total number of subjects	418

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)	212
From 65 to 84 years	802
85 years and over	38

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 137 sites in Australia, Brazil, Canada, China, France, Germany, Hungary, Italy, Japan, Lithuania, Peru, Russia, Taiwan, Spain, & the United States during global phase. Participants were enrolled at 21 sites in China during China extension. OLE period in China was not started as study was terminated early by Sponsor.

Pre-assignment

Screening details:

A total of 985 participants with early (prodromal to mild) Alzheimer's Disease (AD) were randomized to gantenerumab (n=499) or placebo arm (n=485) to enter double-blind treatment (DBT) period of the global phase. 68 early (prodromal to mild) AD participants were randomized in China extension phase to gantenerumab (n=35) or placebo (n=33) arm.

Period 1

Period 1 title	Double-Blind Treatment (DBT) Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The sponsor was also blinded during the DBT period.

Arms

Are arms mutually exclusive?	Yes
Arm title	Global – DBT Period: Placebo

Arm description:

Participants received gantenerumab matching placebo, SC injection, every four weeks (Q4W) up to Week 36 and then every two weeks (Q2W) up to approximately 110 weeks of the DBT period.

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

Dosage and administration details:

Gantenerumab matching placebo, SC injection, Q4W up to Week 36 and then Q2W up to approximately 114 weeks of the DBT period.

Arm title	Global – DBT Period: Gantenerumab

Arm description:

Participants received gantenerumab, SC injection with gradual up-titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and 510 mg, Q4W for 3 doses. Following this, from Week 36 onwards, participants received gantenerumab, SC injection at a dose of 510 mg, Q2W up to Week 114 of the DBT period.

Arm type	Experimental
Investigational medicinal product name	Gantenerumab
Investigational medicinal product code	RO4909832
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Gantenerumab, SC injection with gradual up-titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and 510 mg, Q4W for 3 doses, and 510 mg, Q4W for 3 doses.

After Week 36 gantenerumab, SC injection administered at a dose of 510 mg, Q2W up to Week 114 of the DBT period.

Arm title	China Extension – DBT Period: Placebo

Arm description:

Participants received gantenerumab matching placebo, SC injection, Q4W up to Week 36 and then Q2W up to approximately 110 weeks of the DBT period.

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

Dosage and administration details:

Gantenerumab matching placebo, SC injection, Q4W up to Week 36 and then Q2W up to approximately 110 weeks of the DBT period.

Arm title	China Extension – DBT Period: Gantenerumab

Arm description:

Participants received gantenerumab, SC injection with gradual up-titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and 510 mg, Q4W for 3 doses. Following this, from Week 36 onwards, participants received gantenerumab, SC injection at a dose of 510 mg, Q2W up to approximately 110 weeks of the DBT period.

Arm type	Experimental
Investigational medicinal product name	Gantenerumab
Investigational medicinal product code	RO4909832
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Gantenerumab, SC injection with gradual up-titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and 510 mg, Q4W for 3 doses. After Week 36 gantenerumab, SC injection administered at a dose of 510 mg, Q2W up to approximately 110 weeks of the DBT period.

Number of subjects in period 1	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab	China Extension – DBT Period: Placebo
Started	485	499	33
Completed	387	375	0
Not completed	98	124	33
Adverse event, serious fatal	10	2	-
Consent withdrawn by subject	56	63	2
Physician decision	3	11	-
Adverse event, non-fatal	7	29	-
Protocol Deviation	4	3	-
Study Terminated By Sponsor	-	-	30
Lost to follow-up	1	-	-

Reason not Specified	17	16	1

Number of subjects in period 1	China Extension – DBT Period: Gantenerumab
Started	35
Completed	0
Not completed	35
Adverse event, serious fatal	-
Consent withdrawn by subject	-
Physician decision	-
Adverse event, non-fatal	-
Protocol Deviation	-
Study Terminated By Sponsor	35
Lost to follow-up	-
Reason not Specified	-

Period 2

Period 2 title	Open-Label Extension (OLE) Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Global – OLE Period: Placebo (DBT) to Gantenerumab

Arm description:

Participants who received gantenerumab matching placebo in the DBT period received gantenerumab SC injections with gradual up titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and then at a dose of 510 mg, Q4W up to Week 34 of the OLE period. To maintain the blind to previous treatment assignment, participants received Q2W, SC injections, with alternate doses containing gantenerumab matching placebo.

Arm type	Experimental
Investigational medicinal product name	Gantenerumab
Investigational medicinal product code	RO4909832
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Gantenerumab SC injections with gradual up titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and then at a dose of 510 mg, Q4W up to Week 34 of the OLE period. To maintain the blind to previous treatment assignment, participants received Q2W, SC injections, with alternate doses containing gantenerumab matching placebo.

Arm title	Global – OLE Period: Gantenerumab (DBT) to Gantenerumab

Arm description:

Participants who received gantenerumab in the DBT period continued receiving gantenerumab, SC injections, 510 mg, Q2W up to Week 34 of the OLE period.

Arm type	Experimental

Investigational medicinal product name	Gantenerumab
Investigational medicinal product code	RO4909832
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Gantenerumab, SC injections, 510 mg, Q2W up to Week 34 of the OLE period.

Number of subjects in period 2[1]	Global – OLE Period: Placebo (DBT) to Gantenerumab	Global – OLE Period: Gantenerumab (DBT) to Gantenerumab
Started	10	19
Completed	7	17
Not completed	3	2
Adverse event, serious fatal	1	-
Consent withdrawn by subject	1	2
Physician decision	1	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Participants who completed the DBT Period enrolled in the OLE Period or chose to enter the safety follow-up or rolled over to the PostGraduate OLE (WN42171) study.

Baseline characteristics

Reporting groups	
Reporting group title	Global – DBT Period: Placebo
Reporting group description:	
Participants received gantenerumab matching placebo, SC injection, every four weeks (Q4W) up to Week 36 and then every two weeks (Q2W) up to approximately 110 weeks of the DBT period.	
Reporting group title	Global – DBT Period: Gantenerumab
Reporting group description:	
Participants received gantenerumab, SC injection with gradual up-titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and 510 mg, Q4W for 3 doses. Following this, from Week 36 onwards, participants received gantenerumab, SC injection at a dose of 510 mg, Q2W up to Week 114 of the DBT period.	
Reporting group title	China Extension – DBT Period: Placebo
Reporting group description:	
Participants received gantenerumab matching placebo, SC injection, Q4W up to Week 36 and then Q2W up to approximately 110 weeks of the DBT period.	
Reporting group title	China Extension – DBT Period: Gantenerumab
Reporting group description:	
Participants received gantenerumab, SC injection with gradual up-titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and 510 mg, Q4W for 3 doses. Following this, from Week 36 onwards, participants received gantenerumab, SC injection at a dose of 510 mg, Q2W up to approximately 110 weeks of the DBT period.	

Reporting group values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab	China Extension – DBT Period: Placebo
Number of subjects	485	499	33
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	72.1	71.1	65.9
standard deviation	± 7.8	± 7.9	± 8.5
Sex: Female, Male Units: participants			
Female	255	290	16
Male	230	209	17
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	18	18	0
Asian	53	52	33
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	6	1	0
White	398	414	0
More than one race	0	0	0
Unknown or Not Reported	10	14	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	58	52	0
Not Hispanic or Latino	422	439	32

Unknown or Not Reported	5	8	1

China Extension: Clinical Dementia Rating-Sum of Boxes (CDR-SB)			
CDR was derived through semi-structured interview with participant and appropriate informant. It rated impairment across 6 domains: memory,orientation,judgment,and problem solving,community affairs,home and hobbies, and personal care on a 5-point scale for which 0=no impairment, 0.5=questionable impairment, and 1, 2, and 3=mild, moderate, severe impairment respectively. The CDR-SB is based on summing each of the domain box scores with total score ranging from 0-18 with higher scores reflecting greater cognitive and functional impairment. 9999: Analysed for China extension			
Units: score on a scale			
arithmetic mean	9999	9999	3.29
standard deviation	± 9999	± 9999	± 1.22
DBT Period: CDR-SB			
CDR was derived through semi-structured interview with participant and appropriate informant. It rated impairment across 6 domains: memory,orientation,judgment,and problem solving,community affairs,home and hobbies, and personal care on a 5-point scale for which 0=no impairment, 0.5=questionable impairment, and 1, 2, and 3=mild, moderate, severe impairment respectively. The CDR-SB is based on summing each of the domain box scores with total score ranging from 0-18 with higher scores reflecting greater cognitive and functional impairment. 9999: Analysed for the global part			
Units: score on a scale			
arithmetic mean	3.71	3.71	9999
standard deviation	± 1.67	± 1.57	± 9999

Reporting group values	China Extension – DBT Period: Gantenerumab	Total	
Number of subjects	35	1052	
Age categorical			
Units: Subjects			

Age Continuous			
Units: years			
arithmetic mean	68.5		
standard deviation	± 7.3	-	
Sex: Female, Male			
Units: participants			
Female	18	579	
Male	17	473	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	36	
Asian	35	173	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	7	
White	0	812	
More than one race	0	0	
Unknown or Not Reported	0	24	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	110	
Not Hispanic or Latino	34	927	
Unknown or Not Reported	1	15	

China Extension: Clinical Dementia Rating-Sum of Boxes (CDR-SB)			
CDR was derived through semi-structured interview with participant and appropriate informant. It rated impairment across 6 domains: memory,orientation,judgment,and problem solving,community affairs,home and hobbies, and personal care on a 5-point scale for which 0=no impairment, 0.5=questionable impairment, and 1, 2, and 3=mild, moderate, severe impairment respectively. The CDR-SB is based on summing each of the domain box scores with total score ranging from 0-18 with higher scores reflecting greater cognitive and functional impairment. 9999: Analysed for China extension			
Units: score on a scale			
arithmetic mean	3.69		
standard deviation	± 1.50	-	
DBT Period: CDR-SB			
CDR was derived through semi-structured interview with participant and appropriate informant. It rated impairment across 6 domains: memory,orientation,judgment,and problem solving,community affairs,home and hobbies, and personal care on a 5-point scale for which 0=no impairment, 0.5=questionable impairment, and 1, 2, and 3=mild, moderate, severe impairment respectively. The CDR-SB is based on summing each of the domain box scores with total score ranging from 0-18 with higher scores reflecting greater cognitive and functional impairment. 9999: Analysed for the global part			
Units: score on a scale			
arithmetic mean	9999		
standard deviation	± 9999	-	

End points reporting groups

Reporting group title	Global – DBT Period: Placebo

Reporting group description:

Participants received gantenerumab matching placebo, SC injection, every four weeks (Q4W) up to Week 36 and then every two weeks (Q2W) up to approximately 110 weeks of the DBT period.

Reporting group title	Global – DBT Period: Gantenerumab

Reporting group description:

Participants received gantenerumab, SC injection with gradual up-titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and 510 mg, Q4W for 3 doses. Following this, from Week 36 onwards, participants received gantenerumab, SC injection at a dose of 510 mg, Q2W up to Week 114 of the DBT period.

Reporting group title	China Extension – DBT Period: Placebo

Reporting group description:

Participants received gantenerumab matching placebo, SC injection, Q4W up to Week 36 and then Q2W up to approximately 110 weeks of the DBT period.

Reporting group title	China Extension – DBT Period: Gantenerumab

Reporting group description:

Participants received gantenerumab, SC injection with gradual up-titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and 510 mg, Q4W for 3 doses. Following this, from Week 36 onwards, participants received gantenerumab, SC injection at a dose of 510 mg, Q2W up to approximately 110 weeks of the DBT period.

Reporting group title	Global – OLE Period: Placebo (DBT) to Gantenerumab

Reporting group description:

Participants who received gantenerumab matching placebo in the DBT period received gantenerumab SC injections with gradual up titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and then at a dose of 510 mg, Q4W up to Week 34 of the OLE period. To maintain the blind to previous treatment assignment, participants received Q2W, SC injections, with alternate doses containing gantenerumab matching placebo.

Reporting group title	Global – OLE Period: Gantenerumab (DBT) to Gantenerumab

Reporting group description:

Participants who received gantenerumab in the DBT period continued receiving gantenerumab, SC injections, 510 mg, Q2W up to Week 34 of the OLE period.

Subject analysis set title	Global – DBT Period: Gantenerumab
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received gantenerumab, SC injection with gradual up-titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and 510 mg, Q4W for 3 doses, and 510 mg, Q4W for 3 doses. Following this, from Week 36 onwards, participants received gantenerumab, SC injection at a dose of 510 mg, Q2W up to Week 114 of the DBT period.

Subject analysis set title	Global – OLE Period: Gantenerumab (DBT) to Gantenerumab
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who received gantenerumab in the DBT period continued receiving gantenerumab, SC injections, 510 mg, Q2W up to Week 34 of the OLE period.

Primary: China Extension: DBT Period: Change From Baseline to Week 116 in Global Outcome, as Measured by CDR-SB

End point title	China Extension: DBT Period: Change From Baseline to Week 116 in Global Outcome, as Measured by CDR-SB[1][2]

End point description:

CDR was derived through semi-structured interview with the participant and an appropriate informant, and it rated impairment across six domains: memory, orientation, judgment, and problem solving, community affairs, home and hobbies, and personal care on a 5-point scale for which 0=no impairment, 0.5=questionable impairment, and 1, 2, and 3=mild, moderate, and severe impairment, respectively. The CDR-SB is based on summing each of the domain box scores with total score ranging from 0-18

with higher scores reflecting greater cognitive and functional impairment. A negative change from baseline indicates improvement. The study was terminated early by the sponsor before any participant had reached Week 116 visit in the China extension phase.

End point type	Primary

End point timeframe:

Baseline, Week 116

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics were planned to be analyzed for this endpoint.

[2] - 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: The endpoint represents data for DBT period only.

End point values	China Extension – DBT Period: Placebo	China Extension – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[3]	0[4]		
Units: score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[3] - Study terminated early by sponsor before any participant reached Week 116 in China extension phase.
[4] - Study terminated early by sponsor before any participant reached Week 116 in China extension phase.

Statistical analyses

No statistical analyses for this end point

Primary: DBT Period: Change From Baseline to Week 116 in Global Outcome, as Measured by CDR-SB

End point title	DBT Period: Change From Baseline to Week 116 in Global Outcome, as Measured by CDR-SB[5]

End point description:

CDR was derived through semi-structured interview with the participant and an appropriate informant, and it rated impairment across six domains: memory, orientation, judgment, and problem solving, community affairs, home and hobbies, and personal care on a 5-point scale for which 0=no impairment, 0.5=questionable impairment, and 1, 2, and 3=mild, moderate, and severe impairment, respectively. The CDR-SB is based on summing each of the domain box scores with total score ranging from 0-18 with higher scores reflecting greater cognitive and functional impairment. A negative change from baseline indicates improvement. ITT analysis set included all participants randomized during the global phase, who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Baseline, Week 116

Notes:

[5] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	485	499		
Units: score on a scale				
arithmetic mean (standard error)	3.65 (± 0.16)	3.35 (± 0.14)		

Statistical analyses

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab

Statistical analysis description:

Change from Baseline was calculated based on ANCOVA analysis model which included the following covariates and stratification factors =Treatment + Baseline (BL) + Geographic Region + Disease Stage + AD Medication at BL + Apolipoprotein E, Allele e4 (APOE e4) + Baseline Alzheimer Disease Assessment Scale-Cognition Subscale 13 (ADAS-Cog13) Score + Baseline Alzheimer Disease Cooperative Study Group-Activities of Daily Living (ADCS-ADL).

Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	984
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0954
Method	ANCOVA
Parameter estimate	Difference in adjusted mean
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.18

Secondary: DBT Period: Change from Baseline to Week 116 in Alzheimer Disease Assessment Scale-Cognition Subscale 13 (ADAS-Cog13) Score

End point title	DBT Period: Change from Baseline to Week 116 in Alzheimer Disease Assessment Scale-Cognition Subscale 13 (ADAS-Cog13) Score[6]

End point description:

The ADAS-Cog13 total score includes all of the items in the ADAS-Cog11 in addition to delayed word recall and the number cancellation. For the ADAS-cog 13 the range is 0-85 (score range for Delayed Word Recall [DWR] score is 0-10 and for Number Cancellation [NC] is 0-5, thus the score is ADAS-cog 11[0-70] plus the scores for DWR and NC). A higher score indicates worse performance. A negative change from baseline indicates improvement in cognitive function. ITT analysis set included all participants randomized during the global phase, who received at least one dose of study drug. Overall number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[6] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	480	497		
Units: score on a scale				
arithmetic mean (standard error)	9.82 (± 0.57)	8.57 (± 0.47)		

Statistical analyses

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab

Statistical analysis description:

Change from BL was calculated based on ANCOVA analysis model which included the following covariates and stratification factors = Treatment + Baseline + Geographical Region + Disease Stage + AD Medication at BL + APOE e4.

Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	977
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0544
Method	ANCOVA
Parameter estimate	Difference in adjusted mean
Point estimate	-1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.52
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.65

Secondary: DBT Period: Change From Baseline to Week 116 in Alzheimer's Disease Cooperative Study- Activities of Daily Living (ADCS-ADL) Total Score

End point title	DBT Period: Change From Baseline to Week 116 in Alzheimer's Disease Cooperative Study- Activities of Daily Living (ADCS-ADL) Total Score[7]

End point description:

ADCS-ADL is a 23-item rater-administered, observer-reported outcome (ObsRO) that captures a participant’s ability to perform basic activities of daily living (e.g., eating and toileting) and more complex ADL or instrumental activities of daily living (iADL, e.g., using the telephone, managing finances, preparing a meal). Total score ranges from 0-78, with higher scores reflecting better functioning. A positive change from baseline indicates improvement. ITT analysis set included all participants randomized during the global phase, who received at least one dose of study drug. Overall number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[7] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	479	497		
Units: score on a scale				
arithmetic mean (standard error)	-12.32 (± 0.68)	-11.21 (± 0.60)		

Statistical analyses

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab

Statistical analysis description:

Change from BL was calculated based on ANCOVA analysis model which included the following covariates and stratification factors = Treatment + Baseline + Region + Disease Stage + AD Medication at BL + APOE e4.

Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	976
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1729
Method	ANCOVA
Parameter estimate	Difference in adjusted mean
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	2.7
Variability estimate	Standard error of the mean
Dispersion value	0.81

Secondary: DBT Period: Change From Baseline to Week 116 in Functional Activities Questionnaire (FAQ) Score

End point title	DBT Period: Change From Baseline to Week 116 in Functional Activities Questionnaire (FAQ) Score[8]

End point description:

FAQ is a rater-administered ObsRO (informant-based measure) that measures a participant's functional ability to perform complex higher-order activities. The observer provides performance ratings of the target person on ten complex higher-order activities. Total score that ranges from 0-30, with higher scores reflecting greater functional impairment. A negative change from baseline indicates improvement. ITT analysis set included all participants randomized during the global phase, who received at least one dose of study drug. Overall number analyzed is the number of participants with

data available for analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[8] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	479	498		
Units: score on a scale				
arithmetic mean (standard error)	8.13 (± 0.33)	7.28 (± 0.30)		

Statistical analyses

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab

Statistical analysis description:

Change from BL was calculated based on ANCOVA analysis model which included the following covariates and stratification factors = Treatment + Baseline + Geographical Region + Disease Stage + AD Medication at BL + APOE e4.

Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	977
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0425
Method	ANCOVA
Parameter estimate	Difference in adjusted mean
Point estimate	-0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.68
upper limit	-0.03
Variability estimate	Standard error of the mean
Dispersion value	0.42

Secondary: DBT Period: Change From Baseline to Week 116 in Mini-Mental State Examination (MMSE) Total Score

End point title	DBT Period: Change From Baseline to Week 116 in Mini-Mental State Examination (MMSE) Total Score[9]

End point description:

MMSE is a rater-administered performance-based outcome (PerfO) that includes a set of standardized questions used to evaluate possible cognitive impairment and help stage the severity level of this impairment. The questions target six areas: orientation, registration, attention, short-term recall, language, and constructional praxis/visuospatial abilities. Total score ranges from 0-30, with lower

scores indicating greater impairment. A positive change from baseline indicates improvement. ITT analysis set included all participants randomized during the global phase, who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[9] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	485	499		
Units: score on a scale				
arithmetic mean (standard error)	-5.18 (± 0.25)	-4.86 (± 0.23)		

Statistical analyses

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab

Statistical analysis description:

Change from Baseline was calculated based on ANCOVA analysis model which included the following covariates and stratification factors =Treatment + Baseline + Geographic Region + Disease Stage + AD Medication at BL + APOE e4.

Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	984
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2904
Method	ANCOVA
Parameter estimate	Difference in adjusted mean
Point estimate	0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.93
Variability estimate	Standard error of the mean
Dispersion value	0.31

Secondary: DBT Period: Change From Baseline to Week 116 in Verbal Fluency Task (VFT) Score

End point title	DBT Period: Change From Baseline to Week 116 in Verbal Fluency Task (VFT) Score[10]

End point description:

VFT is a rater administered PerfO that measures speed and flexibility of verbal thought with a total score that ranges from 0-99 (lower scores indicating lower performance). A positive change from baseline

indicates improvement. ITT analysis set included all participants randomized during the global phase, who received at least one dose of study drug. Overall number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[10] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	481	499		
Units: score on a scale				
arithmetic mean (standard error)	-3.46 (± 0.31)	-3.53 (± 0.30)		

Statistical analyses

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab

Statistical analysis description:

Change from BL was calculated based on ANCOVA analysis model which included the following covariates and stratification factors = Treatment + Baseline + Geographical Region + Disease Stage + AD Medication at BL + APOE e4.

Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	980
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8468
Method	ANCOVA
Parameter estimate	Difference in adjusted mean
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	0.65
Variability estimate	Standard error of the mean
Dispersion value	0.37

Secondary: DBT Period: Change From Baseline to Week 116 in Alzheimer Disease Assessment Scale-Cognition Subscale 11 (ADAS-Cog11) Score

End point title	DBT Period: Change From Baseline to Week 116 in Alzheimer Disease Assessment Scale-Cognition Subscale 11 (ADAS-Cog11) Score[11]

End point description:

ADAS-Cog11 was designed to measure cognitive symptom change in participants with Alzheimer's Disease (AD) & consisted of 11 tasks. The standard 11 items (& corresponding score range) were: word recall (0-10), commands (0-5), constructional praxis (0-5), naming objects & fingers (0-5), ideational praxis (0-5), orientation (0-8), word recognition (0-12), spoken language ability (0-5), comprehension of spoken language (0-5), word-finding difficulty (0-5), & remembering test instructions (0-5). Test included 7 performance items & 4 clinician-rated items. ADAS-Cog11 total score was sum of all 11 individual items, with total score ranging from 0 (no impairment) to 70 (severe impairment). Higher scores indicated more severe cognitive impairment. Negative change from baseline indicates improvement. ITT analysis set= all participants randomized during global phase, who received at least one dose of study drug. Overall number analyzed= number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[11] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	481	498		
Units: score on a scale				
arithmetic mean (standard error)	8.42 (± 0.52)	7.44 (± 0.43)		

Statistical analyses

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab

Statistical analysis description:

Change from BL was calculated based on ANCOVA analysis model which included the following covariates and stratification factors = Treatment + Baseline + Geographical Region + Disease Stage + AD Medication at BL + APOE e4.

Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	979
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1036
Method	ANCOVA
Parameter estimate	Difference in adjusted mean
Point estimate	-0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.14
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.6

Secondary: DBT Period: Change from Baseline to Week 116 in the Coding (Digit Symbol Substitution Test [DSST]) Subtest

End point title	DBT Period: Change from Baseline to Week 116 in the Coding (Digit Symbol Substitution Test [DSST]) Subtest[12]

End point description:

Coding, also called DSST is a rater administered PerfO that measures speed of processing and associative memory with a total score that ranges from 0-135 (lower scores indicating lower performance). The DSST was adapted from the Wechsler Adult Intelligence Scale. The 120-second version of the test was used in this study. Positive change from baseline indicates improvement. ITT analysis set included all participants randomized during the global phase, who received at least one dose of study drug. Overall number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[12] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	480	498		
Units: score on a scale				
arithmetic mean (standard error)	-6.47 (± 0.64)	-6.27 (± 0.54)		

Statistical analyses

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab

Statistical analysis description:

Change from BL was calculated based on ANCOVA analysis model which included the following covariates and stratification factors = Treatment + Baseline + Geographical Region + Disease Stage + AD Medication at BL + APOE e4.

Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	978
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.803
Method	ANCOVA
Parameter estimate	Difference in adjusted mean
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.35
upper limit	1.74

Variability estimate	Standard error of the mean
Dispersion value	0.79

Secondary: DBT Period: Number of Participants with at Least One Adverse Event (AE)

End point title	DBT Period: Number of Participants with at Least One Adverse Event (AE)[13]

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant administered a pharmaceutical product, regardless of causal attribution. Safety evaluable (SE) analysis set included all participants randomized during the global phase who received at least one dose of study drug. In the DBT period, four participants randomized to placebo arm received at least one dose of gantenerumab and were considered in the gantenerumab arm for safety analysis set.

End point type	Secondary

End point timeframe:

From Day 1 up to 14 weeks after the last dose of blinded study drug (up to 131 weeks)

Notes:

[13] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	481	503		
Units: participants	423	454		

Statistical analyses

No statistical analyses for this end point

Secondary: DBT Period: Number of Participants with Post-baseline Suicidal Ideation or Suicidal Behavior as Measured Using Columbia-Suicide Severity Rating Scale (C-SSRS)

End point title	DBT Period: Number of Participants with Post-baseline Suicidal Ideation or Suicidal Behavior as Measured Using Columbia-Suicide Severity Rating Scale (C-SSRS)[14]

End point description:

C-SSRS= used to assess lifetime suicidality of participant & any new instances of suicidality. Structured interview prompts recollection of suicidal ideation, including intensity of ideation, behavior& attempts with actual/potential lethality. Responses to categories: yes/no[Wish to be Dead;Non-specific Active Suicidal Thoughts; Active Suicidal Ideation with Any Methods without Intent to Act;Active Suicidal Ideation with Some Intent to Act, without Specific Plan;Active Suicidal Ideation with Specific Plan &Intent, Preparatory Acts &Behavior; Aborted Attempt; Interrupted Attempt; Actual Attempt (non-fatal)]; Completed Suicide. Suicidal ideation/behavior is indicated by "yes" answer to any of listed categories. Score=0, if no suicide risk is present. Score=1/higher indicates suicidal ideation/behavior. SE analysis set was used. In DBT period, 4 participants randomized to placebo received atleast 1 dose of gantenerumab & were considered in the gantenerumab arm for safety analysis set.

End point type	Secondary

End point timeframe:

From Day 1 up to 14 weeks after the last dose of blinded study drug (up to 131 weeks)

Notes:

[14] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	467	489		
Units: participants				
Suicidal Ideation: Passive	13	17		
Suicidal Ideation: Active-Nonspecific	1	3		
Suicidal Ideation: Active-Method, No Intent/Plan	6	3		
Suicidal Ideation: Active-Method&Intent; No Plan	2	0		
Suicidal Ideation: Active-Method, Intent, & Plan	2	0		
Suicidal Ideation: No Event	443	466		
Suicidal Behavior: Interrupted Attempt	0	1		
Suicidal Behavior: No Event	467	488		
Self-injurious Behavior Without Intent: No Event	467	489		

Statistical analyses

No statistical analyses for this end point

Secondary: DBT Period: Change From Baseline to Week 116 in Alzheimer's Disease Cooperative Study-Instrumental Activities of Daily Living (ADCS-iADL) Instrumental Score

End point title	DBT Period: Change From Baseline to Week 116 in Alzheimer's Disease Cooperative Study-Instrumental Activities of Daily Living (ADCS-iADL) Instrumental Score[15]

End point description:

The ADCS-iADL measures activities such as using the telephone, shopping and preparing a meal. The ADCS-iADL consists of 16 questions with a score range of 0 to 56 where a higher score represents better function. Positive change from baseline indicates improvement. ITT analysis set included all participants randomized during the global phase, who received at least one dose of study drug. Overall number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[15] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	479	497		
Units: score on a scale				
arithmetic mean (standard error)	-10.80 (± 0.56)	-9.80 (± 0.51)		

Statistical analyses

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab
Statistical analysis description:	
Change from BL was calculated based on ANCOVA analysis model which included the following covariates and stratification factors = Treatment + Baseline + Geographical Region + Disease Stage + AD Medication at BL + APOE e4.	
Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	976
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1439
Method	ANCOVA
Parameter estimate	Difference in adjusted mean
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	2.34
Variability estimate	Standard error of the mean
Dispersion value	0.68

Secondary: DBT Period: Number of Participants with Injection-Site Reactions

End point title	DBT Period: Number of Participants with Injection-Site Reactions[16]
End point description:	
An AE is any unfavorable and unintended sign, symptom, or disease temporally associated with the use of an investigational product or other protocol-imposed intervention, regardless of attribution. Local injection reactions (or injection site reactions) are defined as AEs related to the injection site that occur during or within 24 hours after study drug administration that are judged to be related to the study drug injection. SE analysis set included all participants randomized during the global phase who received at least one dose of study drug. In the DBT period, four participants randomized to placebo arm received at least one dose of gantenerumab and were considered in the gantenerumab arm for safety analysis set.	
End point type	Secondary
End point timeframe:	
From Day 1 up to 14 weeks after the last dose of blinded study drug (up to 131 weeks)	

Notes:

[16] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	481	503		
Units: participants	43	94		

Statistical analyses

No statistical analyses for this end point

Secondary: DBT Period: Number of Participants with Anti-Drug Antibodies (ADA) to Gantenerumab

End point title	DBT Period: Number of Participants with Anti-Drug Antibodies (ADA) to Gantenerumab

End point description:

The number of participants with positive results for ADA against gantenerumab at any of the post-baseline assessment time-points were reported. Participant with an ADA assay result from at least one post-baseline sample was defined as a post-baseline evaluable participant. Treatment Emergent ADA = A participant with a negative or missing baseline ADA result(s) and at least one positive post-baseline ADA result. SE analysis set included all participants randomized during the global phase who received at least one dose of study drug. In the DBT period, four participants randomized to placebo arm received at least one dose of gantenerumab and were considered in the gantenerumab arm for safety analysis set. Overall number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

From Day 1 up to 14 weeks after the last dose of blinded study drug (up to 131 weeks)

End point values	Global – DBT Period: Gantenerumab			
Subject group type	Subject analysis set			
Number of subjects analysed	489			
Units: participants	10			

Statistical analyses

No statistical analyses for this end point

Secondary: DBT Period: Number of Participants with at Least One Amyloid-Related Imaging Abnormalities-Haemosiderin Deposition (ARIA-H) MRI Finding

End point title	DBT Period: Number of Participants with at Least One Amyloid-Related Imaging Abnormalities-Haemosiderin Deposition

	(ARIA-H) MRI Finding[17]

End point description:

ARIA are an identified risk with anti-amyloid antibodies, including gantenerumab. These changes can be identified on brain MRI. ARIA-H (H for hemosiderosis) are small foci of signal loss observed on MRI sequences sensitive for paramagnetic tissue properties and comprise cerebral microbleeds (small foci of bleeding in the brain parenchyma) and leptomeningeal hemosiderosis (small foci of bleeding on the surface of the brain). These changes also occur sporadically in AD. SEMRI analysis set included all participants in the SE analysis set who had at least one post-baseline safety MRI scan.

End point type	Secondary

End point timeframe:

From Day 1 up to 14 weeks after the last dose of blinded study drug (up to 131 weeks)

Notes:

[17] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	476	497		
Units: participants	6	40		

Statistical analyses

No statistical analyses for this end point

Secondary: DBT Period: Number of Participants with at Least One Amyloid-Related Imaging Abnormalities-Edema (ARIA-E) Magnetic Resonance Imaging (MRI) Finding

End point title	DBT Period: Number of Participants with at Least One Amyloid-Related Imaging Abnormalities-Edema (ARIA-E) Magnetic Resonance Imaging (MRI) Finding[18]

End point description:

ARIA are an identified risk with anti-amyloid antibodies, including gantenerumab. These changes can be identified on brain MRI. In ARIA-E, (E for oedema or effusion), oedema can be seen in different areas of the brain on MRI, representing fluid leakage into the brain parenchyma or sulcal spaces. Safety Magnetic Resonance Imaging (MRI)-evaluable (SEMRI) analysis set included all participants in the SE analysis set who had at least one post-baseline safety MRI scan.

End point type	Secondary

End point timeframe:

From Day 1 up to 14 weeks after the last dose of blinded study drug (up to 131 weeks)

Notes:

[18] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	476	497		
Units: participants	5	105		

Statistical analyses

No statistical analyses for this end point

Secondary: DBT Period: Change from Baseline to Week 116 in Brain Amyloid Load as Measured by Amyloid Positron Emission Tomography (PET) Scan in a Subset of Participants

End point title	DBT Period: Change from Baseline to Week 116 in Brain Amyloid Load as Measured by Amyloid Positron Emission Tomography (PET) Scan in a Subset of Participants[19]

End point description:

Brain amyloid load over time was assessed using [18F] florbetaben or [18F] flutemetamol tracers. These are PET radioligand selective to amyloid. Amyloid PET burden was measured in composite region of interest by using standardized uptake value ratio (SUVR) mapped to centiloid scale. Centiloid scale anchor points are 0 & 100, where 0=high-certainty amyloid negative scan & 100=amount of global amyloid deposition found in typical AD scan. Amyloid-PET modified ITT (mITT) analysis set= all participants in ITT analysis set who participated in Amyloid-PET substudy & who had at least 1 Amyloid-PET scan with valid quantitative measurement performed with either florbetaben or flutemetamol & who did not withdraw from Amyloid-PET substudy before randomization. Overall number analyzed is number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[19] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	49		
Units: score on a scale				
arithmetic mean (standard error)	9.06 (± 3.046)	-57.38 (± 2.841)		

Statistical analyses

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab

Statistical analysis description:

Change from BL was calculated based on mixed-effect model of repeated measure which included the following covariates and stratification factors = Baseline + APOE e4 status + Type of Tracer + Analysis Visit + Treatment + Treatment*Analysis Visit + Analysis Visit*Baseline.

Comparison groups	Global – DBT Period: Placebo v Global – DBT Period:

	Gantenerumab
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference in adjusted means
Point estimate	-66.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-74.71
upper limit	-58.16
Variability estimate	Standard error of the mean
Dispersion value	4.171

Secondary: DBT Period: Change From Baseline to Week 116 in Brain Tau Load, as Measured by Tau PET Scan in a Subset of Participants

End point title	DBT Period: Change From Baseline to Week 116 in Brain Tau Load, as Measured by Tau PET Scan in a Subset of Participants[20]

End point description:

Change in tau load represents amount of neurofibrillary tau pathology present in brain assessed with PET Scan. [18F] GTP1= tau PET radioligand. Tau load was measured with SUVR in 4 composite target ROIs(both left & right): Temporal composite target region included; Medial temporal composite region excluding hippocampus; Frontal lobe; Parietal lobe. Inferior cerebellar grey matter= reference region for calculating SUVRs for all 4 target regions. As pre-specified in protocol/SAP, single tau PET substudy analyzed participants from 2 studies i.e. WN29922 (NCT03444870) & WN39658 (NCT03443973), hence data for Tau PET was analyzed at pooled level of WN29922 &WN39658. Tau-PET-mITT analysis set=all participants in ITT analysis set who participated in Tau PET sub-study & who had atleast 1 Tau PET scan with valid quantitative measurement & who did not withdraw from Tau PET substudy before randomization. Overall number analyzed=number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[20] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	48		
Units: SUVR				
arithmetic mean (standard error)				
ROI: Temporal Composite Region	0.12 (± 0.018)	0.13 (± 0.014)		
ROI: Medial Temporal Composite Region	0.08 (± 0.014)	0.09 (± 0.011)		
ROI: Frontal Lobe	0.08 (± 0.012)	0.08 (± 0.009)		
ROI: Parietal Lobe	0.09 (± 0.020)	0.09 (± 0.016)		

Statistical analyses

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab
Statistical analysis description:	
Temporal Composite Region: Change from BL was calculated based on mixed-effect model of repeated measure which included the following covariates and stratification factors = Baseline + APOE e4 status + Study + Analysis Visit + Treatment + Treatment*Analysis Visit + Analysis Visit*Baseline.	
Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7816
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference in adjusted mean
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.023

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab
Statistical analysis description:	
Parietal Lobe: Change from BL was calculated based on mixed-effect model of repeated measure which included the following covariates and stratification factors = Baseline + APOE e4 status + Study + Analysis Visit + Treatment + Treatment*Analysis Visit + Analysis Visit*Baseline.	
Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9022
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference in adjusted means
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.05

Variability estimate	Standard error of the mean
Dispersion value	0.026

Statistical analysis title	DBT Period: Placebo, DBT Period: Placebo

Statistical analysis description:

Frontal Lobe: Change from BL was calculated based on mixed-effect model of repeated measure which included the following covariates and stratification factors = Baseline + APOE e4 status + Study + Analysis Visit + Treatment + Treatment*Analysis Visit + Analysis Visit*Baseline.

Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7754
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference in adjusted means
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.015

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab

Statistical analysis description:

Medial Temporal Composite Region: Change from BL was calculated based on mixed-effect model of repeated measure which included the following covariates and stratification factors = Baseline + APOE e4 status + Study + Analysis Visit + Treatment + Treatment*Analysis Visit + Analysis Visit*Baseline.

Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6203
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference in adjusted means
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.018

Secondary: DBT Period: Percent Change From Baseline to Week 116 in Cerebrospinal Fluid (CSF) Marker of Disease in a Subset of Participants - Total Tau (tTau)

End point title	DBT Period: Percent Change From Baseline to Week 116 in Cerebrospinal Fluid (CSF) Marker of Disease in a Subset of Participants - Total Tau (tTau)[21]

End point description:

CSF biomarker tTau has been considered as a general marker of neurodegeneration. An elevation in levels of tau, as well as specific pTau species, is thought to be a marker for progressive cellular degeneration in AD. CSF mITT Analysis Set included all participants in the ITT analysis set who had at least one valid quantitative CSF measurement. Overall number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[21] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	91		
Units: percent change in tTau				
geometric mean (confidence interval 95%)	3.2 (-1.74 to 8.37)	-16.6 (-20.40 to -12.54)		

Statistical analyses

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab

Statistical analysis description:

Parietal Lobe: Change from BL was calculated based on mixed-effect model of repeated measure which included the following covariates and stratification factors = Baseline + APOE e4 status + Study + Analysis Visit + Treatment + Treatment*Analysis Visit + Analysis Visit*Baseline.

Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA

Secondary: DBT Period: Percent Change From Baseline to Week 116 in CSF Marker of Disease in a Subset of Participants - Phosphorylated Tau (pTau-181)

End point title	DBT Period: Percent Change From Baseline to Week 116 in CSF

	Marker of Disease in a Subset of Participants - Phosphorylated Tau (pTau-181)[22]

End point description:

CSF phospho-tau is an indicator of neuronal injury and neurodegeneration. CSF biomarker tTau has been considered as a general marker of neurodegeneration. An elevation in levels of pTau species, is thought to be a marker for progressive cellular degeneration in AD. CSF modified ITT analysis set included all participants in the ITT analysis set who had at least one valid quantitative CSF measurement. Overall number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[22] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	89		
Units: percent change in pTau-181				
geometric mean (confidence interval 95%)	1.1 (-3.76 to 6.20)	-25.2 (-28.65 to -21.49)		

Statistical analyses

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab
Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA

Secondary: DBT Period: Percent Change From Baseline to Week 116 in CSF Marker of Disease in a Subset of Participants - Neurofilament Light Chain (NFL)

End point title	DBT Period: Percent Change From Baseline to Week 116 in CSF Marker of Disease in a Subset of Participants - Neurofilament Light Chain (NFL)[23]

End point description:

NFL is a neuronal cytoplasmic protein highly expressed in large, myelinated axons. Its levels increase in CSF and blood proportionally to the degree of axonal damage in a variety of neurological disorders, including AD. CSF mITT Analysis Set included all participants in the ITT analysis set who had at least one valid quantitative CSF measurement. Overall number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[23] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	93		
Units: percent change in NFL				
geometric mean (confidence interval 95%)	15.8 (9.67 to 22.32)	12.1 (6.41 to 18.11)		

Statistical analyses

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab
Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.396
Method	ANCOVA

Secondary: DBT Period: Percent Change From Baseline to Week 116 in CSF Marker of Disease in a Subset of Participants – Neurogranin

End point title	DBT Period: Percent Change From Baseline to Week 116 in CSF Marker of Disease in a Subset of Participants – Neurogranin[24]

End point description:

CSF mITT Analysis Set included all participants in the ITT analysis set who had at least one valid quantitative CSF measurement. Overall number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[24] - 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: The endpoint represents data for DBT period only.

End point values	Global – DBT Period: Placebo	Global – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	93		
Units: percent change in neurogranin				
geometric mean (confidence interval 95%)	-0.6 (-5.93 to 5.05)	-22.3 (-26.28 to -18.13)		

Statistical analyses

Statistical analysis title	DBT Period: Placebo, DBT Period: Gantenerumab
Comparison groups	Global – DBT Period: Placebo v Global – DBT Period: Gantenerumab
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA

Secondary: China – DBT Period: DBT Period: Change From Baseline to Week 116 in MMSE Total Score

End point title	China – DBT Period: DBT Period: Change From Baseline to Week 116 in MMSE Total Score[25]

End point description:

MMSE is a rater-administered PerfO that includes a set of standardized questions used to evaluate possible cognitive impairment and help stage the severity level of this impairment. The questions target six areas: orientation, registration, attention, short-term recall, language, and constructional praxis/visuospatial abilities. Total score ranges from 0-30, with lower scores indicating greater impairment. A positive change from baseline indicates improvement. The study was terminated early by the sponsor before any participant had reached Week 116 visit in the China extension phase.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[25] - 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: The endpoint represents data for DBT period only.

End point values	China Extension – DBT Period: Placebo	China Extension – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[26]	0[27]		
Units: score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[26] - Study terminated early by sponsor before any participant reached Week 116 in China extension phase.
[27] - Study terminated early by sponsor before any participant reached Week 116 in China extension phase.

Statistical analyses

No statistical analyses for this end point

Secondary: China – DBT Period: Change From Baseline to Week 116 in FAQ Score

End point title	China – DBT Period: Change From Baseline to Week 116 in FAQ Score[28]

End point description:

FAQ is a rater-administered ObsRO (informant-based measure) that measures a participant's functional ability to perform complex higher-order activities. The observer provides performance ratings of the target person on ten complex higher-order activities. Total score that ranges from 0-30, with higher scores reflecting greater functional impairment. A negative change from baseline indicates improvement. The study was terminated early by the sponsor before any participant had reached Week 116 visit in the China extension phase.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[28] - 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: The endpoint represents data for DBT period only.

End point values	China Extension – DBT Period: Placebo	China Extension – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[29]	0[30]		
Units: score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[29] - Study terminated early by sponsor before any participant reached Week 116 in China extension phase.
[30] - Study terminated early by sponsor before any participant reached Week 116 in China extension phase.

Statistical analyses

No statistical analyses for this end point

Secondary: China – DBT Period: Change From Baseline to Week 116 in ADCS-ADL Total Score

End point title	China – DBT Period: Change From Baseline to Week 116 in ADCS-ADL Total Score[31]

End point description:

ADCS-ADL is a 23-item rater-administered, ObsRO that captures a participant's ability to perform basic activities of daily living (e.g., eating and toileting) and more complex ADL or instrumental activities of daily living (iADL, e.g., using the telephone, managing finances, preparing a meal). Total score ranges from 0-78, with higher scores reflecting better functioning. A positive change from baseline indicates improvement. The study was terminated early by the sponsor before any participant had reached Week 116 visit in the China extension phase.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[31] - 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: The endpoint represents data for DBT period only.

End point values	China Extension – DBT Period: Placebo	China Extension – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[32]	0[33]		
Units: score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[32] - Study terminated early by sponsor before any participant reached Week 116 in China extension phase.
[33] - Study terminated early by sponsor before any participant reached Week 116 in China extension phase.

Statistical analyses

No statistical analyses for this end point

Secondary: China – DBT Period: Change from Baseline to Week 116 in ADAS-Cog13 Score

End point title	China – DBT Period: Change from Baseline to Week 116 in ADAS-Cog13 Score[34]

End point description:

The ADAS-Cog13 total score includes all of the items in the ADAS-Cog11 in addition to delayed word recall and the number cancellation. For the ADAS-cog 13 the range is 0-85 (score range for Delayed Word Recall [DWR] score is 0-10 and for Number Cancellation [NC] is 0-5, thus the score is ADAS-cog 11[0-70] plus the scores for DWR and NC). A higher score indicates worse performance. A negative change from baseline indicates improvement in cognitive function. The study was terminated early by the sponsor before any participant had reached Week 116 visit in the China extension phase.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[34] - 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: The endpoint represents data for DBT period only.

End point values	China Extension – DBT Period: Placebo	China Extension – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[35]	0[36]		
Units: score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[35] - Study terminated early by sponsor before any participant reached Week 116 in China extension phase.
[36] - Study terminated early by sponsor before any participant reached Week 116 in China extension phase.

Statistical analyses

No statistical analyses for this end point

Secondary: China – DBT Period: Number of Participants with Post-baseline Suicidal Ideation or Suicidal Behavior as Measured Using C-SSRS

End point title	China – DBT Period: Number of Participants with Post-baseline Suicidal Ideation or Suicidal Behavior as Measured Using C-SSRS[37]

End point description:

C-SSRS=assessment tool used to assess lifetime suicidality of participant and any new instances of suicidality. Structured interview prompts recollection of suicidal ideation, including intensity of ideation, behavior& attempts with actual/potential lethality. Responses to categories: yes/no[Wish to be Dead;Non-specific Active Suicidal Thoughts; Active Suicidal Ideation with Any Methods without Intent to Act;Active Suicidal Ideation with Some Intent to Act, without Specific Plan;Active Suicidal Ideation with Specific Plan &Intent, Preparatory Acts &Behavior; Aborted Attempt; Interrupted Attempt; Actual Attempt (non-fatal)]; Completed Suicide. Suicidal ideation/behavior is indicated by a "yes" answer to any of the listed categories. Score=0, if no suicide risk is present. Score=1/higher indicates suicidal ideation/behavior. SE analysis set (China) was used. Overall number analyzed=number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

From Day 1 up to 14 weeks after the last dose of blinded study drug (up to 124 weeks)

Notes:

[37] - 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: The endpoint represents data for DBT period only.

End point values	China Extension – DBT Period: Placebo	China Extension – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	30		
Units: participants				
Suicidal Ideation: Passive	1	1		
Suicidal Ideation: Active-Nonspecific	0	1		
Suicidal Ideation: Active-Method & intent, no plan	1	0		
Suicidal Ideation: No Event	23	28		
Suicidal Behavior: No Event	25	30		
Self-injurious Behavior Without Intent: No Event	25	30		

Statistical analyses

No statistical analyses for this end point

Secondary: China – DBT Period: Number of Participants with at Least One AEs

End point title	China – DBT Period: Number of Participants with at Least One AEs[38]

End point description:

An adverse event is any untoward medical occurrence in a clinical investigation participant administered a pharmaceutical product, regardless of causal attribution. Total number of participants with at least one event (AEs) have been reported here. SE analysis set (China) included all participants enrolled in China in the China extension phase who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From Day 1 up to 14 weeks after the last dose of blinded study drug (up to 124 weeks)

Notes:

[38] - 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: The endpoint represents data for DBT period only.

End point values	China Extension – DBT Period: Placebo	China Extension – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	35		
Units: participants	17	24		

Statistical analyses

No statistical analyses for this end point

Secondary: China – DBT Period: Change From Baseline to Week 116 in VFT Score

End point title	China – DBT Period: Change From Baseline to Week 116 in VFT Score[39]

End point description:

VFT is a rater administered PerfO that measures speed and flexibility of verbal thought with a total score that ranges from 0-99 (lower scores indicating lower performance). A positive change from baseline indicates improvement. The study was terminated early by the sponsor before any participant had reached Week 116 visit in the China extension phase.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[39] - 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: The endpoint represents data for DBT period only.

End point values	China Extension – DBT Period: Placebo	China Extension – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[40]	0[41]		
Units: score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[40] - Study terminated early by sponsor before any participant reached Week 116 in China extension phase.
[41] - Study terminated early by sponsor before any participant reached Week 116 in China extension phase.

Statistical analyses

No statistical analyses for this end point

Secondary: China – DBT Period: Change from Baseline to Week 116 in the Coding (DSST) Subtest

End point title	China – DBT Period: Change from Baseline to Week 116 in the Coding (DSST) Subtest[42]

End point description:

Coding, also called DSST is a rater administered PerfO that measures speed of processing and associative memory with a total score that ranges from 0-135 (lower scores indicating lower performance). The DSST was adapted from the Wechsler Adult Intelligence Scale. The 120-second version of the test was used in this study. Positive change from baseline indicates improvement. The study was terminated early by the sponsor before any participant had reached Week 116 visit in the China extension phase.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[42] - 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: The endpoint represents data for DBT period only.

End point values	China Extension – DBT Period: Placebo	China Extension – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[43]	0[44]		
Units: score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[43] - Study terminated early by sponsor before any participant reached Week 116 in China extension phase.
[44] - Study terminated early by sponsor before any participant reached Week 116 in China extension phase.

Statistical analyses

No statistical analyses for this end point

Secondary: China – DBT Period: Change From Baseline to Week 116 in ADAS-Cog11 Score

End point title	China – DBT Period: Change From Baseline to Week 116 in ADAS-Cog11 Score[45]

End point description:

ADAS-Cog11 was designed to measure cognitive symptom change in participants with AD, consisted of 11 tasks. Standard 11 items & score range were: word recall(0-10),commands(0-5),constructional praxis(0-5),naming objects & fingers(0-5), ideational praxis(0-5),orientation(0-8),word recognition(0-12),spoken language ability(0-5),comprehension of spoken language(0-5),word-finding difficulty(0-5) & remembering test instructions(0-5). Test included 7 performance items & 4 clinician-rated items. ADAS-Cog11 total score=sum of all 11 individual items, with total score ranging from 0 (no impairment)-70 (severe impairment). Higher scores indicated more severe cognitive impairment. Negative change from baseline indicates improvement. The study was terminated early by the sponsor before any participant had reached Week 116 visit in the China extension phase.

End point type	Secondary

End point timeframe:

Baseline, Week 116

Notes:

[45] - 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: The endpoint represents data for DBT period only.

End point values	China Extension – DBT Period: Placebo	China Extension – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[46]	0[47]		
Units: score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[46] - Study terminated early by sponsor before any participant reached Week 116 in China extension phase.
[47] - Study terminated early by sponsor before any participant reached Week 116 in China extension phase.

Statistical analyses

No statistical analyses for this end point

Secondary: China – DBT Period: Number of Participants with Injection-Site Reactions

End point title	China – DBT Period: Number of Participants with Injection-Site Reactions[48]

End point description:

An AE is any unfavorable and unintended sign, symptom, or disease temporally associated with the use of an investigational product or other protocol-imposed intervention, regardless of attribution. Local injection reactions (or injection site reactions) are defined as AEs related to the injection site that occur during or within 24 hours after study drug administration that are judged to be related to the study drug injection. SE analysis set (China) included all participants enrolled in China in the China extension phase who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From Day 1 up to 14 weeks after the last dose of blinded study drug (up to 124 weeks)

Notes:

[48] - 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: The endpoint represents data for DBT period only.

End point values	China Extension – DBT Period: Placebo	China Extension – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	35		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: China – DBT Period: Number of Participants with at Least One ARIA-H MRI Finding

End point title	China – DBT Period: Number of Participants with at Least One ARIA-H MRI Finding[49]

End point description:

ARIA are an identified risk with anti-amyloid antibodies, including gantenerumab. These changes can be identified on brain MRI. ARIA-H (H for hemosiderosis) are small foci of signal loss observed on MRI sequences sensitive for paramagnetic tissue properties and comprise cerebral microbleeds (small foci of bleeding in the brain parenchyma) and leptomeningeal hemosiderosis (small foci of bleeding on the surface of the brain). These changes also occur sporadically in AD. SE analysis set (China) included all participants enrolled in China in the China extension phase who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From Day 1 up to 14 weeks after the last dose of blinded study drug (up to 124 weeks)

Notes:

[49] - 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: The endpoint represents data for DBT period only.

End point values	China Extension – DBT Period: Placebo	China Extension – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	35		
Units: participants	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: China – DBT Period: Number of Participants with at Least One ARIA-E MRI Finding

End point title	China – DBT Period: Number of Participants with at Least One ARIA-E MRI Finding[50]

End point description:

ARIA are an identified risk with anti-amyloid antibodies, including gantenerumab. These changes can be identified on brain MRI. In ARIA-E, (E for oedema or effusion), oedema can be seen in different areas of the brain on MRI, representing fluid leakage into the brain parenchyma or sulcal spaces. SE analysis set (China) included all participants enrolled in China in the China extension phase who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From Day 1 up to 14 weeks after the last dose of blinded study drug (up to 124 weeks)

Notes:

[50] - 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: The endpoint represents data for DBT period only.

End point values	China Extension – DBT Period: Placebo	China Extension – DBT Period: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	35		
Units: participants	1	4		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Number of Participants with at Least One ARIA-H MRI Finding

End point title	OLE Period: Number of Participants with at Least One ARIA-H MRI Finding

End point description:

ARIA are an identified risk with anti-amyloid antibodies, including gantenerumab. These changes can be identified on brain MRI. ARIA-H (H for hemosiderosis) are small foci of signal loss observed on MRI sequences sensitive for paramagnetic tissue properties and comprise cerebral microbleeds (small foci of bleeding in the brain parenchyma) and leptomeningeal hemosiderosis (small foci of bleeding on the surface of the brain). These changes also occur sporadically in AD. SEMRI analysis set included all participants in the SE analysis set who had at least one post-baseline safety MRI scan. Overall number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

From day of first dose in OLE period up to 14 weeks after the last OLE dose (up to 68 weeks)

End point values	Global – OLE Period: Placebo (DBT) to Gantenerumab	Global – OLE Period: Gantenerumab (DBT) to Gantenerumab		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9	20		
Units: participants	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Number of Participants with Post-baseline Suicidal Ideation or Suicidal Behavior as Measured Using C-SSRS

End point title	OLE Period: Number of Participants with Post-baseline Suicidal Ideation or Suicidal Behavior as Measured Using C-SSRS

End point description:

C-SSRS= used to assess suicidality in participants,both lifetime & any new instances. Structured interview prompts recollection of suicidal ideation, including intensity of ideation, behavior& attempts with actual/potential lethality. Responses to categories: yes/no[Wish to be Dead;Non-specific Active Suicidal Thoughts; Active Suicidal Ideation with Any Methods without Intent to Act;Active Suicidal Ideation with Some Intent to Act, without Specific Plan;Active Suicidal Ideation with Specific Plan &Intent, Preparatory Acts &Behavior; Aborted Attempt; Interrupted Attempt; Actual Attempt (non-fatal)]; Completed Suicide. Suicidal ideation/behavior is indicated by "yes" answer to any of listed

categories. Score=0, if no suicide risk is present. Score=1/higher indicates suicidal ideation/behavior. SE set was used where in DBT period, 4 participants randomized to placebo received atleast 1 dose of gantenerumab & were considered in gantenerumab arm, of which 1 participant entered OLE period.

End point type	Secondary

End point timeframe:

From day of first dose in OLE period up to 14 weeks after the last OLE dose (up to 68 weeks)

End point values	Global – OLE Period: Placebo (DBT) to Gantenerumab	Global – OLE Period: Gantenerumab (DBT) to Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	19		
Units: participants				
Suicidal Ideation: Active-Method, no intent/plan	0	1		
Suicidal Ideation: No Event	6	18		
Suicidal Behavior: No Event	6	19		
Self-injurious Behavior Without Intent: No event	6	19		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Number of Participants with at Least One AE

End point title	OLE Period: Number of Participants with at Least One AE

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant administered a pharmaceutical product, regardless of causal attribution. SE analysis set included all participants randomized during the global phase who received at least one dose of study drug. In the DBT period, 4 participants randomized to placebo arm received at least one dose of gantenerumab and were considered in the gantenerumab arm for safety analysis set, of which one participant entered OLE period.

End point type	Secondary

End point timeframe:

From day of first dose in OLE period up to 14 weeks after the last OLE dose (up to 68 weeks)

End point values	Global – OLE Period: Placebo (DBT) to Gantenerumab	Global – OLE Period: Gantenerumab (DBT) to Gantenerumab		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9	20		
Units: participants	8	16		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Number of Participants with at Least One ARIA-E MRI Finding

End point title	OLE Period: Number of Participants with at Least One ARIA-E MRI Finding

End point description:

ARIA are an identified risk with anti-amyloid antibodies, including gantenerumab. These changes can be identified on brain MRI. In ARIA-E, (E for oedema or effusion), oedema can be seen in different areas of the brain on MRI, representing fluid leakage into the brain parenchyma or sulcal spaces. SEMRI analysis set included all participants in the SE analysis set who had at least one post-baseline safety MRI scan. Overall number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

From day of first dose in OLE period up to 14 weeks after the last OLE dose (up to 68 weeks)

End point values	Global – OLE Period: Placebo (DBT) to Gantenerumab	Global – OLE Period: Gantenerumab (DBT) to Gantenerumab		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9	20		
Units: participants	3	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

DBT: Day 1 to 14 weeks post last dose (131 weeks); OLE: OLE Day 1 to 14 weeks post last OLE dose (68 weeks) China DBT: Day 1 to 14 weeks post last dose (124 weeks); Deaths: DBT: Day 1 to end of study (164 weeks); OLE: OLE Day 1 to end of study (86 weeks)

Adverse event reporting additional description:

SE analysis set=all participants randomized during global phase &received atleast 1dose of study drug. In DBT,4 participants randomized to placebo received atleast 1dose of gantenerumab &were considered in gantenerumab arm for safety analysis.SE analysis set (China)=all participants enrolled in China extension &received atleast 1dose of study drug

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	Global – DBT Period: Placebo

Reporting group description:

Participants received gantenerumab matching placebo, SC injection, every four weeks (Q4W) up to Week 36 and then every two weeks (Q2W) up to approximately 110 weeks of the DBT period.

Reporting group title	China Extension – DBT Period: Gantenerumab

Reporting group description:

Participants received gantenerumab, SC injection with gradual up-titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and 510 mg, Q4W for 3 doses. Following this, from Week 36 onwards, participants received gantenerumab, SC injection at a dose of 510 mg, Q2W up to approximately 110 weeks of the DBT period.

Reporting group title	Global – OLE Period: Gantenerumab (DBT) to Gantenerumab

Reporting group description:

Participants who received gantenerumab in the DBT period continued receiving gantenerumab, SC injections, 510 mg, Q2W up to Week 34 of the OLE period.

Reporting group title	China Extension – DBT Period: Placebo

Reporting group description:

Participants received gantenerumab matching placebo, SC injection, Q4W up to Week 36 and then Q2W up to approximately 110 weeks of the DBT period.

Reporting group title	Global – DBT Period: Gantenerumab

Reporting group description:

Participants received gantenerumab, SC injection with gradual up-titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and 510 mg, Q4W for 3 doses. Following this, from Week 36 onwards, participants received gantenerumab, SC injection at a dose of 510 mg, Q2W up to Week 114 of the DBT period.

Reporting group title	Global – OLE Period: Placebo (DBT) to Gantenerumab

Reporting group description:

Participants who received gantenerumab matching placebo in the DBT period received gantenerumab SC injections with gradual up titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and then at a dose of 510 mg, Q4W up to Week 34 of the OLE period. To maintain the blind to previous treatment assignment, participants received Q2W, SC injections, with alternate doses containing gantenerumab matching placebo.

Serious adverse events	Global – DBT Period: Placebo	China Extension – DBT Period: Gantenerumab	Global – OLE Period: Gantenerumab (DBT) to Gantenerumab
Total subjects affected by serious adverse events			
subjects affected / exposed	95 / 481 (19.75%)	2 / 35 (5.71%)	2 / 20 (10.00%)
number of deaths (all causes)	11	0	0
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gingival cancer			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder neoplasm			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric leiomyoma			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma of the cervix			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal adenocarcinoma			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer stage I			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma			

subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatic adenoma			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of the vulva			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma metastatic			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal squamous cell carcinoma			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer recurrent			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			

subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery thrombosis			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superficial vein thrombosis			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial occlusive disease			

subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic aneurysm			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden cardiac death			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine prolapse			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Uterine cyst			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Lung infiltration			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive airways disorder			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Emphysema			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute pulmonary oedema			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Asthma			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Paranoia			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aggression			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychomotor retardation			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			

subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Wrist fracture			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ilium fracture			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bones fracture			

subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	3 / 481 (0.62%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Upper limb fracture			

subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Paroxysmal atrioventricular block			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			

subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus node dysfunction			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia supraventricular			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			

subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic encephalopathy			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient global amnesia			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			

subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural hygroma			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebrobasilar artery dissection			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			

subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemianopia			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Tremor			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clonic convulsion			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myoclonus			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			

subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphasia			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIth nerve paresis			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thalamic infarction			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			

Acute vestibular syndrome			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deafness unilateral			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertigo			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Glaucoma			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia strangulated			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Large intestine perforation			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral hernia strangulated			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			

subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic cirrhosis			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	1 / 481 (0.21%)	1 / 35 (2.86%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder diverticulum			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			

Hypothyroidism			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rotator cuff syndrome			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Greater trochanteric pain syndrome			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	3 / 481 (0.62%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Diverticulitis intestinal perforated			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Urosepsis			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	5 / 481 (1.04%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device site abscess			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			

subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	3 / 481 (0.62%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	9 / 481 (1.87%)	1 / 35 (2.86%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 9	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 4	0 / 0	0 / 0
Suspected COVID-19			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			

subjects affected / exposed	3 / 481 (0.62%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear infection			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			

subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	China Extension – DBT Period: Placebo	Global – DBT Period: Gantenerumab	Global – OLE Period: Placebo (DBT) to Gantenerumab
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 33 (0.00%)	76 / 503 (15.11%)	2 / 9 (22.22%)
number of deaths (all causes)	0	3	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gingival cancer			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder neoplasm			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric leiomyoma			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma of the cervix			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal adenocarcinoma			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Colon cancer stage I			

subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatic adenoma			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of the vulva			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma metastatic			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal squamous cell carcinoma			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer recurrent			

subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 33 (0.00%)	2 / 503 (0.40%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery thrombosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superficial vein thrombosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			

subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial occlusive disease			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic aneurysm			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 33 (0.00%)	2 / 503 (0.40%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden cardiac death			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Reproductive system and breast disorders			
Uterine prolapse			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Benign prostatic hyperplasia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine cyst			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 33 (0.00%)	5 / 503 (0.99%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infiltration			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive airways disorder			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Emphysema			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Acute pulmonary oedema			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Paranoia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aggression			
subjects affected / exposed	0 / 33 (0.00%)	2 / 503 (0.40%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychomotor retardation			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			

subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 33 (0.00%)	2 / 503 (0.40%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Wrist fracture			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 33 (0.00%)	2 / 503 (0.40%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Ilium fracture			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			

subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bones fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			

subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 33 (0.00%)	6 / 503 (1.19%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 33 (0.00%)	2 / 503 (0.40%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Paroxysmal atrioventricular block			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			

subjects affected / exposed	0 / 33 (0.00%)	2 / 503 (0.40%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus node dysfunction			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia supraventricular			

subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic encephalopathy			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
subjects affected / exposed	0 / 33 (0.00%)	2 / 503 (0.40%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient global amnesia			

subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural hygroma			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebrobasilar artery dissection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			

subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemianopia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clonic convulsion			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myoclonus			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			

subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	0 / 33 (0.00%)	7 / 503 (1.39%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	8 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphasia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIth nerve paresis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 33 (0.00%)	2 / 503 (0.40%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thalamic infarction			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			

subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Acute vestibular syndrome			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deafness unilateral			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertigo			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Inguinal hernia strangulated			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral hernia strangulated			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			

subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic cirrhosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder diverticulum			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			

subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rotator cuff syndrome			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Greater trochanteric pain syndrome			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 33 (0.00%)	2 / 503 (0.40%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Diverticulitis intestinal perforated			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device site abscess			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 33 (0.00%)	3 / 503 (0.60%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suspected COVID-19			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cellulitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			

subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 33 (0.00%)	2 / 503 (0.40%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear infection			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			

subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Global – DBT Period: Placebo	China Extension – DBT Period: Gantenerumab	Global – OLE Period: Gantenerumab (DBT) to Gantenerumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	329 / 481 (68.40%)	20 / 35 (57.14%)	16 / 20 (80.00%)
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	35 / 481 (7.28%)	1 / 35 (2.86%)	1 / 20 (5.00%)
occurrences (all)	38	2	1
Hypotension			
subjects affected / exposed	7 / 481 (1.46%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	8	0	0
Peripheral ischaemia			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	43 / 481 (8.94%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	95	0	1
Vaccination site pain			
subjects affected / exposed	3 / 481 (0.62%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	3	0	1
Pyrexia			

subjects affected / exposed	12 / 481 (2.49%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	14	0	1
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	7 / 481 (1.46%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	7	0	0
Cough			
subjects affected / exposed	11 / 481 (2.29%)	3 / 35 (8.57%)	2 / 20 (10.00%)
occurrences (all)	13	3	2
Psychiatric disorders			
Agitation			
subjects affected / exposed	15 / 481 (3.12%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	18	0	1
Disorientation			
subjects affected / exposed	3 / 481 (0.62%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	3	0	1
Insomnia			
subjects affected / exposed	21 / 481 (4.37%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	23	0	1
Depression			
subjects affected / exposed	22 / 481 (4.57%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	22	0	1
Anxiety			
subjects affected / exposed	19 / 481 (3.95%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	21	0	1
Depressed mood			
subjects affected / exposed	4 / 481 (0.83%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	4	0	1
Investigations			
Blood pressure increased			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	2 / 20 (10.00%)
occurrences (all)	2	0	2
Blood glucose increased			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Joint dislocation			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Contusion			
subjects affected / exposed	13 / 481 (2.70%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	18	0	1
Hip fracture			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Spinal compression fracture			
subjects affected / exposed	2 / 481 (0.42%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Rib fracture			
subjects affected / exposed	3 / 481 (0.62%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	3	0	0
Fall			
subjects affected / exposed	62 / 481 (12.89%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	82	0	1
Ligament sprain			
subjects affected / exposed	8 / 481 (1.66%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	8	0	1
Ankle fracture			
subjects affected / exposed	0 / 481 (0.00%)	2 / 35 (5.71%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Cardiac disorders			
Cardiac failure chronic			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Myocardial ischaemia			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Arrhythmia			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	3
Sinus bradycardia			

subjects affected / exposed	2 / 481 (0.42%)	1 / 35 (2.86%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	41 / 481 (8.52%)	1 / 35 (2.86%)	1 / 20 (5.00%)
occurrences (all)	49	1	1
Headache			
subjects affected / exposed	42 / 481 (8.73%)	1 / 35 (2.86%)	1 / 20 (5.00%)
occurrences (all)	85	1	1
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	5 / 481 (1.04%)	4 / 35 (11.43%)	2 / 20 (10.00%)
occurrences (all)	5	5	3
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
subjects affected / exposed	4 / 481 (0.83%)	1 / 35 (2.86%)	0 / 20 (0.00%)
occurrences (all)	5	1	0
Focal dyscognitive seizures			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Dysarthria			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ischaemic stroke			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	6 / 481 (1.25%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	7	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	17 / 481 (3.53%)	2 / 35 (5.71%)	0 / 20 (0.00%)
occurrences (all)	20	2	0
Diarrhoea			
subjects affected / exposed	26 / 481 (5.41%)	1 / 35 (2.86%)	0 / 20 (0.00%)
occurrences (all)	29	2	0
Dysphagia			

subjects affected / exposed	3 / 481 (0.62%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	3	0	1
Toothache			
subjects affected / exposed	9 / 481 (1.87%)	2 / 35 (5.71%)	0 / 20 (0.00%)
occurrences (all)	10	5	0
Large intestine polyp			
subjects affected / exposed	5 / 481 (1.04%)	1 / 35 (2.86%)	0 / 20 (0.00%)
occurrences (all)	5	1	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	13 / 481 (2.70%)	1 / 35 (2.86%)	1 / 20 (5.00%)
occurrences (all)	13	1	1
Erythema			
subjects affected / exposed	7 / 481 (1.46%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	8	0	0
Alopecia			
subjects affected / exposed	3 / 481 (0.62%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	3	0	0
Eczema			
subjects affected / exposed	6 / 481 (1.25%)	2 / 35 (5.71%)	0 / 20 (0.00%)
occurrences (all)	6	2	0
Dermatitis			
subjects affected / exposed	1 / 481 (0.21%)	3 / 35 (8.57%)	0 / 20 (0.00%)
occurrences (all)	1	3	0
Renal and urinary disorders			
Bladder irritation			
subjects affected / exposed	0 / 481 (0.00%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	4 / 481 (0.83%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	4	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	40 / 481 (8.32%)	1 / 35 (2.86%)	1 / 20 (5.00%)
occurrences (all)	51	1	1
Arthralgia			

subjects affected / exposed	29 / 481 (6.03%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	36	0	1
Muscle spasms			
subjects affected / exposed	3 / 481 (0.62%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	4	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	35 / 481 (7.28%)	4 / 35 (11.43%)	1 / 20 (5.00%)
occurrences (all)	35	4	1
Rhinitis			
subjects affected / exposed	6 / 481 (1.25%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	6	0	1
Influenza			
subjects affected / exposed	5 / 481 (1.04%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	5	0	1
Gingivitis			
subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	33 / 481 (6.86%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	37	0	0
Urinary tract infection			
subjects affected / exposed	28 / 481 (5.82%)	1 / 35 (2.86%)	2 / 20 (10.00%)
occurrences (all)	39	1	3
Respiratory tract infection			
subjects affected / exposed	3 / 481 (0.62%)	0 / 35 (0.00%)	1 / 20 (5.00%)
occurrences (all)	6	0	1
Coronavirus infection			
subjects affected / exposed	0 / 481 (0.00%)	3 / 35 (8.57%)	0 / 20 (0.00%)
occurrences (all)	0	3	0
Upper respiratory tract infection			
subjects affected / exposed	19 / 481 (3.95%)	3 / 35 (8.57%)	0 / 20 (0.00%)
occurrences (all)	23	6	0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	1 / 481 (0.21%)	0 / 35 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	China Extension – DBT Period: Placebo	Global – DBT Period: Gantenerumab	Global – OLE Period: Placebo (DBT) to Gantenerumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 33 (33.33%)	366 / 503 (72.76%)	8 / 9 (88.89%)
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	0 / 33 (0.00%)	41 / 503 (8.15%)	0 / 9 (0.00%)
occurrences (all)	0	54	0
Hypotension			
subjects affected / exposed	0 / 33 (0.00%)	12 / 503 (2.39%)	2 / 9 (22.22%)
occurrences (all)	0	13	2
Peripheral ischaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	0 / 33 (0.00%)	94 / 503 (18.69%)	1 / 9 (11.11%)
occurrences (all)	0	392	1
Vaccination site pain			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	1 / 33 (3.03%)	6 / 503 (1.19%)	0 / 9 (0.00%)
occurrences (all)	1	6	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 33 (0.00%)	5 / 503 (0.99%)	1 / 9 (11.11%)
occurrences (all)	0	7	1
Cough			

subjects affected / exposed	0 / 33 (0.00%)	19 / 503 (3.78%)	0 / 9 (0.00%)
occurrences (all)	0	19	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 33 (0.00%)	10 / 503 (1.99%)	0 / 9 (0.00%)
occurrences (all)	0	10	0
Disorientation			
subjects affected / exposed	0 / 33 (0.00%)	2 / 503 (0.40%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Insomnia			
subjects affected / exposed	0 / 33 (0.00%)	25 / 503 (4.97%)	0 / 9 (0.00%)
occurrences (all)	0	26	0
Depression			
subjects affected / exposed	1 / 33 (3.03%)	28 / 503 (5.57%)	0 / 9 (0.00%)
occurrences (all)	1	28	0
Anxiety			
subjects affected / exposed	0 / 33 (0.00%)	19 / 503 (3.78%)	1 / 9 (11.11%)
occurrences (all)	0	21	1
Depressed mood			
subjects affected / exposed	0 / 33 (0.00%)	5 / 503 (0.99%)	0 / 9 (0.00%)
occurrences (all)	0	5	0
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 33 (0.00%)	3 / 503 (0.60%)	0 / 9 (0.00%)
occurrences (all)	0	4	0
Blood glucose increased			
subjects affected / exposed	0 / 33 (0.00%)	4 / 503 (0.80%)	1 / 9 (11.11%)
occurrences (all)	0	4	1
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 33 (0.00%)	21 / 503 (4.17%)	0 / 9 (0.00%)
occurrences (all)	0	23	0
Hip fracture			

subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Spinal compression fracture			
subjects affected / exposed	0 / 33 (0.00%)	4 / 503 (0.80%)	0 / 9 (0.00%)
occurrences (all)	0	4	0
Rib fracture			
subjects affected / exposed	0 / 33 (0.00%)	2 / 503 (0.40%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
Fall			
subjects affected / exposed	0 / 33 (0.00%)	60 / 503 (11.93%)	2 / 9 (22.22%)
occurrences (all)	0	94	2
Ligament sprain			
subjects affected / exposed	0 / 33 (0.00%)	8 / 503 (1.59%)	0 / 9 (0.00%)
occurrences (all)	0	8	0
Ankle fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Cardiac failure chronic			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Myocardial ischaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Arrhythmia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	3 / 33 (9.09%)	5 / 503 (0.99%)	0 / 9 (0.00%)
occurrences (all)	4	5	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 33 (0.00%)	45 / 503 (8.95%)	0 / 9 (0.00%)
occurrences (all)	0	64	0
Headache			

subjects affected / exposed	1 / 33 (3.03%)	60 / 503 (11.93%)	0 / 9 (0.00%)
occurrences (all)	1	99	0
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	1 / 33 (3.03%)	102 / 503 (20.28%)	3 / 9 (33.33%)
occurrences (all)	1	161	4
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
subjects affected / exposed	0 / 33 (0.00%)	33 / 503 (6.56%)	0 / 9 (0.00%)
occurrences (all)	0	35	0
Focal dyscognitive seizures			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dysarthria			
subjects affected / exposed	0 / 33 (0.00%)	3 / 503 (0.60%)	1 / 9 (11.11%)
occurrences (all)	0	3	1
Ischaemic stroke			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Somnolence			
subjects affected / exposed	0 / 33 (0.00%)	2 / 503 (0.40%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 33 (0.00%)	26 / 503 (5.17%)	0 / 9 (0.00%)
occurrences (all)	0	43	0
Diarrhoea			
subjects affected / exposed	0 / 33 (0.00%)	33 / 503 (6.56%)	0 / 9 (0.00%)
occurrences (all)	0	48	0
Dysphagia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Toothache			
subjects affected / exposed	0 / 33 (0.00%)	13 / 503 (2.58%)	0 / 9 (0.00%)
occurrences (all)	0	13	0
Large intestine polyp			

subjects affected / exposed	2 / 33 (6.06%)	3 / 503 (0.60%)	0 / 9 (0.00%)
occurrences (all)	2	3	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 33 (0.00%)	12 / 503 (2.39%)	0 / 9 (0.00%)
occurrences (all)	0	15	0
Erythema			
subjects affected / exposed	0 / 33 (0.00%)	8 / 503 (1.59%)	1 / 9 (11.11%)
occurrences (all)	0	8	1
Alopecia			
subjects affected / exposed	0 / 33 (0.00%)	2 / 503 (0.40%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
Eczema			
subjects affected / exposed	0 / 33 (0.00%)	9 / 503 (1.79%)	0 / 9 (0.00%)
occurrences (all)	0	9	0
Dermatitis			
subjects affected / exposed	0 / 33 (0.00%)	2 / 503 (0.40%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Renal and urinary disorders			
Bladder irritation			
subjects affected / exposed	0 / 33 (0.00%)	0 / 503 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 33 (0.00%)	43 / 503 (8.55%)	0 / 9 (0.00%)
occurrences (all)	0	49	0
Arthralgia			
subjects affected / exposed	0 / 33 (0.00%)	37 / 503 (7.36%)	0 / 9 (0.00%)
occurrences (all)	0	51	0
Muscle spasms			
subjects affected / exposed	0 / 33 (0.00%)	13 / 503 (2.58%)	1 / 9 (11.11%)
occurrences (all)	0	15	1
Infections and infestations			

COVID-19			
subjects affected / exposed	3 / 33 (9.09%)	26 / 503 (5.17%)	1 / 9 (11.11%)
occurrences (all)	3	26	1
Rhinitis			
subjects affected / exposed	0 / 33 (0.00%)	9 / 503 (1.79%)	0 / 9 (0.00%)
occurrences (all)	0	10	0
Influenza			
subjects affected / exposed	1 / 33 (3.03%)	1 / 503 (0.20%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
Gingivitis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 503 (0.20%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Nasopharyngitis			
subjects affected / exposed	1 / 33 (3.03%)	46 / 503 (9.15%)	0 / 9 (0.00%)
occurrences (all)	1	60	0
Urinary tract infection			
subjects affected / exposed	0 / 33 (0.00%)	30 / 503 (5.96%)	1 / 9 (11.11%)
occurrences (all)	0	37	3
Respiratory tract infection			
subjects affected / exposed	0 / 33 (0.00%)	4 / 503 (0.80%)	0 / 9 (0.00%)
occurrences (all)	0	4	0
Coronavirus infection			
subjects affected / exposed	1 / 33 (3.03%)	0 / 503 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 33 (6.06%)	19 / 503 (3.78%)	0 / 9 (0.00%)
occurrences (all)	2	24	0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 33 (0.00%)	3 / 503 (0.60%)	1 / 9 (11.11%)
occurrences (all)	0	4	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 February 2018	1. This amendment presented the results of the relative bioavailability study (WP40052). The dosing regimen of GRADUATE I study was also adjusted according to these results. 2. The entry criteria of the study population were revised to increase the homogeneity of the study population and to better target the appropriate study population.
16 January 2020	1. The sample size of the study was updated. The sample size was increased from 760 participants to 1,016 (508 participants randomized to gantenerumab and 508 randomized to placebo). 2. The protocol was amended to allow the first participants enrolled in the study to enroll in an OLE as planned. Details on this procedure and the OLE Schedule of Activities was also added.
23 May 2020	1. This amendment extended the DBT period (originally 104 weeks) by 12 weeks in order to mitigate the impact of missed administrations and preserve the scientific integrity of the study by enabling more participants to receive study drug at the initially intended exposures. 2. The amendment also allowed the option of further extending the double-blind treatment period by another 12 weeks (to 128 weeks). 3. The upper limit of the sample size was increased from 1,140 to 1,322 participants. This further extension of the double-blind treatment period to 128 weeks was not implemented, nor was the sample size increased.
02 August 2021	1. The pharmacokinetic (PK) objective of the study was changed to an exploratory PK objective to be consistent with the sparse PK sampling design and population modeling used to analyse the dose concentration–time data of gantenerumab. 2. The corresponding endpoints for the pharmacodynamic (PD) biomarker objective was revised to clarify the duration of change as a measurement from baseline to Week 116 when assessing brain amyloid load, brain tau load and cerebral spinal fluid markers. 3. Sections were updated to clarify that the open-label extension (OLE) of Study WN29922 is not applicable in countries that cannot run Study WN42171.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
11 November 2022	Following results of a pre-planned primary analysis of the safety and efficacy of Gant in Graduate I&II (WN29922/WN39658) a decision was made to terminate development of Gantenerumab for treatment of prodromal/mild/early stage Alzheimer's disease.	-

Notes:

Limitations and caveats

None reported