Clinical trial results:
An Open-Label, Multicenter, Rollover Study to Evaluate the Safety, Tolerability, and Efficacy of Long-Term Gantenerumab Administration in Participants with Alzheimer's Disease

Summary

EudraCT number	2020-000766-42
Trial protocol	GB DK PT PL HU DE FR IT LT NL BE FI HR
Global end of trial date	06 March 2023

Results information

Result version number	v1 (current)
This version publication date	20 March 2024
First version publication date	20 March 2024

Trial information

Trial identification

Sponsor protocol code	WN42171

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04374253
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
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	06 March 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 March 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 safety and tolerability of long-term gantenerumab administered by subcutaneous (SC) injection.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 January 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 38
Country: Number of subjects enrolled	Australia: 48
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Brazil: 15
Country: Number of subjects enrolled	Canada: 36
Country: Number of subjects enrolled	Chile: 37
Country: Number of subjects enrolled	China: 2
Country: Number of subjects enrolled	Germany: 73
Country: Number of subjects enrolled	Denmark: 16
Country: Number of subjects enrolled	Spain: 239
Country: Number of subjects enrolled	Finland: 17
Country: Number of subjects enrolled	France: 33
Country: Number of subjects enrolled	United Kingdom: 34
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Italy: 58
Country: Number of subjects enrolled	Japan: 115
Country: Number of subjects enrolled	Korea, Republic of: 45
Country: Number of subjects enrolled	Lithuania: 11
Country: Number of subjects enrolled	Mexico: 37
Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Peru: 28
Country: Number of subjects enrolled	Poland: 89

Country: Number of subjects enrolled	Portugal: 27
Country: Number of subjects enrolled	Russian Federation: 57
Country: Number of subjects enrolled	Sweden: 17
Country: Number of subjects enrolled	Türkiye: 1
Country: Number of subjects enrolled	Taiwan: 24
Country: Number of subjects enrolled	United States: 266
Worldwide total number of subjects	1381
EEA total number of subjects	598

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)	186
From 65 to 84 years	1116
85 years and over	79

Subject disposition

Recruitment

Recruitment details:

Participants took part at 258 investigative centers across 28 countries from 26 January 2021 to 06 March 2023. A total of 1381 participants who completed either double-blind (DB) part or open-label extension (OLE) part in GRADUATE parent studies WN29922 (NCT03444870) or WN39658 (NCT03443973) were enrolled to receive open-label gantenerumab.

Pre-assignment

Screening details:

Participants who completed DB and OLE part received gantenerumab approximately 2 weeks after OLE Week 34 visit or final OLE dose visit in the parent study. Participants who completed DB part and did not enter the OLE part received gantenerumab approximately 2 weeks after the Week 116 visit of the parent study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo: Participated in Graduate OLE

Arm description:

Participants treated with placebo in the DB part and who completed the DB and OLE up titration in study WN29922 (GRADUATE I) or WN39658 (GRADUATE II), continued receiving open-label gantenerumab, 510 milligrams (mg), SC, every two weeks (Q2W).

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 administered as SC injections at a dose of 510 mg, Q2W.

Arm title	Placebo: No Participation in Graduate OLE

Arm description:

Participants treated with placebo in the DB part and who did not enter the OLE part of study WN29922 (GRADUATE I) or WN39658 (GRADUATE II) received gantenerumab SC injections with gradual up titration starting at a dose of 120 mg, every four weeks (Q4W) for 3 doses, followed by 255 mg, Q4W for 3 doses, and then at a dose of 510 mg, Q4W for 3 doses before receiving open-label gantenerumab, 510 mg SC injections, Q2W. 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 administered as 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 3 doses before receiving open label gantenerumab, 510 mg SC injections, Q2W. To maintain the blind to previous treatment assignment, participants received Q2W, SC injections, with alternate doses

containing gantenerumab matching placebo.

Arm title	Gantenerumab: Participated in Graduate OLE
Arm description:	
Participants treated with gantenerumab in the DB part and who completed the DB and OLE part of study WN29922 (GRADUATE I) or WN39658 (GRADUATE II) continued receiving open-label gantenerumab, 510 mg, SC, Q2W.	
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 administered as SC injections at a dose of 510 mg, Q2W.	

Arm title	Gantenerumab: No Participation in Graduate OLE
Arm description:	
Participants treated with gantenerumab in the DB part and who did not enter the OLE part of study WN29922 (GRADUATE I) or WN39658 (GRADUATE II) continued receiving open-label gantenerumab 510 mg SC, Q2W.	
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 administered as SC injections at a dose of 510 mg, Q2W.	

Number of subjects in period 1	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE
Started	15	696	28
Completed	0	0	0
Not completed	15	696	28
Adverse event, serious fatal	-	3	1
Physician decision	1	10	1
Consent withdrawn by subject	-	55	3
Adverse event, non-fatal	-	26	2
Reason Not Specified	-	8	-
Study terminated by sponsor	13	593	21
Lost to follow-up	1	1	-
Protocol deviation	-	-	-

Lack of efficacy	-	-	-

Number of subjects in period 1	Gantenerumab: No Participation in Graduate OLE
Started	642
Completed	0
Not completed	642
Adverse event, serious fatal	1
Physician decision	10
Consent withdrawn by subject	40
Adverse event, non-fatal	12
Reason Not Specified	8
Study terminated by sponsor	566
Lost to follow-up	2
Protocol deviation	2
Lack of efficacy	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo: Participated in Graduate OLE
Reporting group description:	
Participants treated with placebo in the DB part and who completed the DB and OLE up titration in study WN29922 (GRADUATE I) or WN39658 (GRADUATE II), continued receiving open-label gantenerumab, 510 milligrams (mg), SC, every two weeks (Q2W).	
Reporting group title	Placebo: No Participation in Graduate OLE
Reporting group description:	
Participants treated with placebo in the DB part and who did not enter the OLE part of study WN29922 (GRADUATE I) or WN39658 (GRADUATE II) received gantenerumab SC injections with gradual up titration starting at a dose of 120 mg, every four weeks (Q4W) for 3 doses, followed by 255 mg, Q4W for 3 doses, and then at a dose of 510 mg, Q4W for 3 doses before receiving open-label gantenerumab, 510 mg SC injections, Q2W. To maintain the blind to previous treatment assignment, participants received Q2W, SC injections, with alternate doses containing gantenerumab matching placebo.	
Reporting group title	Gantenerumab: Participated in Graduate OLE
Reporting group description:	
Participants treated with gantenerumab in the DB part and who completed the DB and OLE part of study WN29922 (GRADUATE I) or WN39658 (GRADUATE II) continued receiving open-label gantenerumab, 510 mg, SC, Q2W.	
Reporting group title	Gantenerumab: No Participation in Graduate OLE
Reporting group description:	
Participants treated with gantenerumab in the DB part and who did not enter the OLE part of study WN29922 (GRADUATE I) or WN39658 (GRADUATE II) continued receiving open-label gantenerumab 510 mg SC, Q2W.	

Reporting group values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE
Number of subjects	15	696	28
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	76.7	73.6	74.1
standard deviation	± 7.8	± 7.4	± 8.0
Sex: Female, Male Units: participants			
Female	11	387	14
Male	4	309	14
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	25	4
Asian	1	104	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	6	0
White	14	549	22
More than one race	0	0	0
Unknown or Not Reported	0	12	1
Ethnicity (NIH/OMB)			

Units: Subjects			
Hispanic or Latino	6	116	14
Not Hispanic or Latino	9	576	14
Unknown or Not Reported	0	4	0

Reporting group values	Gantenerumab: No Participation in Graduate OLE	Total	
Number of subjects	642	1381	
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	73.0		
standard deviation	± 7.7	-	
Sex: Female, Male Units: participants			
Female	382	794	
Male	260	587	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	18	47	
Asian	87	193	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	4	10	
White	518	1103	
More than one race	0	0	
Unknown or Not Reported	15	28	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	89	225	
Not Hispanic or Latino	548	1147	
Unknown or Not Reported	5	9	

End points

End points reporting groups

Reporting group title	Placebo: Participated in Graduate OLE

Reporting group description:

Participants treated with placebo in the DB part and who completed the DB and OLE up titration in study WN29922 (GRADUATE I) or WN39658 (GRADUATE II), continued receiving open-label gantenerumab, 510 milligrams (mg), SC, every two weeks (Q2W).

Reporting group title	Placebo: No Participation in Graduate OLE

Reporting group description:

Participants treated with placebo in the DB part and who did not enter the OLE part of study WN29922 (GRADUATE I) or WN39658 (GRADUATE II) received gantenerumab SC injections with gradual up titration starting at a dose of 120 mg, every four weeks (Q4W) for 3 doses, followed by 255 mg, Q4W for 3 doses, and then at a dose of 510 mg, Q4W for 3 doses before receiving open-label gantenerumab, 510 mg SC injections, Q2W. To maintain the blind to previous treatment assignment, participants received Q2W, SC injections, with alternate doses containing gantenerumab matching placebo.

Reporting group title	Gantenerumab: Participated in Graduate OLE

Reporting group description:

Participants treated with gantenerumab in the DB part and who completed the DB and OLE part of study WN29922 (GRADUATE I) or WN39658 (GRADUATE II) continued receiving open-label gantenerumab, 510 mg, SC, Q2W.

Reporting group title	Gantenerumab: No Participation in Graduate OLE

Reporting group description:

Participants treated with gantenerumab in the DB part and who did not enter the OLE part of study WN29922 (GRADUATE I) or WN39658 (GRADUATE II) continued receiving open-label gantenerumab 510 mg SC, Q2W.

Subject analysis set title	Gantenerumab: Participated in Graduate OLE
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants treated with gantenerumab in the DB part and who completed the DB and OLE part of study WN29922 (GRADUATE I) or WN39658 (GRADUATE II) continued receiving open-label gantenerumab, 510 mg, SC, Q2W.

Subject analysis set title	Gantenerumab: No Participation in Graduate OLE
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants treated with gantenerumab in the DB part and who did not enter the OLE part of Study WN29922 (GRADUATE I) or WN39658 (GRADUATE II), continued receiving open-label gantenerumab 510 mg SC, Q2W.

Primary: Number of Participants With at Least One Adverse Event (AE) and Serious Adverse Event (SAE)

End point title	Number of Participants With at Least One Adverse Event (AE) and Serious Adverse Event (SAE)[1][2]

End point description:

AE is any untoward medical occurrence in clinical investigation participant administered a pharmaceutical product, regardless of casual attribution. SAE is any fatal AE, life threatening, requires or prolongs inpatient hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect in a neonate/infant born to a mother exposed to study drug or a significant medical event in investigator's judgment. Safety evaluable (SE) analysis set included all participants enrolled who received at least one dose of study drug in this study or in OLE part of parent studies (GRADUATE I or GRADUATE II). 6 participants randomized to placebo arm during double-blind treatment in parent studies received at least one dose of gantenerumab and were considered in gantenerumab arm for safety evaluable set. First dosing visit in OLE (first dosing in current study or first dosing in OLE period of parent GRADUATE studies) was considered as baseline (OLE Day 1).

End point type	Primary

End point timeframe:

From Baseline (OLE Day 1) up to 14 weeks after the last dose (up to 134 weeks)

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 was planned 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: Data for all arms of the study is reported. Due to difference in overall number analyzed, arms: 'Gantenerumab: Participated in Graduate OLE' and 'Gantenerumab: No Participation in Graduate OLE' are added as subject analysis set.

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE	Gantenerumab: No Participation in Graduate OLE
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	14	691	29	647
Units: participants				
AEs	13	510	25	487
SAEs	2	72	4	54

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Post-baseline Suicidal Ideation or Suicidal Behavior as Measured Using Columbia–Suicide Severity Rating Scale (C-SSRS) Score

End point title	Number of Participants With Post-baseline Suicidal Ideation or Suicidal Behavior as Measured Using Columbia–Suicide Severity Rating Scale (C-SSRS) Score[3][4]

End point description:

C-SSRS assesses lifetime suicidality of participant (baseline) & any new instances of suicidality (since last visit). Structured interview prompts recollection of suicidal ideation (intensity of ideation, behavior, & attempts with actual/potential lethality). Categories have yes/no responses, include Wish to be Dead; Non-specific Active Suicidal Thoughts; Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act; Active Suicidal Ideation with Some Intent to Act, without Specific Plan; Active Suicidal Ideation with Specific Plan and Intent, Preparatory Acts and Behavior; Aborted/Interrupted Attempt; Actual Attempt (non-fatal); Completed Suicide.Suicidal ideation/behavior="yes" to any of listed categories. Score 0= no suicide risk. Score 1 or higher=suicidal ideation or behavior. Categories with non-zero values are only reported here. First dosing visit in OLE (first dosing in current study or OLE period of parent GRADUATE studies)=baseline (OLE Day 1).SE analysis set.

End point type	Primary

End point timeframe:

From Baseline (OLE Day 1) up to 14 weeks after the last dose (up to 134 weeks)

Notes:

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

[4] - 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: Data for all arms of the study is reported. Due to difference in overall number analyzed, arms: 'Gantenerumab: Participated in Graduate OLE' is added as subject analysis set.

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	14	631	588	29
Units: participants				
Suicidal Ideation (SI): Passive	1	11	11	1
SI: Active-Nonspecific (No Intent, or Plan)	0	3	2	0
SI: Active-Method, but No Intent or Plan	1	0	0	1
Suicidal Ideation: No event	12	617	575	27
Suicidal Behavior: Aborted Attempt	0	1	0	0
Suicidal Behavior: Preparatory Actions	0	1	0	0
Suicidal Behavior: No event	14	629	586	29
Self-Injurious Behavior - No Suicidal Intent	0	2	0	0
Self-Injurious Behavior Without Intent: No event	14	629	588	29
Suicidal Behaviour: Completed Suicide	0	0	2	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with at Least One Amyloid-Related Imaging Abnormalities-Edema (ARIA-E) Confirmed by MRI

End point title	Number of Participants with at Least One Amyloid-Related Imaging Abnormalities-Edema (ARIA-E) Confirmed by MRI[5][6]

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. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1). M-SE analysis set included all participants in the SE analysis set who had at least one post-baseline safety MRI scan.

End point type	Primary

End point timeframe:

From Baseline (OLE Day 1) up to 14 weeks after the last dose (up to 134 weeks)

Notes:

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

[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: Data for all arms of the study is reported. Due to difference in overall number analyzed, arms: 'Gantenerumab: Participated in Graduate OLE' and 'Gantenerumab: No Participation in Graduate OLE' are added as subject analysis set.

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	14	671	627	29
Units: participants	6	104	27	5

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with at Least One Amyloid-Related Imaging Abnormalities-Haemosiderin Deposition (ARIA-H) Confirmed by MRI

End point title	Number of Participants with at Least One Amyloid-Related Imaging Abnormalities-Haemosiderin Deposition (ARIA-H) Confirmed by MRI[7][8]

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. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1). M-SE analysis set included all participants in the SE analysis set who had at least one post-baseline safety MRI scan.

End point type	Primary

End point timeframe:

From Baseline (OLE Day 1) up to 14 weeks after the last dose (up to 134 weeks)

Notes:

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

[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: Data for all arms of the study is reported. Due to difference in overall number analyzed, arms: 'Gantenerumab: Participated in Graduate OLE' and 'Gantenerumab: No Participation in Graduate OLE' are added as subject analysis set.

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	14	671	627	29
Units: participants	3	85	40	4

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Injection-Site Reactions (ISRs)

End point title	Number of Participants with Injection-Site Reactions (ISRs)[9]

	[10]

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 enrolled who received at least one dose of study drug in this study or in the OLE part of the parent studies (GRADUATE I or GRADUATE II). Six participants randomized to placebo arm during the double-blind treatment in the parent studies received at least one dose of gantenerumab and were considered in the gantenerumab arm for safety evaluable set. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

End point type	Primary

End point timeframe:

From Baseline (OLE Day 1) up to 14 weeks after the last dose (up to 134 weeks)

Notes:

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

[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: Data for all arms of the study is reported. Due to difference in overall number analyzed, arms: 'Gantenerumab: Participated in Graduate OLE' and 'Gantenerumab: No Participation in Graduate OLE' are added as subject analysis set.

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE	Gantenerumab: No Participation in Graduate OLE
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	14	691	29	647
Units: participants	3	63	1	80

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With at Least One Adverse Event of Special Interest (AESI)

End point title	Number of Participants With at Least One Adverse Event of Special Interest (AESI)[11][12]

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant administered a pharmaceutical product, regardless of casual attribution. AEs that were considered to be of special interest for this study included cases of potential drug-induced liver injury that include an elevated ALT or AST in combination with either an elevated bilirubin or clinical jaundice, as defined by Hy's Law and suspected transmission of an infectious agent by the study drug. Participants in SE analysis set were analysed. Six participants randomized to placebo arm during the double-blind treatment in the parent studies received at least one dose of gantenerumab and were considered in the gantenerumab arm for safety evaluable set. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

End point type	Primary

End point timeframe:

From Baseline (OLE Day 1) up to 14 weeks after the last dose (up to 134 weeks)

Notes:

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

[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: Data for all arms of the study is reported. Due to difference in overall number analyzed, arms: 'Gantenerumab: Participated in Graduate OLE' and 'Gantenerumab: No Participation in Graduate OLE' are added as subject analysis set.

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE	Gantenerumab: No Participation in Graduate OLE
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	14	691	29	647
Units: participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Discontinued the Study Due an AE

End point title	Number of Participants Who Discontinued the Study Due an

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant administered a pharmaceutical product, regardless of casual attribution. SE analysis set included all participants enrolled who received at least one dose of study drug in this study or in the OLE part of the parent studies (GRADUATE I or GRADUATE II). Six participants randomized to placebo arm during the double-blind treatment in the parent studies received at least one dose of gantenerumab and were considered in the gantenerumab arm for safety evaluable set. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

End point type	Primary

End point timeframe:

From Baseline (OLE Day 1) up to 14 weeks after the last dose (up to 134 weeks)

Notes:

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

[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: Data for all arms of the study is reported. Due to difference in overall number analyzed, arms: 'Gantenerumab: Participated in Graduate OLE' and 'Gantenerumab: No Participation in Graduate OLE' are added as subject analysis set.

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE	Gantenerumab: No Participation in Graduate OLE
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	14	691	29	647
Units: participants	0	9	1	7

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in Clinical Dementia Rating – Global Score (CDR-GS)

End point title	Change From Baseline Over Time in Clinical Dementia Rating – Global Score (CDR-GS)

End point description:

CDR was derived through semi-structured interview with participant and an appropriate informant, and 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=normal, 0.5=very mild dementia, 1=mild dementia, 2=moderate dementia, and 3= severe dementia. Score range for CDR-GS is from 0 to 3 and a high score on the CDR-GS would indicate a high disease severity. A negative change from baseline indicates improvement. Participants in ITT analysis set were analysed. Overall number analyzed is number of participants with data available for analyses. Number of participants analyzed indicates number of participants with data available for analyses at specified timepoint. First dosing visit in OLE (first dosing in current study or first dosing in OLE period of parent GRADUATE studies) was considered as baseline (OLE Day 1).

End point type	Secondary

End point timeframe:

Baseline (OLE Day 1), Weeks 24, 36, 52, 76 and 104

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE	Gantenerumab: No Participation in Graduate OLE
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	693	25	641
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 24 (n=15,611,25,561)	0.4 (± 0.50)	0.1 (± 0.43)	0.1 (± 0.53)	0.1 (± 0.41)
Change from Baseline at Week 36 (n=5,107,9,89)	0.4 (± 0.55)	0.3 (± 0.55)	0.1 (± 0.42)	0.2 (± 0.47)
Change from Baseline at Week 52 (n=14,336,20,327)	0.3 (± 0.46)	0.2 (± 0.44)	-0.1 (± 0.43)	0.2 (± 0.46)
Change from Baseline at Week 76 (n=11,169,19,161)	0.5 (± 0.69)	0.3 (± 0.47)	0.2 (± 0.75)	0.3 (± 0.44)
Change from Baseline at Week 104 (n=5,19,13,20)	0.6 (± 0.89)	0.6 (± 0.52)	0.2 (± 0.43)	0.3 (± 0.50)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in Clinical Dementia Rating (CDR) – Sum of Boxes (SB)

End point title	Change From Baseline Over Time in Clinical Dementia Rating (CDR) – Sum of Boxes (SB)

End point description:

CDR 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, and severe impairment, respectively. CDR-SB is based on summing each of 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. Overall number analyzed is the number of participants with data available for analyses. The number of participants analyzed indicates the number of participants with data available for analyses at the specified timepoint. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

End point type	Secondary

End point timeframe:

Baseline (OLE Day 1), Weeks 24, 36, 52, 76 and 104

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE	Gantenerumab: No Participation in Graduate OLE
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	693	28	641
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 24 (n=15,611,25,561)	2.10 (± 2.473)	0.83 (± 1.787)	1.00 (± 2.529)	0.70 (± 1.754)
Change from Baseline at Week 36 (n=5,107,9,89)	2.90 (± 2.608)	1.39 (± 2.397)	0.72 (± 2.265)	1.11 (± 2.161)
Change from Baseline at Week 52 (n=14,336,20,327)	2.57 (± 2.286)	1.60 (± 1.906)	0.80 (± 1.351)	1.50 (± 2.051)
Change from Baseline at Week 76 (n=11,169,19,161)	2.68 (± 3.133)	2.20 (± 1.994)	1.95 (± 3.218)	1.97 (± 2.249)
Change from Baseline at Week 104 (n=5,19,13,20)	3.80 (± 3.213)	3.26 (± 2.751)	1.15 (± 2.470)	1.80 (± 1.949)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in Mini-Mental State Examination (MMSE) Score

End point title	Change From Baseline Over Time in Mini-Mental State Examination (MMSE) Score

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. Overall number analyzed is the number of participants with data available for analyses. The number of participants analyzed indicates the number of participants with data available for analyses at

the specified timepoint. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

End point type	Secondary

End point timeframe:

Baseline (OLE Day 1), Weeks 24, 36, 52, 76 and 104

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab : Participated in Graduate OLE	Gantenerumab : No Participation in Graduate OLE
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	694	28	641
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 24 (n=15,622,27,571)	-0.3 (± 2.41)	-1.2 (± 2.87)	-0.9 (± 2.39)	-1.1 (± 2.69)
Change from Baseline at Week 36 (n=5,111,9,93)	-1.8 (± 3.35)	-1.6 (± 2.83)	-0.3 (± 1.66)	-1.7 (± 3.18)
Change from Baseline at Week 52 (n=15,346,21,337)	-1.9 (± 2.94)	-2.3 (± 3.15)	-2.0 (± 3.49)	-2.1 (± 3.14)
Change from Baseline at Week 76 (n=12,173,20,165)	-2.9 (± 3.20)	-3.2 (± 3.39)	-2.9 (± 3.97)	-3.0 (± 3.56)
Change from Baseline at Week 104 (n=5,19,14,21)	-3.6 (± 5.13)	-4.3 (± 3.93)	-2.9 (± 3.92)	-3.0 (± 4.12)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in Alzheimer Disease Assessment Scale-Cognition, Subscale 11 (ADAS-Cog11) Score

End point title	Change From Baseline Over Time in Alzheimer Disease Assessment Scale-Cognition, Subscale 11 (ADAS-Cog11) Score

End point description:

The ADAS-Cog11 was designed to measure cognitive symptom change in participants with Alzheimer's Disease (AD) and consisted of 11 tasks. The test included 7 performance items and 4 clinician-rated items. The total score was the sum of all 11 individual items, ranging from 0 (no impairment) to 70 (severe impairment). ITT analysis set included all enrolled participants, who received at least one dose of study drug. Participants will be analyzed by the treatment they were randomized to in the parent studies (GRADUATE I or GRADUATE II). Overall number analyzed is the number of participants with data available for analyses. The number of participants analyzed indicates the number of participants with data available for analyses at the specified timepoint. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

End point type	Secondary

End point timeframe:

Baseline (OLE Day 1), Weeks 24, 36, 52, 76 and 104

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE	Gantenerumab: No Participation in Graduate OLE
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	688	28	630
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 24 (n=14,611,27,549)	2.4 (± 5.56)	2.4 (± 5.47)	1.6 (± 5.29)	2.8 (± 5.22)
Change from Baseline at Week 36 (n=5,107,9,86)	12.0 (± 10.00)	3.9 (± 6.80)	-3.7 (± 5.50)	4.0 (± 5.46)
Change from Baseline at Week 52 (n=14,332,20,326)	5.6 (± 9.55)	3.7 (± 6.13)	1.9 (± 5.89)	4.7 (± 6.61)
Change from Baseline at Week 76 (n=11,170,20,162)	6.6 (± 10.90)	5.9 (± 7.52)	7.0 (± 9.50)	6.1 (± 7.80)
Change from Baseline at Week 104 (n=5,19,13,22)	8.4 (± 14.12)	7.8 (± 7.65)	3.8 (± 6.67)	8.2 (± 10.26)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in Alzheimer Disease Assessment Scale-Cognition, Subscale 13 (ADAS-Cog13) Score

End point title	Change From Baseline Over Time in Alzheimer Disease Assessment Scale-Cognition, Subscale 13 (ADAS-Cog13) Score

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. Overall number analyzed is the number of participants with data available for analyses. The number of participants analyzed indicates the number of participants with data available for analyses at the specified timepoint. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

End point type	Secondary

End point timeframe:

Baseline (OLE Day 1), Weeks 24, 36, 52, 76 and 104

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE	Gantenerumab: No Participation in Graduate OLE
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	677	28	623
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 24 (n=14,597,27,542)	2.9 (± 6.29)	3.0 (± 5.73)	2.0 (± 5.53)	3.3 (± 5.45)
Change from Baseline at Week 36 (n=5,104,9,84)	13.2 (± 11.52)	4.7 (± 7.05)	-3.4 (± 5.39)	4.7 (± 5.85)

Change from Baseline at Week 52 (n=14,325,20,319)	6.7 (± 10.13)	4.3 (± 6.45)	2.7 (± 6.01)	5.3 (± 6.94)
Change from Baseline at Week 76 (n=11,164,20,161)	7.9 (± 11.89)	6.8 (± 7.85)	7.7 (± 9.76)	6.7 (± 8.22)
Change from Baseline at Week 104 (n=5,19,13,22)	10.4 (± 14.98)	8.7 (± 8.13)	4.8 (± 6.74)	8.8 (± 10.22)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in Verbal Fluency Task Score

End point title	Change From Baseline Over Time in Verbal Fluency Task Score

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 enrolled participants, who received at least one dose of study drug. Participants will be analyzed by the treatment they were randomized to in the parent studies (GRADUATE I or GRADUATE II). Overall number analyzed is the number of participants with data available for analyses. The number of participants analyzed indicates the number of participants with data available for analyses at the specified timepoint. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

End point type	Secondary

End point timeframe:

Baseline (OLE Day 1), Weeks 24, 36, 52, 76 and 104

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE	Gantenerumab: No Participation in Graduate OLE
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	693	28	641
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 24 (n=15,622,27,567)	0.2 (± 2.73)	-0.9 (± 3.15)	-1.0 (± 2.83)	-0.6 (± 4.73)
Change from Baseline at Week 36 (n=5,108,9,90)	-2.2 (± 3.42)	-1.2 (± 3.07)	-0.6 (± 2.70)	-1.4 (± 3.45)
Change from Baseline at Week 52 (n=15,346,20,337)	-1.5 (± 3.02)	-1.5 (± 3.60)	-0.4 (± 2.39)	-1.5 (± 5.77)
Change from Baseline at Week 76 (n=12,176,19,164)	-1.3 (± 2.83)	-2.1 (± 3.66)	-1.3 (± 4.36)	-2.8 (± 7.54)
Change from Baseline at Week 104 (n=5,19,13,21)	-0.6 (± 4.22)	-3.8 (± 3.79)	-0.8 (± 4.09)	-3.3 (± 2.50)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in Coding (Digit Symbol Substitution Test [DSST]) Subset

End point title	Change From Baseline Over Time in Coding (Digit Symbol Substitution Test [DSST]) Subset

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 enrolled participants, who received at least one dose of study drug. Participants will be analyzed by the treatment they were randomized to in the parent studies (GRADUATE I or GRADUATE II). Overall number analyzed is the number of participants with data available for analyses. The number of participants analyzed indicates the number of participants with data available for analyses at the specified timepoint. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

End point type	Secondary

End point timeframe:

Baseline (OLE Day 1), Weeks 24, 36, 52, 76 and 104

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE	Gantenerumab: No Participation in Graduate OLE
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	693	28	640
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 24 (n=14,617,27,563)	-0.5 (± 6.31)	-2.8 (± 7.84)	-0.3 (± 9.02)	-2.3 (± 8.04)
Change from Baseline at Week 36 (n=5,107,9,89)	-8.0 (± 10.00)	-4.8 (± 8.09)	6.2 (± 13.96)	-3.0 (± 9.66)
Change from Baseline at Week 52 (n=15,343,20,333)	-3.1 (± 7.61)	-5.0 (± 8.60)	-2.8 (± 14.00)	-4.7 (± 8.79)
Change from Baseline at Week 76 (n=11,171,19,164)	-3.4 (± 8.49)	-7.2 (± 10.12)	-7.1 (± 8.99)	-6.0 (± 9.71)
Change from Baseline at Week 104 (n=5,19,13,21)	0.4 (± 9.94)	-4.5 (± 13.25)	-5.2 (± 11.95)	-7.0 (± 11.04)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Functional Activities Questionnaire (FAQ) Score

End point title	Change in Functional Activities Questionnaire (FAQ) Score

End point description:

FAQ is a rater-administered observer-reported outcomes (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. Overall number analyzed is the number of participants with data available for analyses. The number of participants analyzed indicates the number of participants with data available for analyses at the specified timepoint. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

End point type	Secondary

End point timeframe:

Baseline (OLE Day 1), Weeks 24, 36, 52, 76 and 104

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE	Gantenerumab: No Participation in Graduate OLE
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	694	27	637
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 24 (n=15,618,25,568)	1.2 (± 4.04)	1.6 (± 4.36)	0.1 (± 3.15)	1.5 (± 4.09)
Change from Baseline at Week 36 (n=5,111,9,96)	-1.0 (± 1.87)	2.7 (± 5.07)	1.3 (± 6.18)	1.7 (± 4.92)
Change from Baseline at Week 52 (n=14,346,19,333)	2.1 (± 3.80)	2.6 (± 4.39)	2.7 (± 3.73)	2.6 (± 4.81)
Change from Baseline at Week 76 (n=13,172,20,162)	2.3 (± 3.66)	4.0 (± 4.55)	3.3 (± 3.95)	3.5 (± 5.12)
Change from Baseline at Week 104 (n=5,17,13,21)	3.2 (± 4.92)	4.5 (± 4.09)	4.1 (± 4.91)	1.7 (± 5.07)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Alzheimer Disease Cooperative Study Group-Activities of Daily Living (ADCS-ADL) Score

End point title	Change in Alzheimer Disease Cooperative Study Group-Activities of Daily Living (ADCS-ADL) Score

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. ITT analysis set. Overall number analyzed is the number of participants with data available for analyses. The number of participants analyzed indicates the number of participants with data available for analyses at the specified timepoint. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

End point type	Secondary

End point timeframe:

Baseline (OLE Day 1), Weeks 24, 36, 52, 76 and 104

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE	Gantenerumab: No Participation in Graduate OLE
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	694	27	639
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 24 (n=15,618,25,569)	-4.7 (± 5.15)	-2.9 (± 7.07)	-2.0 (± 7.10)	-3.2 (± 6.69)
Change from Baseline at Week 36 (n=4,111,9,96)	-12.5 (± 12.40)	-5.6 (± 9.55)	-2.1 (± 6.23)	-4.9 (± 8.53)
Change from Baseline at Week 52 (n=14,344,19,334)	-9.4 (± 7.49)	-5.9 (± 8.97)	-4.4 (± 8.09)	-6.2 (± 8.38)
Change from Baseline at Week 76 (n=13,172,20,162)	-10.8 (± 11.19)	-7.8 (± 9.87)	-8.3 (± 11.22)	-6.9 (± 9.62)
Change from Baseline at Week 104 (n=5,17,13,21)	-11.6 (± 17.99)	-6.6 (± 10.20)	-6.3 (± 13.52)	-9.9 (± 12.21)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-drug Antibody (ADA) to Gantenerumab

End point title	Number of Participants with Anti-drug Antibody (ADA) to Gantenerumab[15]

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. Evaluable participant during OLE was participant with an ADA assay result from at least one sample during OLE. 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 enrolled who received at least one dose of study drug in this study or in the OLE part of the parent studies (GRADUATE I or GRADUATE II). Six participants randomized to placebo arm during the double-blind treatment in the parent studies received at least one dose of gantenerumab and were considered in the gantenerumab arm for safety evaluable set. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

End point type	Secondary

End point timeframe:

Baseline (OLE Day 1) up to 14 weeks after the last dose (up to 134 weeks)

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: Data for all arms of the study is reported. Due to difference in overall number analyzed, arms: 'Gantenerumab: Participated in Graduate OLE' and 'Gantenerumab: No Participation in Graduate OLE' are added as subject analysis set.

End point values	Placebo: Participated in Graduate OLE	Placebo: No Participation in Graduate OLE	Gantenerumab: Participated in Graduate OLE	Gantenerumab: No Participation in Graduate OLE
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	14	656	29	617
Units: participants	1	17	1	14

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline (OLE Day 1) up to 14 weeks after the last dose (up to 110 weeks)

Adverse event reporting additional description:

SE analysis set. 6 participants randomized to placebo arm during double-blind treatment in parent studies received at least 1 dose of gantenerumab and were considered in gantenerumab arm for SE set. 1st dosing visit in OLE (1st dosing in current study or first dosing in OLE period of parent GRADUATE studies) was considered as baseline (OLE Day 1).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Placebo: Participated in Graduate OLE

Reporting group description:

Participants treated with placebo in the DB part and who completed the DB and OLE up titration part of WN29922 or WN39658, were enrolled in this arm and continued receiving open-label gantenerumab, 510 mg, SC, Q2W.

Reporting group title	Gantenerumab: Participated in Graduate OLE

Reporting group description:

Participants treated with gantenerumab in the DB part and who completed the DB and OLE part of Study WN29922 or WN39658, were enrolled in this arm and continued receiving open-label gantenerumab, 510 mg, SC, Q2W.

Reporting group title	Gantenerumab: No Participation in Graduate OLE

Reporting group description:

Participants treated with gantenerumab in the DB part and who did not enter the OLE part of Study WN29922 or WN39658, were enrolled in this arm and continued receiving open-label gantenerumab 510 mg SC, Q2W.

Reporting group title	Placebo: No Participation in Graduate OLE

Reporting group description:

Participants treated with placebo in the DB part and who did not enter the OLE part of Study WN29922 or WN39658, were enrolled in this arm to receive 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, 510 mg Q4W for 3 doses before receiving open-label gantenerumab, 510 mg SC injections, Q2W. To maintain the blind to previous treatment assignment, participants received Q2W, SC injections, with alternate doses containing gantenerumab matching placebo.

Serious adverse events	Placebo: Participated in Graduate OLE	Gantenerumab: Participated in Graduate OLE	Gantenerumab: No Participation in Graduate OLE
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 14 (14.29%)	4 / 29 (13.79%)	54 / 647 (8.35%)
number of deaths (all causes)	0	1	4
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			

subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric leiomyoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pancreatic carcinoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary neoplasm			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Melanoma recurrent			

subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive breast carcinoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Glioblastoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Malignant melanoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery aneurysm			

subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 dissection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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			
Pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Chest pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Pyrexia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 oedema			

subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal prolapse			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			

subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delusion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Investigations			
Troponin increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Contusion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Accidental overdose			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Wound			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Fracture displacement			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Spinal compression fracture			
subjects affected / exposed	0 / 14 (0.00%)	1 / 29 (3.45%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post-traumatic pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			

subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 14 (0.00%)	1 / 29 (3.45%)	0 / 647 (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
Road traffic accident			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 14 (0.00%)	1 / 29 (3.45%)	4 / 647 (0.62%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrioventricular block complete			

subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Myocardial infarction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Tachycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cor pulmonale acute			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			

subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	2 / 647 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Upper motor neurone lesion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	2 / 647 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	2 / 647 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasogenic cerebral oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Presyncope			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Headache			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epileptic encephalopathy			

subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Hydrocephalus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 / 14 (0.00%)	1 / 29 (3.45%)	0 / 647 (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 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thalamus haemorrhage			

subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Motor dysfunction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Dysstasia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Meniere's disease			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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			
Cataract			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 ulcer			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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
Decubitus ulcer			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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			
Urinary retention			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus bladder			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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			
Escherichia urinary tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 29 (3.45%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Wound infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	3 / 647 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Diverticulitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	2 / 647 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	2 / 647 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Skin infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			

subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	0 / 647 (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	1 / 14 (7.14%)	0 / 29 (0.00%)	2 / 647 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	0 / 14 (0.00%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo: No		

	Participation in Graduate OLE		
Total subjects affected by serious adverse events			
subjects affected / exposed	72 / 691 (10.42%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric leiomyoma			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatic carcinoma			
subjects affected / exposed	2 / 691 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Colon cancer			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary neoplasm			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Bladder cancer				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Melanoma recurrent				
subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Invasive breast carcinoma				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Glioblastoma				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric cancer				
subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic myeloid leukaemia				
subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				

Deep vein thrombosis				
subjects affected / exposed	3 / 691 (0.43%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Peripheral artery aneurysm				
subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral arterial occlusive disease				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aortic dissection				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Pain				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Pyrexia			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Generalised oedema			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostatitis			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vaginal prolapse			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	5 / 691 (0.72%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			

subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Agitation			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Confusional state			
subjects affected / exposed	2 / 691 (0.29%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Mental status changes			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Delusion			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Troponin increased			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Contusion			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Accidental overdose			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subdural haemorrhage			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Radius fracture			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fracture displacement			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post-traumatic pain			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Head injury			

subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Concussion				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	3 / 691 (0.43%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Fall				
subjects affected / exposed	4 / 691 (0.58%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	2 / 691 (0.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				

subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrioventricular block complete				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bradycardia				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tachycardia				
subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cor pulmonale acute				
subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	2 / 691 (0.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Cardiac arrest				

subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	2 / 691 (0.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Nervous system disorders				
Upper motor neurone lesion				
subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Loss of consciousness				
subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vasogenic cerebral oedema				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral ischaemia				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Headache				

subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epileptic encephalopathy				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cerebral infarction				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hydrocephalus				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	3 / 691 (0.43%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Amyloid related imaging abnormality-oedema/effusion				
subjects affected / exposed	2 / 691 (0.29%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				

subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thalamus haemorrhage			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subdural hygroma			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Motor dysfunction			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dysstasia			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Meniere's disease			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anal ulcer			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal fistula			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			

Cholecystitis			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Decubitus ulcer			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Calculus bladder			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Escherichia urinary tract infection			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			

subjects affected / exposed	2 / 691 (0.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	3 / 691 (0.43%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	3 / 691 (0.43%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	1 / 691 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin infection				
subjects affected / exposed	0 / 691 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19 pneumonia				

subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malnutrition			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo: Participated in Graduate OLE	Gantenerumab: Participated in Graduate OLE	Gantenerumab: No Participation in Graduate OLE
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 14 (92.86%)	21 / 29 (72.41%)	358 / 647 (55.33%)
Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 14 (14.29%)	0 / 29 (0.00%)	11 / 647 (1.70%)
occurrences (all)	2	0	11
Hypertensive crisis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	1	0	0
Arteriosclerosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences (all)	1	0	1
Hypertension			
subjects affected / exposed	3 / 14 (21.43%)	2 / 29 (6.90%)	19 / 647 (2.94%)
occurrences (all)	3	2	22
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	3 / 14 (21.43%)	1 / 29 (3.45%)	80 / 647 (12.36%)
occurrences (all)	5	10	266
Fatigue			
subjects affected / exposed	0 / 14 (0.00%)	2 / 29 (6.90%)	10 / 647 (1.55%)
occurrences (all)	0	2	10
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	2 / 14 (14.29%)	1 / 29 (3.45%)	1 / 647 (0.15%)
occurrences (all)	2	1	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 29 (3.45%)	16 / 647 (2.47%)
occurrences (all)	1	1	16
Hallucination			

subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences (all)	1	0	1
Aggression			
subjects affected / exposed	1 / 14 (7.14%)	1 / 29 (3.45%)	3 / 647 (0.46%)
occurrences (all)	2	1	3
Confusional state			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	9 / 647 (1.39%)
occurrences (all)	1	0	13
Irritability			
subjects affected / exposed	0 / 14 (0.00%)	2 / 29 (6.90%)	4 / 647 (0.62%)
occurrences (all)	0	2	4
Anxiety			
subjects affected / exposed	1 / 14 (7.14%)	1 / 29 (3.45%)	14 / 647 (2.16%)
occurrences (all)	1	1	14
Depression			
subjects affected / exposed	0 / 14 (0.00%)	2 / 29 (6.90%)	5 / 647 (0.77%)
occurrences (all)	0	2	5
Delusion			
subjects affected / exposed	0 / 14 (0.00%)	2 / 29 (6.90%)	4 / 647 (0.62%)
occurrences (all)	0	2	4
Investigations			
Vitamin B12 decreased			
subjects affected / exposed	0 / 14 (0.00%)	2 / 29 (6.90%)	5 / 647 (0.77%)
occurrences (all)	0	2	5
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 14 (7.14%)	1 / 29 (3.45%)	4 / 647 (0.62%)
occurrences (all)	1	1	4
Contusion			
subjects affected / exposed	3 / 14 (21.43%)	2 / 29 (6.90%)	13 / 647 (2.01%)
occurrences (all)	4	2	35
Wrist fracture			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	1	0	0
Procedural pain			

subjects affected / exposed	2 / 14 (14.29%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	2	0	0
Fall			
subjects affected / exposed	4 / 14 (28.57%)	6 / 29 (20.69%)	59 / 647 (9.12%)
occurrences (all)	7	10	92
Spinal compression fracture			
subjects affected / exposed	0 / 14 (0.00%)	2 / 29 (6.90%)	2 / 647 (0.31%)
occurrences (all)	0	2	3
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Cardiac failure chronic			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	1	0	0
Myocardial ischaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	1	0	0
Arrhythmia			
subjects affected / exposed	1 / 14 (7.14%)	2 / 29 (6.90%)	0 / 647 (0.00%)
occurrences (all)	1	3	0
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences (all)	2	0	1
Dysarthria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	1	0	0
Neuralgia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences (all)	1	0	1
Cerebral haemorrhage			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	1	0	0
Amyloid related imaging abnormality-microhaemorrhages and			

haemosiderin deposits			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	7 / 647 (1.08%)
occurrences (all)	1	0	7
Migraine			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences (all)	1	0	1
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	5 / 14 (35.71%)	3 / 29 (10.34%)	16 / 647 (2.47%)
occurrences (all)	5	4	17
Dizziness			
subjects affected / exposed	0 / 14 (0.00%)	4 / 29 (13.79%)	22 / 647 (3.40%)
occurrences (all)	0	5	23
Headache			
subjects affected / exposed	1 / 14 (7.14%)	1 / 29 (3.45%)	24 / 647 (3.71%)
occurrences (all)	1	1	46
Somnolence			
subjects affected / exposed	1 / 14 (7.14%)	2 / 29 (6.90%)	3 / 647 (0.46%)
occurrences (all)	1	2	3
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	2 / 647 (0.31%)
occurrences (all)	1	0	2
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	2 / 647 (0.31%)
occurrences (all)	1	0	2
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	23 / 647 (3.55%)
occurrences (all)	1	0	29
Anal incontinence			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	6 / 647 (0.93%)
occurrences (all)	1	0	7
Diarrhoea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	17 / 647 (2.63%)
occurrences (all)	1	0	20

Umbilical hernia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	1	0	0
Dysphagia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 29 (3.45%)	1 / 647 (0.15%)
occurrences (all)	1	1	1
Colitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	13 / 647 (2.01%)
occurrences (all)	1	0	13
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 14 (7.14%)	2 / 29 (6.90%)	9 / 647 (1.39%)
occurrences (all)	1	2	12
Alopecia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences (all)	1	0	1
Dermatosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	8 / 647 (1.24%)
occurrences (all)	1	0	8
Renal and urinary disorders			
Bladder irritation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	1	0	0
Stress urinary incontinence			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	1	0	0
Incontinence			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			

subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	4 / 647 (0.62%)
occurrences (all)	1	0	4
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 14 (0.00%)	2 / 29 (6.90%)	32 / 647 (4.95%)
occurrences (all)	0	2	36
Osteoporosis			
subjects affected / exposed	0 / 14 (0.00%)	2 / 29 (6.90%)	0 / 647 (0.00%)
occurrences (all)	0	2	0
Neck pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 29 (3.45%)	5 / 647 (0.77%)
occurrences (all)	1	1	6
Myalgia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 29 (6.90%)	3 / 647 (0.46%)
occurrences (all)	0	2	3
Arthritis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences (all)	1	0	1
Arthralgia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 29 (3.45%)	33 / 647 (5.10%)
occurrences (all)	0	1	39
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	3 / 14 (21.43%)	1 / 29 (3.45%)	37 / 647 (5.72%)
occurrences (all)	9	2	52
Urosepsis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	3	0	0
COVID-19			
subjects affected / exposed	3 / 14 (21.43%)	3 / 29 (10.34%)	90 / 647 (13.91%)
occurrences (all)	3	3	92
Sinusitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	1	0	0
Bacteriuria			

subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	1 / 647 (0.15%)
occurrences (all)	1	0	1
Dacryocystitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	2	0	0
Pharyngitis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 29 (3.45%)	1 / 647 (0.15%)
occurrences (all)	1	1	1
Dermatophytosis of nail			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 14 (0.00%)	2 / 29 (6.90%)	1 / 647 (0.15%)
occurrences (all)	0	2	1
Pelvic inflammatory disease			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	0 / 647 (0.00%)
occurrences (all)	2	0	0
Gastroenteritis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	6 / 647 (0.93%)
occurrences (all)	1	0	7
Nasopharyngitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 29 (0.00%)	29 / 647 (4.48%)
occurrences (all)	2	0	30
Metabolism and nutrition disorders			
Vitamin B12 deficiency			
subjects affected / exposed	0 / 14 (0.00%)	2 / 29 (6.90%)	15 / 647 (2.32%)
occurrences (all)	0	2	15

Non-serious adverse events	Placebo: No Participation in Graduate OLE		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	395 / 691 (57.16%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	10 / 691 (1.45%)		
occurrences (all)	10		
Hypertensive crisis			

subjects affected / exposed	1 / 691 (0.14%)		
occurrences (all)	1		
Arteriosclerosis			
subjects affected / exposed	4 / 691 (0.58%)		
occurrences (all)	4		
Hypertension			
subjects affected / exposed	14 / 691 (2.03%)		
occurrences (all)	15		
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	63 / 691 (9.12%)		
occurrences (all)	157		
Fatigue			
subjects affected / exposed	17 / 691 (2.46%)		
occurrences (all)	20		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	3 / 691 (0.43%)		
occurrences (all)	3		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	16 / 691 (2.32%)		
occurrences (all)	17		
Hallucination			
subjects affected / exposed	4 / 691 (0.58%)		
occurrences (all)	4		
Aggression			
subjects affected / exposed	8 / 691 (1.16%)		
occurrences (all)	8		
Confusional state			
subjects affected / exposed	11 / 691 (1.59%)		
occurrences (all)	12		
Irritability			
subjects affected / exposed	5 / 691 (0.72%)		
occurrences (all)	5		
Anxiety			

subjects affected / exposed	11 / 691 (1.59%)		
occurrences (all)	11		
Depression			
subjects affected / exposed	12 / 691 (1.74%)		
occurrences (all)	12		
Delusion			
subjects affected / exposed	2 / 691 (0.29%)		
occurrences (all)	2		
Investigations			
Vitamin B12 decreased			
subjects affected / exposed	11 / 691 (1.59%)		
occurrences (all)	12		
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	5 / 691 (0.72%)		
occurrences (all)	5		
Contusion			
subjects affected / exposed	20 / 691 (2.89%)		
occurrences (all)	21		
Wrist fracture			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences (all)	1		
Procedural pain			
subjects affected / exposed	2 / 691 (0.29%)		
occurrences (all)	4		
Fall			
subjects affected / exposed	50 / 691 (7.24%)		
occurrences (all)	67		
Spinal compression fracture			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences (all)	0		
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences (all)	1		
Cardiac disorders			

Cardiac failure chronic			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences (all)	0		
Myocardial ischaemia			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences (all)	0		
Arrhythmia			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	3 / 691 (0.43%)		
occurrences (all)	3		
Dysarthria			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences (all)	0		
Neuralgia			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences (all)	1		
Cerebral haemorrhage			
subjects affected / exposed	2 / 691 (0.29%)		
occurrences (all)	2		
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
subjects affected / exposed	21 / 691 (3.04%)		
occurrences (all)	22		
Migraine			
subjects affected / exposed	3 / 691 (0.43%)		
occurrences (all)	3		
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	67 / 691 (9.70%)		
occurrences (all)	76		
Dizziness			
subjects affected / exposed	23 / 691 (3.33%)		
occurrences (all)	27		
Headache			

subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all)	33 / 691 (4.78%) 41 8 / 691 (1.16%) 10		
Blood and lymphatic system disorders Iron deficiency anaemia subjects affected / exposed occurrences (all)	 4 / 691 (0.58%) 4		
Eye disorders Dry eye subjects affected / exposed occurrences (all)	 3 / 691 (0.43%) 3		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Anal incontinence subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Umbilical hernia subjects affected / exposed occurrences (all) Dysphagia subjects affected / exposed occurrences (all) Colitis subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all)	 10 / 691 (1.45%) 15 5 / 691 (0.72%) 5 13 / 691 (1.88%) 15 0 / 691 (0.00%) 0 2 / 691 (0.29%) 2 1 / 691 (0.14%) 1 14 / 691 (2.03%) 14		
Skin and subcutaneous tissue disorders			

Rash subjects affected / exposed occurrences (all)	11 / 691 (1.59%) 12		
Alopecia subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1		
Dermatosis subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0		
Erythema subjects affected / exposed occurrences (all)	4 / 691 (0.58%) 4		
Renal and urinary disorders Bladder irritation subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0		
Stress urinary incontinence subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0		
Incontinence subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0		
Urinary incontinence subjects affected / exposed occurrences (all)	6 / 691 (0.87%) 6		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	15 / 691 (2.17%) 16		
Osteoporosis subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1		
Neck pain subjects affected / exposed occurrences (all)	6 / 691 (0.87%) 6		
Myalgia			

subjects affected / exposed	3 / 691 (0.43%)		
occurrences (all)	3		
Arthritis			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	25 / 691 (3.62%)		
occurrences (all)	26		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	30 / 691 (4.34%)		
occurrences (all)	38		
Urosepsis			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	114 / 691 (16.50%)		
occurrences (all)	116		
Sinusitis			
subjects affected / exposed	4 / 691 (0.58%)		
occurrences (all)	5		
Bacteriuria			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences (all)	0		
Dacryocystitis			
subjects affected / exposed	0 / 691 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	4 / 691 (0.58%)		
occurrences (all)	4		
Dermatophytosis of nail			
subjects affected / exposed	3 / 691 (0.43%)		
occurrences (all)	3		
Respiratory tract infection viral			
subjects affected / exposed	1 / 691 (0.14%)		
occurrences (all)	1		

Pelvic inflammatory disease subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0		
Gastroenteritis subjects affected / exposed occurrences (all)	4 / 691 (0.58%) 4		
Nasopharyngitis subjects affected / exposed occurrences (all)	25 / 691 (3.62%) 28		
Metabolism and nutrition disorders Vitamin B12 deficiency subjects affected / exposed occurrences (all)	14 / 691 (2.03%) 14		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 December 2021	The purpose of this update was primarily to include the requirement to agree not to donate blood or blood products during the study and for one year after final dose and to include the requirement for a caregiver during the study, consistent with the parent studies. In addition, an assessment of the impact of the COVID-19 pandemic on POSTGRADUATE and an assessment of concomitant administration of the COVID-19 vaccine with gantenerumab was added. Finally, this update clarified that the pharmacokinetic (PK) and biomarker objectives were exploratory. Changes to the protocol, along with a rationale for each change, are summarized in Protocol Amendment v2.
10 May 2022	Protocol Amendment v3 was never submitted to any Health Authorities or Institutional Review Boards (IRBs)/Ethics Committees (ECs) due to some typographical errors that occurred during editing. Although not submitted, it was decided that to maintain version control, an updated version of the document was required to ensure clarity of information.
11 May 2022	The purpose of this update was primarily to extend the POSTGRADUATE OLE treatment period from 2 to 4 years. Changes to the protocol, along with a rationale for each change, are summarized in Protocol Amendment v4.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
06 March 2023	Decision to terminate development of Gantenerumab for treatment of prodromal/mild/early-stage Alzheimer's disease following results of a pre-planned analysis of the safety and efficacy of Gant in Graduate I&II (WN29922/WN39658).	-

Notes:

Limitations and caveats

None reported