Clinical trial results:
A Phase III, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter, Efficacy and Safety Study of Gantenerumab in Patients With Mild Alzheimer's Disease; Part II: Open-Label Extension For Participating Patients

Summary

EudraCT number	2013-003390-95
Trial protocol	GB DE SE ES PT IT NL BE HU FI BG DK FR
Global end of trial date	16 April 2021

Results information

Result version number	v2 (current)
This version publication date	22 July 2022
First version publication date	25 April 2022
Version creation reason	• Correction of full data set Updated pre-assignment details, updated overall number of participants analysed, timeframe, and unit of measure in the endpoint.

Trial information

Trial identification

Sponsor protocol code	WN28745

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02051608
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH4070
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	16 April 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of subcutaneous Gantenerumab on cognition and function in mild Alzheimer’s disease.

Protection of trial subjects:

All study subjects were required to sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 March 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Argentina: 7
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Canada: 34
Country: Number of subjects enrolled	Switzerland: 4
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Denmark: 14
Country: Number of subjects enrolled	Spain: 31
Country: Number of subjects enrolled	Finland: 4
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Japan: 21
Country: Number of subjects enrolled	Korea, Republic of: 22
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Portugal: 6
Country: Number of subjects enrolled	Russian Federation: 28
Country: Number of subjects enrolled	Sweden: 14
Country: Number of subjects enrolled	Turkey: 13

Country: Number of subjects enrolled	United States: 95
Worldwide total number of subjects	387
EEA total number of subjects	136

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)	105
From 65 to 84 years	273
85 years and over	9

Subject disposition

Recruitment

Recruitment details:

Part 1 of the study was conducted at 116 centers in 21 countries and part 2 was conducted at 75 centers in 17 countries.

Pre-assignment

Screening details:

A total of 389 participants were enrolled out of which 387 randomised and treated (192=gantenerumab and 195=placebo) in part 1 of study. Of these, a total of 230 participants enrolled in Part 2 of study:225 participants received at least one dose of study drug. Participants who discontinued from Part 1 of study were not allowed to enroll in Part 2.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: Placebo

Arm description:

Participants received matching placebo by SC injection Q4W up to 100 weeks during Part 1 of the study.

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

Dosage and administration details:

Participants received gantenerumab matching placebo SC injection Q4W.

Arm title	Part 1: Gantenerumab

Arm description:

Participants received 105 mg Gantenerumab by SC injection Q4W for 24 weeks and if eligible 225 mg SC injection Q4W from weeks 28-100 during Part 1 of the study.

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

Dosage and administration details:

Participants received gantenerumab SC injection Q4W.

Number of subjects in period 1	Part 1: Placebo	Part 1: Gantenerumab
Started	195	192
Completed	134	136
Not completed	61	56
Physician decision	2	4
Non-Compliance	2	4
Part 1 Terminated by Sponsor	3	2
Death	3	3
Not specified	6	3
Adverse event	2	8
Lost to follow-up	1	2
Withdrawal by subject	42	29
Protocol deviation	-	1

Period 2

Period 2 title	Part 2: Open-label Extension
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 2 (OLE treatment): Placebo switched to Gant to 1200 mg

Arm description:

Participants who had received Placebo in Part 1, received Gantenerumab at doses up to 1200 mg by SC injection Q4W for up to 2 years. Additionally, participants were given the option to continue receiving open-label gantenerumab treatment for 3 years.

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

Dosage and administration details:

Participants received gantenerumab SC injection Q4W

Arm title	Part 2 (OLE treatment): Gantenerumab up to 1200 mg

Arm description:

Participants who had received Gantenerumab in Part 1, received treatment at doses up to 1200 mg by SC injection Q4W for up to 2 years. Additionally, participants were given the option to continue receiving open-label gantenerumab treatment for 3 years.

Arm type	Experimental

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

Dosage and administration details:

Participants received gantenerumab SC injection Q4W

Number of subjects in period 2[1]	Part 2 (OLE treatment): Placebo switched to Gant to 1200 mg	Part 2 (OLE treatment): Gantenerumab up to 1200 mg
Started	119	111
Completed	49	50
Not completed	70	61
Non-Compliance	1	1
Physician decision	8	5
Study Terminated By Sponsor	-	1
Death	7	4
Not specified	9	9
Adverse event	6	8
Withdrawal by subjects	39	32
Lost to follow-up	-	1

Notes:

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

Justification: A total of 230 participants were enrolled in OLE. Of these, 225 were treated in OLE phase.

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: Placebo
Reporting group description:	
Participants received matching placebo by SC injection Q4W up to 100 weeks during Part 1 of the study.	
Reporting group title	Part 1: Gantenerumab
Reporting group description:	
Participants received 105 mg Gantenerumab by SC injection Q4W for 24 weeks and if eligible 225 mg SC injection Q4W from weeks 28-100 during Part 1 of the study.	

Reporting group values	Part 1: Placebo	Part 1: Gantenerumab	Total
Number of subjects	195	192	387
Age categorical Units: Participants			
Age Continuous Units: years			
arithmetic mean	70.1	69.7	
standard deviation	± 8.6	± 8.9	-
Sex: Female, Male Units: Participants			
Female	113	98	211
Male	82	94	176
Ethnicity Units: Subjects			
Hispanic or Latino	11	12	23
Not Hispanic or Latino	178	176	354
Unknown or Not Reported	6	4	10
Race Units: Subjects			
Asian	23	21	44
Black or African American	2	2	4
Native Hawaiian or other Pacific Islander	0	1	1
White	164	166	330
More than one race	1	0	1
Unknown or Not Reported	5	2	7
American Indian or Alaska Native	0	0	0

Subject analysis sets	
Subject analysis set title	Part 2 (OLE): Placebo switched to Gantenerumab up to 1200 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants who had received Placebo in Part 1, received Gantenerumab at doses up to 1200 mg by SC injection Q4W for up to 2 years. Additionally, participants were given the option to continue receiving open-label gantenerumab treatment for 3 years.	
Subject analysis set title	Part 2 (OLE): Gantenerumab up to 1200 mg

Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who had received Gantenerumab in Part 1, received treatment at doses up to 1200 mg by SC injection Q4W for up to 2 years. Additionally, participants were given the option to continue receiving open-label gantenerumab treatment for 3 years.

Subject analysis set title	Part 2 (OLE): Gantenerumab 1200 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who had received placebo or gantenerumab in Part 1, received gantenerumab at doses up to 1200 mg by SC injection Q4W for up to 2 years. Additionally, participants were given the option to continue receiving open-label gantenerumab treatment for 3 years.

Reporting group values	Part 2 (OLE): Placebo switched to Gantenerumab up to 1200 mg	Part 2 (OLE): Gantenerumab up to 1200 mg	Part 2 (OLE): Gantenerumab 1200 mg
Number of subjects	117	108	223
Age categorical Units: Participants			
Age Continuous Units: years			
arithmetic mean	71.82	71.01	
standard deviation	± 8.09	± 9.31	±
Sex: Female, Male Units: Participants			
Female	69	61	
Male	48	47	
Ethnicity Units: Subjects			
Hispanic or Latino	9	10	
Not Hispanic or Latino	108	96	
Unknown or Not Reported	0	2	
Race Units: Subjects			
Asian	19	19	
Black or African American	2	2	
Native Hawaiian or other Pacific Islander	0	1	
White	94	85	
More than one race	0	0	
Unknown or Not Reported	2	1	
American Indian or Alaska Native	0	0	

End points

End points reporting groups

Reporting group title	Part 1: Placebo
Reporting group description:	
Participants received matching placebo by SC injection Q4W up to 100 weeks during Part 1 of the study.	
Reporting group title	Part 1: Gantenerumab
Reporting group description:	
Participants received 105 mg Gantenerumab by SC injection Q4W for 24 weeks and if eligible 225 mg SC injection Q4W from weeks 28-100 during Part 1 of the study.	
Reporting group title	Part 2 (OLE treatment): Placebo switched to Gant to 1200 mg
Reporting group description:	
Participants who had received Placebo in Part 1, received Gantenerumab at doses up to 1200 mg by SC injection Q4W for up to 2 years. Additionally, participants were given the option to continue receiving open-label gantenerumab treatment for 3 years.	
Reporting group title	Part 2 (OLE treatment): Gantenerumab up to 1200 mg
Reporting group description:	
Participants who had received Gantenerumab in Part 1, received treatment at doses up to 1200 mg by SC injection Q4W for up to 2 years. Additionally, participants were given the option to continue receiving open-label gantenerumab treatment for 3 years.	
Subject analysis set title	Part 2 (OLE): Placebo switched to Gantenerumab up to 1200 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants who had received Placebo in Part 1, received Gantenerumab at doses up to 1200 mg by SC injection Q4W for up to 2 years. Additionally, participants were given the option to continue receiving open-label gantenerumab treatment for 3 years.	
Subject analysis set title	Part 2 (OLE): Gantenerumab up to 1200 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants who had received Gantenerumab in Part 1, received treatment at doses up to 1200 mg by SC injection Q4W for up to 2 years. Additionally, participants were given the option to continue receiving open-label gantenerumab treatment for 3 years.	
Subject analysis set title	Part 2 (OLE): Gantenerumab 1200 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who had received placebo or gantenerumab in Part 1, received gantenerumab at doses up to 1200 mg by SC injection Q4W for up to 2 years. Additionally, participants were given the option to continue receiving open-label gantenerumab treatment for 3 years.	

Primary: Part 2: Percentage of Participants with Adverse Events (AEs) or Serious Adverse Events (SAEs)

End point title	Part 2: Percentage of Participants with Adverse Events (AEs) or Serious Adverse Events (SAEs)[1]
End point description:	
An AE is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. SAE is any adverse event that is fatal or which requires or prolongs inpatient hospitalization or results in persistent or significant disability/incapacity or causes congenital anomaly/birth defect or results in a significant medical event in the investigator's judgment.	
End point type	Primary
End point timeframe:	
First dose up to 4 weeks after the last dose of study drug (up to 249 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: No statistical analyses were performed

End point values	Part 2 (OLE treatment): Placebo switched to Gant to 1200 mg	Part 2 (OLE treatment): Gantenerumab up to 1200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117	108		
Units: Percentage of Participants				
number (not applicable)				
AEs	91.5	95.4		
SAEs	24.8	38.0		

Statistical analyses

No statistical analyses for this end point

Primary: Part 2: Percentage of Participants with Treatment Emergent Anti-Drug Antibodies (ADAs)

End point title	Part 2: Percentage of Participants with Treatment Emergent Anti-Drug Antibodies (ADAs)[2]

End point description:

Participants were considered positive or negative for ADA based on their baseline and post-baseline sample results. The number and percentage of participants with confirmed positive ADA levels were determined for participants previously (in part 1) on Gantenerumab and Placebo. The prevalence of ADA at baseline was calculated as the percentage of participants with confirmed positive ADA levels at baseline relative to the total number of participants with a sample available at baseline. The incidence of treatment-emergent ADAs was determined as the percentage of participants with confirmed post-baseline positive ADAs relative to the total number of participants that had at least one post-baseline sample available for ADA analysis.

End point type	Primary

End point timeframe:

First dose up to last dose (Baseline up to until maximum 5 years)

Notes:

[2] - 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: No statistical analyses were performed

End point values	Part 2 (OLE treatment): Placebo switched to Gant to 1200 mg	Part 2 (OLE treatment): Gantenerumab up to 1200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115[3]	106[4]		
Units: Percentage of Participants				
number (not applicable)	2.6	2.8		

Notes:

[3] - The number of participants analysed indicates the number of participants evaluated for the endpoint.
[4] - The number of participants analysed indicates the number of participants evaluated for the endpoint.

Statistical analyses

No statistical analyses for this end point

Primary: Part 2: Percentage of Participants With Adverse Events Leading to Discontinuation of Treatment

End point title	Part 2: Percentage of Participants With Adverse Events Leading to Discontinuation of Treatment[5]

End point description:

Percentage of participants with adverse events leading to discontinuation from treatment were reported. The safety population consisted of all participants who had received at least one dose of study drug, regardless of whether the participants withdrew prematurely or not.

End point type	Primary

End point timeframe:

First dose up to 4 weeks after the last dose in OLE (Up to approximately 249 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: No statistical analyses were performed

End point values	Part 2 (OLE treatment): Placebo switched to Gant to 1200 mg	Part 2 (OLE treatment): Gantenerumab up to 1200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117	108		
Units: Percentage of Participants				
number (not applicable)	12.0	15.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants With AEs, SAEs

End point title	Part 1: Percentage of Participants With AEs, SAEs

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. SAE is any adverse event that is fatal or which requires or prolongs inpatient hospitalization or results in persistent or significant disability/incapacity or causes congenital anomaly/birth defect or results in a significant medical event in the investigator's judgment.

End point type	Secondary

End point timeframe:

First dose up to last dose (Up to approximately 152 weeks)

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	192		
Units: Percentage of Participants				
number (not applicable)				
AEs	80.5	82.8		
SAEs	12.3	12.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants with Treatment-emergent ADAs

End point title	Part 1: Percentage of Participants with Treatment-emergent ADAs

End point description:

Participants were considered positive or negative for ADA based on their baseline and post-baseline sample results. The number and percentage of participants with confirmed positive ADA levels were determined for Gantenerumab and Placebo groups. The prevalence of ADA at baseline was calculated as the percentage of participants with confirmed positive ADA levels at baseline relative to the total number of participants with a sample available at baseline. The incidence of treatment-emergent ADAs was determined as the percentage of participants with confirmed post-baseline positive ADAs relative to the total number of participants that had at least one post-baseline sample available for ADA analysis.

End point type	Secondary

End point timeframe:

First dose up to last dose (Up to approximately 152 weeks)

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194[6]	191[7]		
Units: Percentage of Participants				
number (not applicable)	3.6	11.5		

Notes:

[6] - The number of participants analysed indicates the number of participants evaluated for the endpoint.

[7] - The number of participants analysed indicates the number of participants evaluated for the endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Gantenerumab Plasma Concentration at Multiple Timepoints

End point title	Part 1: Gantenerumab Plasma Concentration at Multiple Timepoints[8]

End point description:

The pharmacokinetic (PK) evaluable population consisted of all participants that were treated with gantenerumab and provided at least 1 post-baseline PK sample. "n" = number analysed is the number of participants with data available for analyses at the given time-point.

End point type	Secondary

End point timeframe:

Pre-dose: Weeks 4, 8, 12, 24, 48, 72 and Post dose: Day 4

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses were performed

End point values	Part 1: Gantenerumab			
Subject group type	Reporting group			
Number of subjects analysed	192			
Units: µg/mL				
arithmetic mean (standard deviation)				
Day 4 (n=183)	4.11 (± 2.59)			
Week 4 (n=190)	2.06 (± 0.89)			
Week 8 (n=188)	3.11 (± 1.41)			
Week 12 (n=184)	3.35 (± 1.63)			
Week 24 (n=177)	3.71 (± 2.13)			
Week 48 (n=137)	7.61 (± 3.88)			
Week 72 (n=79)	7.66 (± 4.44)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants with Adverse Events Leading to Discontinuation of Treatment

End point title	Part 1: Percentage of Participants with Adverse Events Leading to Discontinuation of Treatment

End point description:

Percentage of participants with adverse events leading to discontinuation from treatment were reported. The safety population consisted of all participants who received at least one dose of study drug, regardless of whether the participants withdrew prematurely or not.

End point type	Secondary

End point timeframe:

First dose up to last dose (Up to approximately 152 weeks)

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	192		
Units: Percentage of Participants				
number (not applicable)	2.6	6.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percent Change From Baseline in Hippocampal Volume at Week 104

End point title	Part 2: Percent Change From Baseline in Hippocampal Volume at Week 104

End point description:

Change from baseline in hippocampal right volume (HRV) and hippocampal left volume (HLV) were analysed at Week 104 using magnetic resonance imaging. The safety population consisted of all participants who received at least one dose of gantenerumab during the OLE and also had at least one post baseline MRI. Number analyzed is the number of participants with data available for analyses at the given time-point.

End point type	Secondary

End point timeframe:

Baseline (Part 1 screening), Week 104

End point values	Part 2 (OLE treatment): Placebo switched to Gant to 1200 mg	Part 2 (OLE treatment): Gantenerumab up to 1200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52[9]	44[10]		
Units: Percent Change				
arithmetic mean (standard deviation)				
HLV- Percent Change at Week 104 (n=50, n=43)	-11.24 (± 4.04)	-12.10 (± 4.45)		
HRV- Percent Change at Week 104 (n=52, n=44)	-12.49 (± 4.03)	-11.34 (± 4.41)		

Notes:

[9] - The number of participants analysed indicates the number of participants evaluated for the endpoint.

[10] - The number of participants analysed indicates the number of participants evaluated for the endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percent Change From Baseline in Whole Brain Volume at Week 104

End point title	Part 2: Percent Change From Baseline in Whole Brain Volume

	at Week 104

End point description:

Change from baseline brain volume were analysed at Week 104 using magnetic resonance imaging. The safety population consisted of all participants who received at least one dose of gantenerumab during the OLE and also had at least one post baseline MRI.

End point type	Secondary

End point timeframe:

Baseline (Part 1 screening), Week 104

End point values	Part 2 (OLE treatment): Placebo switched to Gant to 1200 mg	Part 2 (OLE treatment): Gantenerumab up to 1200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[11]	44[12]		
Units: Percent Change				
arithmetic mean (standard deviation)	-4.89 (± 1.90)	-4.91 (± 1.58)		

Notes:

[11] - The number of participants analysed indicates the number of participants evaluated for the endpoint.
[12] - The number of participants analysed indicates the number of participants evaluated for the endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percent Change From Baseline in Cortical Thickness at Week 104

End point title	Part 2: Percent Change From Baseline in Cortical Thickness at Week 104

End point description:

Change from baseline in cortical thickness were analysed at Week 104 using magnetic resonance imaging. The safety population consisted of all participants who received at least one dose of gantenerumab during the OLE and also had at least one post baseline MRI.

End point type	Secondary

End point timeframe:

Baseline (Part 1 screening), Week 104

End point values	Part 2 (OLE treatment): Placebo switched to Gant to 1200 mg	Part 2 (OLE treatment): Gantenerumab up to 1200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[13]	44[14]		
Units: Percent Change				
arithmetic mean (standard deviation)	-5.84 (± 2.33)	-5.58 (± 1.87)		

Notes:

[13] - The number of participants analysed indicates the number of participants evaluated for the endpoint.
[14] - The number of participants analysed indicates the number of participants evaluated for the endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Ventricular Volume as Measured by MRI at Week 104

End point title	Part 2: Ventricular Volume as Measured by MRI at Week 104

End point description:

Ventricular volume were analysed at Week 104 using magnetic resonance imaging. The safety population consisted of all participants who received at least one dose of gantenerumab during the OLE and also had at least one post baseline MRI.

End point type	Secondary

End point timeframe:

Part 2: Week 104

End point values	Part 2 (OLE treatment): Placebo switched to Gant to 1200 mg	Part 2 (OLE treatment): Gantenerumab up to 1200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63[15]	52[16]		
Units: mL				
arithmetic mean (standard deviation)	86.70 (± 38.37)	86.21 (± 30.49)		

Notes:

[15] - The number of participants analysed indicates the number of participants evaluated for the endpoint.
[16] - The number of participants analysed indicates the number of participants evaluated for the endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Gantenerumab Plasma Concentration at Multiple Timepoints

End point title	Part 2: Gantenerumab Plasma Concentration at Multiple Timepoints

End point description:

Of the 225 participants in the OLE safety evaluable population, evaluable PK information was available from 223 participants. The PK evaluable population consisted of all participants that were treated with gantenerumab and provided at least 1 post-baseline PK sample. "n" = number analysed is the number of participants with data available for analyses at the given time-point.

End point type	Secondary

End point timeframe:

Pre-dose: Weeks 104, 116, 156, 208; Post-dose: Weeks 53, 101

End point values	Part 2 (OLE): Gantenerumab 1200 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	223[17]			
Units: µg/mL				
arithmetic mean (standard deviation)				
Week 53 (n=128)	80.6 (± 38.4)			
Week 101 (n=111)	89.1 (± 33.6)			
Week 104 (n=141)	43.5 (± 22.4)			
Week 116 (n=15)	3.66 (± 2.29)			
Week 156 (n=80)	45.2 (± 22.5)			
Week 208 (n=48)	55.8 (± 37.9)			

Notes:

[17] - The number of participants analysed indicated the number of participants evaluated for the endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in Brain Amyloid Load at Week 156 in a Subset of Participants

End point title	Part 2: Change from Baseline in Brain Amyloid Load at Week 156 in a Subset of Participants

End point description:

Brain amyloid load over time was assessed using a Florbetapir [F18] injection, a positron emission tomography (PET) radioligand selective to amyloid. Analysis was conducted in a subset of participants who signed consent to participate in the PET substudy. Amyloid PET burden was measured in a composite region of interest (ROI) by using standardized uptake value ratio (SUVR) mapped to the centiloid scale. The composite region was composed of the following six bilateral regions: frontal lobe, parietal lobe, temporal lobe, posterior cingulate cortex, anterior cingulate cortex. The reference region used to normalize the composite region was the cerebellar cortex. SUVR is ratio of tracer uptake in each of cingulate, frontal, parietal and temporal cortexes relative to cerebellum. The centiloid scale anchor points are 0 and 100, where 0 represents a high-certainty amyloid negative scan and 100 represents the amount of global amyloid deposition found in a typical AD scans. Safety population.

End point type	Secondary

End point timeframe:

Baseline, Week 156

End point values	Part 2 (OLE treatment): Placebo switched to Gant to 1200 mg	Part 2 (OLE treatment): Gantenerumab up to 1200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13[18]	8[19]		
Units: Score on a scale				
arithmetic mean (standard deviation)	-81.01 (± 47.08)	-84.93 (± 28.38)		

Notes:
[18] - Participants who had discontinued from Part 1 of the study were not allowed to enroll in Part 2.
[19] - Participants who had discontinued from Part 1 of the study were not allowed to enroll in Part 2.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Mean Change from Baseline in Alzheimer's Disease Activity Scale-Cognitive Subscale 13 (ADAS-Cog13) Scores at Week 104

End point title	Part 1: Mean Change from Baseline in Alzheimer's Disease Activity Scale-Cognitive Subscale 13 (ADAS-Cog13) Scores at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:
Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[20]	0[21]		
Units: Units on the scale				
arithmetic mean (standard deviation)	()	()		

Notes:
[20] - For part 1, the efficacy endpoints became exploratory in nature.
[21] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Mean Change From Baseline in Alzheimer's Disease Cooperative Study-Activities of Daily Living (ADCS-ADL) scores at week 104

End point title	Part 1: Mean Change From Baseline in Alzheimer's Disease Cooperative Study-Activities of Daily Living (ADCS-ADL) scores at week 104

End point description:

End point type	Other pre-specified

End point timeframe:
Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[22]	0[23]		
Units: Units on the scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[22] - For part 1, the efficacy endpoints became exploratory in nature.

[23] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Percentage Change From Baseline in Total Tau (t-tau) in CSF at Week 104

End point title	Part 1: Percentage Change From Baseline in Total Tau (t-tau) in CSF at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[24]	0[25]		
Units: Percent Change				
arithmetic mean (standard deviation)	()	()		

Notes:

[24] - For part 1, the efficacy endpoints became exploratory in nature.

[25] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Percentage Change From Baseline in Abeta 1-42 levels in CSF at Week 104

End point title	Part 1: Percentage Change From Baseline in Abeta 1-42 levels in CSF at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[26]	0[27]		
Units: Percent Change				
arithmetic mean (standard deviation)	()	()		

Notes:

[26] - For part 1, the efficacy endpoints became exploratory in nature.

[27] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Percentage Change From Baseline in phosphorylated tau [p-tau] in CSF at Week 104

End point title	Part 1: Percentage Change From Baseline in phosphorylated tau [p-tau] in CSF at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[28]	0[29]		
Units: Percent Change				
arithmetic mean (standard deviation)	()	()		

Notes:

[28] - For part 1, the efficacy endpoints became exploratory in nature.

[29] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Percent Change From Baseline in Hippocampal Volume at Week 104

End point title	Part 1: Percent Change From Baseline in Hippocampal Volume at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[30]	0[31]		
Units: Percent Change				
arithmetic mean (standard deviation)	()	()		

Notes:

[30] - For part 1, the efficacy endpoints became exploratory in nature.

[31] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Percent Change From Baseline in Whole Brain Volume at Week 104

End point title	Part 1: Percent Change From Baseline in Whole Brain Volume at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[32]	0[33]		
Units: Percent Change				
arithmetic mean (standard deviation)	()	()		

Notes:

[32] - For part 1, the efficacy endpoints became exploratory in nature.

[33] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Percent Change From Baseline in Cortical Thickness at Week 104

End point title	Part 1: Percent Change From Baseline in Cortical Thickness at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[34]	0[35]		
Units: Percent Change				
arithmetic mean (standard deviation)	()	()		

Notes:

[34] - For part 1, the efficacy endpoints became exploratory in nature.

[35] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Ventricular Volume as Measured by MRI at Week 104

End point title	Part 1: Ventricular Volume as Measured by MRI at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[36]	0[37]		
Units: ml				
arithmetic mean (standard deviation)	()	()		

Notes:

[36] - For part 1, the efficacy endpoints became exploratory in nature.

[37] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Change From Baseline in Clinical Dementia Rating Global Score (CDR-GS) at Week 104

End point title	Part 1: Change From Baseline in Clinical Dementia Rating Global Score (CDR-GS) at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[38]	0[39]		
Units: Units on the scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[38] - For part 1, the efficacy endpoints became exploratory in nature.

[39] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Change From Baseline in CDR Sum of Boxes (SB) at Week 104

End point title	Part 1: Change From Baseline in CDR Sum of Boxes (SB) at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[40]	0[41]		
Units: Units on the scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[40] - For part 1, the efficacy endpoints became exploratory in nature.

[41] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Change From Baseline in Neuropsychiatric Inventory (NPI) Total Score at Week 104

End point title	Part 1: Change From Baseline in Neuropsychiatric Inventory (NPI) Total Score at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[42]	0[43]		
Units: Units on the scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[42] - For part 1, the efficacy endpoints became exploratory in nature.

[43] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Change From Baseline in NPI Domain Score at Week 104

End point title	Part 1: Change From Baseline in NPI Domain Score at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[44]	0[45]		
Units: Units on the scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[44] - For part 1, the efficacy endpoints became exploratory in nature.

[45] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Change From Baseline in Mini Mental State Examination (MMSE) Total Score at Week 104

End point title	Part 1: Change From Baseline in Mini Mental State Examination (MMSE) Total Score at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[46]	0[47]		
Units: Units on the Scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[46] - For part 1, the efficacy endpoints became exploratory in nature.

[47] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Change From Baseline in Alzheimer's Dementia (QoL-AD) Global Score at Week 104

End point title	Part 1: Change From Baseline in Alzheimer's Dementia (QoL-AD) Global Score at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[48]	0[49]		
Units: Units on the scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[48] - For part 1, the efficacy endpoints became exploratory in nature.

[49] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Change From Baseline in Symptom Guide Facilitated (GAS) at Week 104

End point title	Part 1: Change From Baseline in Symptom Guide Facilitated (GAS) at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[50]	0[51]		
Units: Units on the scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[50] - For part 1, the efficacy endpoints became exploratory in nature.

[51] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Change from Baseline in Dependence Scale (DS) at Week 104

End point title	Part 1: Change from Baseline in Dependence Scale (DS) at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[52]	0[53]		
Units: Units on the scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[52] - For part 1, the efficacy endpoints became exploratory in nature.

[53] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Change From Baseline in Resource Utilization Dementia-Lite (RUD - Lite) Scale at Week 104

End point title	Part 1: Change From Baseline in Resource Utilization Dementia-Lite (RUD - Lite) Scale at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[54]	0[55]		
Units: Units on the scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[54] - For part 1, the efficacy endpoints became exploratory in nature.

[55] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Change From Baseline in Zarit Caregiver Interview for Alzheimer's Disease (ZCI-AD) at Week 104

End point title	Part 1: Change From Baseline in Zarit Caregiver Interview for Alzheimer's Disease (ZCI-AD) at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[56]	0[57]		
Units: Units on the scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[56] - For part 1, the efficacy endpoints became exploratory in nature.

[57] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Time to Clinical Decline

End point title	Part 1: Time to Clinical Decline

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline up to Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[58]	0[59]		
Units: Weeks				
median (full range (min-max))	(to)	(to)		

Notes:

[58] - For part 1, the efficacy endpoints became exploratory in nature.

[59] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Change from Baseline in Clinical Composite Score (Prespecified Items From The ADAS-Cog, MMSE, and CDR) at Week 104

End point title	Part 1: Change from Baseline in Clinical Composite Score (Prespecified Items From The ADAS-Cog, MMSE, and CDR) at Week 104

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline, Week 104

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[60]	0[61]		
Units: Units on the scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[60] - For part 1, the efficacy endpoints became exploratory in nature.

[61] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: Percentage of participants with ADAS-Cog Response

End point title	Part 1: Percentage of participants with ADAS-Cog Response

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline up to Week 152

End point values	Part 1: Placebo	Part 1: Gantenerumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[62]	0[63]		
Units: Units on the scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[62] - For part 1, the efficacy endpoints became exploratory in nature.

[63] - For part 1, the efficacy endpoints became exploratory in nature.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 52 weeks after the last dose of study drug (up to 7 years)

Adverse event reporting additional description:

The safety-evaluable population consisted of all participants who had received at least one dose of study drug, regardless of whether the participants withdrew prematurely or not.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Part 1: Placebo

Reporting group description:

Participants received matching placebo by SC injection Q4W up to 100 weeks during Part 1 of the study.

Reporting group title	Part 1: Gantenerumab

Reporting group description:

Participants received 105 mg Gantenerumab by SC injection Q4W for 24 weeks and if eligible 225 mg SC injection Q4W from weeks 28-100 during Part 1 of the study.

Reporting group title	Part 2 (OLE treatment): Placebo switched to Gant to 1200 mg

Reporting group description:

Participants who had received Placebo in Part 1, received Gantenerumab at doses up to 1200 mg by SC injection Q4W for up to 2 years. Additionally, participants were given the option to continue receiving open-label gantenerumab treatment for 3 years.

Reporting group title	Part 2 (OLE treatment): Gantenerumab up to 1200 mg

Reporting group description:

Participants who had received Gantenerumab in Part 1, received treatment at doses up to 1200 mg by SC injection Q4W for up to 2 years. Additionally, participants were given the option to continue receiving open-label gantenerumab treatment for 3 years.

Serious adverse events	Part 1: Placebo	Part 1: Gantenerumab	Part 2 (OLE treatment): Placebo switched to Gant to 1200 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	53 / 195 (27.18%)	61 / 192 (31.77%)	29 / 117 (24.79%)
number of deaths (all causes)	11	8	8
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 195 (0.51%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebellar tumour			

subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Colon cancer			
subjects affected / exposed	2 / 195 (1.03%)	0 / 192 (0.00%)	2 / 117 (1.71%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Ovarian epithelial cancer			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Rectal cancer			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Squamous cell carcinoma of pharynx			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm rupture			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Deep vein thrombosis			

subjects affected / exposed	1 / 195 (0.51%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Giant cell arteritis			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Hypertension			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Cyst			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Death			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Pain			

subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Epistaxis			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infiltration			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Pleural effusion			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Pulmonary embolism			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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

Tonsillar hypertrophy			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Aggression			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	1 / 195 (0.51%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Psychotic symptom			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide threat			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Investigations			
Electrocardiogram abnormal			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 195 (0.51%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest injury			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Comminuted fracture			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	3 / 195 (1.54%)	5 / 192 (2.60%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 195 (0.51%)	2 / 192 (1.04%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 195 (0.51%)	1 / 192 (0.52%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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

Meniscus injury			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Multiple fractures			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Optic nerve injury			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	2 / 195 (1.03%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Spinal compression fracture			
subjects affected / exposed	0 / 195 (0.00%)	2 / 192 (1.04%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	2 / 195 (1.03%)	2 / 192 (1.04%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	1 / 2	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Upper limb fracture			

subjects affected / exposed	1 / 195 (0.51%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Acute myocardial infarction			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Angina unstable			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 195 (0.00%)	3 / 192 (1.56%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 195 (0.51%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	1 / 195 (0.51%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			

subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 195 (0.51%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myocardial infarction			
subjects affected / exposed	2 / 195 (1.03%)	1 / 192 (0.52%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 1
Nervous system disorders			
ARIA-E			
subjects affected / exposed	2 / 195 (1.03%)	2 / 192 (1.04%)	2 / 117 (1.71%)
occurrences causally related to treatment / all	2 / 2	3 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARIA-H			
subjects affected / exposed	0 / 195 (0.00%)	2 / 192 (1.04%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain stem infarction			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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 haematoma			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			

subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral venous sinus thrombosis			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Cerebrovascular accident			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Dementia Alzheimer's type			
subjects affected / exposed	2 / 195 (1.03%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Dementia of the Alzheimer's type, with delusions			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Encephalopathy			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Epilepsy			
subjects affected / exposed	1 / 195 (0.51%)	2 / 192 (1.04%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	1 / 1	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Haemorrhagic stroke			

subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Hemiplegia			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukoencephalopathy			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Neurotoxicity			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychomotor hyperactivity			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Somnolence			

subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	2 / 195 (1.03%)	2 / 192 (1.04%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	2 / 195 (1.03%)	0 / 192 (0.00%)	2 / 117 (1.71%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebral artery dissection			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Vertebrobasilar stroke			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Ocular hypertension			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			

subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Enteritis			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faeces discoloured			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Haematochezia			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Ileus			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Inguinal hernia			
subjects affected / exposed	0 / 195 (0.00%)	2 / 192 (1.04%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			

subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Umbilical hernia			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Liver disorder			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 195 (0.00%)	2 / 192 (1.04%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Appendiceal abscess			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial sepsis			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Cellulitis			
subjects affected / exposed	0 / 195 (0.00%)	2 / 192 (1.04%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic abscess			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Cystitis			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Erysipelas			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Influenza			

subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Periodontitis			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 195 (1.54%)	1 / 192 (0.52%)	2 / 117 (1.71%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	3 / 195 (1.54%)	0 / 192 (0.00%)	3 / 117 (2.56%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Shunt infection			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Tonsillitis bacterial			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (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
Urinary tract infection			

subjects affected / exposed	3 / 195 (1.54%)	3 / 192 (1.56%)	3 / 117 (2.56%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Hypercalcaemia			
subjects affected / exposed	1 / 195 (0.51%)	0 / 192 (0.00%)	0 / 117 (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
Hypoglycaemia			
subjects affected / exposed	0 / 195 (0.00%)	1 / 192 (0.52%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 195 (0.00%)	2 / 192 (1.04%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2 (OLE treatment): Gantenerumab up to 1200 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	41 / 108 (37.96%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebellar tumour			

subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colon cancer				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Invasive lobular breast carcinoma				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myelodysplastic syndrome				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian epithelial cancer				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal cancer				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of pharynx				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Aortic aneurysm rupture				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				

subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Giant cell arteritis				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cyst				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				

subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung infiltration			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Tonsillar hypertrophy			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aggression			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Agitation			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Delirium			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychotic symptom			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Suicide threat			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Electrocardiogram abnormal			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chest injury			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Comminuted fracture			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hip fracture			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Jaw fracture			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Meniscus injury				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple fractures				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Optic nerve injury				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	2 / 108 (1.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	2 / 108 (1.85%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 1			
Traumatic intracranial haemorrhage				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				

subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute coronary syndrome				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arrhythmia				
subjects affected / exposed	2 / 108 (1.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bradycardia				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				

subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Myocardial infarction				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Nervous system disorders				
ARIA-E				
subjects affected / exposed	2 / 108 (1.85%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
ARIA-H				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Brain stem infarction				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral haematoma				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				

subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral venous sinus thrombosis				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dementia Alzheimer's type				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Dementia of the Alzheimer's type, with delusions				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Generalised tonic-clonic seizure				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic stroke				

subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hemiplegia			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hydrocephalus			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Leukoencephalopathy			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorder			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neurotoxicity			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychomotor hyperactivity			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Somnolence			

subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	2 / 108 (1.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vertebral artery dissection				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vertebrobasilar stroke				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Ocular hypertension				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Constipation				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulum intestinal haemorrhagic				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				

subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Enteritis				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Faeces discoloured				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haematochezia				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	0 / 108 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	2 / 108 (1.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				

subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Umbilical hernia			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver disorder			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			

Appendiceal abscess			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bacterial sepsis			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Colonic abscess			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cystitis			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			

subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Periodontitis			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Shunt infection			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tonsillitis bacterial			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			

subjects affected / exposed	2 / 108 (1.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part 1: Placebo	Part 1: Gantenerumab	Part 2 (OLE treatment): Placebo switched to Gant to 1200 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	147 / 195 (75.38%)	159 / 192 (82.81%)	94 / 117 (80.34%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	12 / 195 (6.15%)	16 / 192 (8.33%)	5 / 117 (4.27%)
occurrences (all)	15	21	7
Fall			
subjects affected / exposed	28 / 195 (14.36%)	35 / 192 (18.23%)	16 / 117 (13.68%)
occurrences (all)	44	69	25

Skin abrasion			
subjects affected / exposed	6 / 195 (3.08%)	12 / 192 (6.25%)	3 / 117 (2.56%)
occurrences (all)	7	17	3
Vascular disorders			
Hypertension			
subjects affected / exposed	13 / 195 (6.67%)	13 / 192 (6.77%)	4 / 117 (3.42%)
occurrences (all)	13	15	4
Nervous system disorders			
ARIA-E			
subjects affected / exposed	32 / 195 (16.41%)	42 / 192 (21.88%)	29 / 117 (24.79%)
occurrences (all)	42	70	35
ARIA-H			
subjects affected / exposed	30 / 195 (15.38%)	36 / 192 (18.75%)	19 / 117 (16.24%)
occurrences (all)	39	42	23
Dizziness			
subjects affected / exposed	18 / 195 (9.23%)	17 / 192 (8.85%)	13 / 117 (11.11%)
occurrences (all)	24	26	13
Headache			
subjects affected / exposed	29 / 195 (14.87%)	22 / 192 (11.46%)	15 / 117 (12.82%)
occurrences (all)	38	44	18
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	49 / 195 (25.13%)	52 / 192 (27.08%)	48 / 117 (41.03%)
occurrences (all)	284	322	281
Oedema peripheral			
subjects affected / exposed	2 / 195 (1.03%)	10 / 192 (5.21%)	1 / 117 (0.85%)
occurrences (all)	2	11	1
Pyrexia			
subjects affected / exposed	4 / 195 (2.05%)	7 / 192 (3.65%)	2 / 117 (1.71%)
occurrences (all)	4	9	2
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	14 / 195 (7.18%)	16 / 192 (8.33%)	6 / 117 (5.13%)
occurrences (all)	15	20	7
Diarrhoea			

subjects affected / exposed	23 / 195 (11.79%)	11 / 192 (5.73%)	11 / 117 (9.40%)
occurrences (all)	27	18	14
Nausea			
subjects affected / exposed	15 / 195 (7.69%)	10 / 192 (5.21%)	3 / 117 (2.56%)
occurrences (all)	24	11	9
Vomiting			
subjects affected / exposed	11 / 195 (5.64%)	14 / 192 (7.29%)	6 / 117 (5.13%)
occurrences (all)	16	18	11
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	9 / 195 (4.62%)	12 / 192 (6.25%)	4 / 117 (3.42%)
occurrences (all)	9	12	4
Psychiatric disorders			
Agitation			
subjects affected / exposed	13 / 195 (6.67%)	18 / 192 (9.38%)	9 / 117 (7.69%)
occurrences (all)	16	21	10
Anxiety			
subjects affected / exposed	13 / 195 (6.67%)	13 / 192 (6.77%)	5 / 117 (4.27%)
occurrences (all)	13	14	5
Depression			
subjects affected / exposed	17 / 195 (8.72%)	13 / 192 (6.77%)	8 / 117 (6.84%)
occurrences (all)	17	14	8
Insomnia			
subjects affected / exposed	12 / 195 (6.15%)	15 / 192 (7.81%)	7 / 117 (5.98%)
occurrences (all)	15	16	8
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	14 / 195 (7.18%)	13 / 192 (6.77%)	8 / 117 (6.84%)
occurrences (all)	15	23	8
Back pain			
subjects affected / exposed	20 / 195 (10.26%)	17 / 192 (8.85%)	8 / 117 (6.84%)
occurrences (all)	21	19	9
Neck pain			
subjects affected / exposed	6 / 195 (3.08%)	2 / 192 (1.04%)	6 / 117 (5.13%)
occurrences (all)	6	2	6
Infections and infestations			

Bronchitis			
subjects affected / exposed	10 / 195 (5.13%)	10 / 192 (5.21%)	6 / 117 (5.13%)
occurrences (all)	13	11	9
Influenza			
subjects affected / exposed	8 / 195 (4.10%)	14 / 192 (7.29%)	4 / 117 (3.42%)
occurrences (all)	10	19	4
Nasopharyngitis			
subjects affected / exposed	27 / 195 (13.85%)	23 / 192 (11.98%)	13 / 117 (11.11%)
occurrences (all)	35	31	14
Upper respiratory tract infection			
subjects affected / exposed	20 / 195 (10.26%)	7 / 192 (3.65%)	10 / 117 (8.55%)
occurrences (all)	30	12	13
Urinary tract infection			
subjects affected / exposed	17 / 195 (8.72%)	18 / 192 (9.38%)	11 / 117 (9.40%)
occurrences (all)	20	28	13

Non-serious adverse events	Part 2 (OLE treatment): Gantenerumab up to 1200 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	91 / 108 (84.26%)		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	8 / 108 (7.41%)		
occurrences (all)	9		
Fall			
subjects affected / exposed	22 / 108 (20.37%)		
occurrences (all)	41		
Skin abrasion			
subjects affected / exposed	5 / 108 (4.63%)		
occurrences (all)	10		
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 108 (4.63%)		
occurrences (all)	5		
Nervous system disorders			

ARIA-E subjects affected / exposed occurrences (all) ARIA-H subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	30 / 108 (27.78%) 51 23 / 108 (21.30%) 27 6 / 108 (5.56%) 6 12 / 108 (11.11%) 24		
General disorders and administration site conditions Injection site reaction subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 44 / 108 (40.74%) 280 8 / 108 (7.41%) 9 6 / 108 (5.56%) 8		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 0 / 108 (0.00%) 15 8 / 108 (7.41%) 13 4 / 108 (3.70%) 4 6 / 108 (5.56%) 7		
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	5 / 108 (4.63%)		
occurrences (all)	5		
Psychiatric disorders			
Agitation			
subjects affected / exposed	8 / 108 (7.41%)		
occurrences (all)	9		
Anxiety			
subjects affected / exposed	6 / 108 (5.56%)		
occurrences (all)	6		
Depression			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Insomnia			
subjects affected / exposed	5 / 108 (4.63%)		
occurrences (all)	5		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 108 (6.48%)		
occurrences (all)	10		
Back pain			
subjects affected / exposed	5 / 108 (4.63%)		
occurrences (all)	5		
Neck pain			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 108 (4.63%)		
occurrences (all)	6		
Influenza			
subjects affected / exposed	10 / 108 (9.26%)		
occurrences (all)	12		
Nasopharyngitis			
subjects affected / exposed	11 / 108 (10.19%)		
occurrences (all)	15		

Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 108 (2.78%) 5		
Urinary tract infection subjects affected / exposed occurrences (all)	7 / 108 (6.48%) 14		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 October 2014	A. Protocol was amended to allow for higher doses of gantenerumab to be examined in an open-label extension and the positron emission tomography (PET) substudy protocol was amended to reflect these changes and to allow subjects participating in the PET substudy to continue their yearly PET scans according to the open label schedule. B. Overview section was updated to explain overall changes. C. Update was made in rationale of study to explain the need for up-titration. D. Study design was updated to allow for transition into open label. Also, to update the number of subjects, treatment allocation and to delete the arterial blood sampling. E. Number of subjects and inclusion criteria was updated F. Schedule of Assessment and Procedures was updated. G. Need for an additional scan was updated in preparation and administration of the radioligand. H. Warnings and precautions, sample size information and overall statistical plan was updated. I. Ongoing review of the PET data by Sponsor included in interim review of study results.
27 October 2015	A. Protocol body was updated to clarify Part 1 from Part 2. B. Protocol was amended to allow for higher doses of gantenerumab to be examined in an open-label extension and to achieve higher dosing using an APOE ε4-based titration schedule and corresponding magnetic resonance imaging monitoring. C. Screening examination and eligibility screening form were updated. D. Update was made to reflect the abbreviated rescreening visit can be combined with baseline visit as long as all procedures required at screening and Baseline are performed. E. Serology requirements for the screening and re-screening visits were specified. F. Schedule of assessments was updated. G. Roche reporting requirements were updated.
02 December 2017	A. Protocol was amended to allow subjects the option to continue receiving open-label gantenerumab until the end of 2020. B. The number of studies in which gantenerumab is investigated were updated in background on Gantenerumab. C. The period of review for independent data monitoring committee has been clarified. D. The Cardiac-PET substudy has been updated to reflect updated status. E. Update was made to reflect MMSE is the only efficacy outcome measure assessed during additional years of part 2. F. Removed the cardiac PET substudy because the substudy has been stopped. G. Pharmacokinetic sampling in case of amyloid-related imaging abnormality findings has been clarified. H. Medical monitor information has been updated to reflect the change in Medical Monitor. I. The reporting of the term “sudden death” has been updated. J. Event reporting for hospitalization has been clarified. K. The process for reviewing and handling protocol deviations has been updated. L. Appendix 2 has been updated to indicate assessments collected during the additional years of OLE.

28 February 2020	A. Protocol was amended to allow participants who complete dosing visits in study WN28745 to enroll in an OLE study (WN41874) without any unnecessary dosing gap, and to enable the use of leftover plasma samples, collected for PK and ADA analysis, for exploratory biomarker research. B. Update was made to clarify that amyloid-related imaging abnormalities (both edema/effusion and hemosiderin depositions) and injection-site reactions are identified risks for gantenerumab and to enable participants to enroll in study WN41874 (open-label rollover study) to continue to receive gantenerumab for 2 more years. Participants who enroll in study WN41874 will not undergo follow-up assessments 16 weeks after their last dose (Follow–Up 2 visit). C. Positron emission tomography tracers used in the substudies associated in this substudy are included as investigational medicinal products (IMPs) or non-IMPs. D. Update was made to enable the use of leftover plasma samples, collected for PK and ADA analysis, for exploratory biomarker research and to clarify the timing of follow-up visits for Part 1 versus Part 2. E. Medical Monitor contact information was updated. F. Documents to be used for reference safety information for the PET tracers have been specified. G. Appendix 2 has been corrected to clarify that treatment is not to be administered at the Follow-Up 1 visit. H. Appendix 2 has been updated to add an optional lumbar puncture at Week 104 for all participants.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

As the participants transitioned early to OLE, most participants did not reach the primary analysis timepoint (Week 104). Hence, the efficacy endpoints for Part 1 became exploratory in nature.

Notes: