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

Summary

EudraCT number	2019-004431-23
Trial protocol	NL ES PL GB DK IT
Global end of trial date	04 January 2023

Results information

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

Trial information

Trial identification

Sponsor protocol code	WN41874

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04339413
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 January 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 January 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of continued treatment with subcutaneous gantenerumab at the target dose in participants with AD who received gantenerumab in the OLEs of SCarlet RoAD (NCT01224106) and Marguerite RoAD (NCT02051608).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 May 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 1
Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	Chile: 1
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Japan: 9
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Mexico: 4
Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	Türkiye: 6
Country: Number of subjects enrolled	United States: 20
Worldwide total number of subjects	116
EEA total number of subjects	46

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)	10
From 65 to 84 years	83
85 years and over	23

Subject disposition

Recruitment

Recruitment details:

Participants took part in Part 1 of the study at 56 centers in the United States, Spain, Canada, Italy, Germany, Japan, Korea, Mexico, Poland, Turkey, Australia, Russia, Argentina, Switzerland, Chile, Denmark, and Netherlands from 22 May 2020 to 04 Jan 2023. The study was terminated before Part 2 was initiated.

Pre-assignment

Screening details:

A total of 116 participants rolled over in this study of which 115 participants received gantenerumab in part 1. 59 participants rolled over from OLE WN25203 & 56 participants rolled over from WN28745. Due to negative pre-planned analysis of studies WN39658 & WN29922, this study was terminated by sponsor, & no participant was rolled over to Part 2.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	SCarlet RoAD

Arm description:

Participants enrolled from the open label extension (OLE) part of parent study WN25203, received gantenerumab, up to 1200 milligram (mg), subcutaneous (SC) injection, every 4 weeks (Q4W) for up to 129 weeks.

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

Dosage and administration details:

Gantenerumab was administered as SC injection Q4W.

Arm title	Marguerite RoAD

Arm description:

Participants enrolled from the OLE part of parent study WN28745, received gantenerumab, up to 1200 mg, SC injection, Q4W for up to 129 weeks.

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

Dosage and administration details:

Gantenerumab was administered as SC injection Q4W.

Number of subjects in period 1	SCarlet RoAD	Marguerite RoAD
Started	59	57
Completed	1	0
Not completed	58	57
Consent withdrawn by subject	9	10
Physician decision	3	1
Adverse event, non-fatal	3	-
Death	2	-
Study terminated by sponsor	30	33
Reason not specified	2	7
Progressive disease	9	6

Baseline characteristics

Reporting groups	
Reporting group title	SCarlet RoAD
Reporting group description:	
Participants enrolled from the open label extension (OLE) part of parent study WN25203, received gantenerumab, up to 1200 milligram (mg), subcutaneous (SC) injection, every 4 weeks (Q4W) for up to 129 weeks.	
Reporting group title	Marguerite RoAD
Reporting group description:	
Participants enrolled from the OLE part of parent study WN28745, received gantenerumab, up to 1200 mg, SC injection, Q4W for up to 129 weeks.	

Reporting group values	SCarlet RoAD	Marguerite RoAD	Total
Number of subjects	59	57	116
Age categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	78.0	75.2	
standard deviation	± 6.7	± 8.3	-
Sex: Female, Male			
Units: Participants			
Female	36	35	71
Male	23	22	45
Ethnicity			
Units: Subjects			
Hispanic or Latino	9	4	13
Not Hispanic or Latino	50	53	103
Race			
Units: Subjects			
American Indian or Alaska Native	2	0	2
Asian	0	13	13
Black or African American	0	1	1
White	56	42	98
Unknown or Not Reported	1	1	2

End points

End points reporting groups

Reporting group title	SCarlet RoAD

Reporting group description:

Participants enrolled from the open label extension (OLE) part of parent study WN25203, received gantenerumab, up to 1200 milligram (mg), subcutaneous (SC) injection, every 4 weeks (Q4W) for up to 129 weeks.

Reporting group title	Marguerite RoAD

Reporting group description:

Participants enrolled from the OLE part of parent study WN28745, received gantenerumab, up to 1200 mg, SC injection, Q4W for up to 129 weeks.

Primary: Number of Participants with Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants with Adverse Events (AEs) and Serious Adverse Events (SAEs)[1]

End point description:

An AE was defined as any untoward medical occurrence in a participant administered with gantenerumab and which does not necessarily have a causal relationship with gantenerumab. A serious adverse event (SAE) is any significant hazard, contraindication, side effect that is fatal or life threatening; requires in-patient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; is medically significant or requires intervention to prevent one or other of the outcomes listed above, and which does not necessarily have a causal relationship with gantenerumab. Safety evaluable population included all the participants who received at least one dose of gantenerumab.

End point type	Primary

End point timeframe:

Baseline [Day 1] up to 4 weeks after the last dose of study drug (Up to Week 133)

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 comparison was planned.

End point values	SCarlet RoAD	Marguerite RoAD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	56		
Units: participants				
AE	54	49		
SAE	11	10		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Change in Any Suicidal Ideation or Behavior as Assessed by Columbia-Suicide Severity Rating Scale (C-SSRS)

End point title	Number of Participants with Change in Any Suicidal Ideation or Behavior as Assessed by Columbia-Suicide Severity Rating Scale (C-SSRS)[2]

End point description:

C-SSRS=assessment tool used to assess lifetime suicidality of a participant (at baseline) as well as any new instances of suicidality (C-SSRS since last visit). Intensity of ideation, behavior, & attempts with actual/potential lethality were categories with binary responses (yes/no) & include Wish to be Dead; Non-specific Active Suicidal Thoughts; Active Suicidal Ideation(SI) with Any Methods (Not Plan) without Intent to Act; Active SI with Some Intent to Act, without Specific Plan; Active SI with Specific Plan and Intent, Preparatory Acts and Behavior; Aborted Attempt; Interrupted Attempt; Actual Attempt (non-fatal); Completed Suicide. Suicidal Ideation/behavior is indicated by a "yes" answer to any of the listed categories. Score of 0= no suicide risk present. Score of 1 or > 1= suicidal ideation/behavior. Number of participants with any suicidal ideation/behavior were reported. SE population was used. n= number analysed is number of participants with data available for analysis.

End point type	Primary

End point timeframe:

Baseline (Day 1), up to Week 104

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 comparison was planned.

End point values	SCarlet RoAD	Marguerite RoAD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	54		
Units: participants				
Baseline (n=56,54)	3	0		
Week 24 (n=52,44)	2	0		
Week 52 (n=48,38)	1	0		
Week 76 (n=37,32)	0	1		
Week 104 (n=30,0)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Anti-drug Antibody (ADA) to Gantenerumab

End point title	Number of Participants With Anti-drug Antibody (ADA) to Gantenerumab[3]

End point description:

Safety evaluable population included all the participants who received at least one dose of gantenerumab.

End point type	Primary

End point timeframe:

Up to Week 133

Notes:

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

End point values	SCarlet RoAD	Marguerite RoAD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	56		
Units: participants	3	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Injection-Site Reactions

End point title	Number of Participants with Injection-Site Reactions[4]

End point description:

Safety evaluable population included all the participants who received at least one dose of gantenerumab.

End point type	Primary

End point timeframe:

Baseline [Day 1] up to 4 weeks after the last dose of study drug (Up to Week 133)

Notes:

[4] - 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 comparison was planned.

End point values	SCarlet RoAD	Marguerite RoAD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	56		
Units: participants	14	7		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Discontinued Treatment due to AEs

End point title	Number of Participants Who Discontinued Treatment due to AEs[5]

End point description:

An AE was defined as any untoward medical occurrence in a participant administered with gantenerumab and which does not necessarily have a causal relationship with gantenerumab. SAE is any significant hazard, contraindication, side effect that is fatal or life threatening; requires in-patient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; is medically significant or requires intervention to prevent one or other of the outcomes listed above, and which does not necessarily have a causal relationship with gantenerumab. Safety evaluable population included all the participants who received at least one dose of gantenerumab.

End point type	Primary

End point timeframe:

Baseline [Day 1] up to 4 weeks after the last dose of study drug (Up to Week 133)

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 comparison was planned.

End point values	SCarlet RoAD	Marguerite RoAD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	56		
Units: participants	3	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Amyloid-Related Imaging Abnormalities-Edema (ARIA-E) AEs

End point title	Number of Participants with Amyloid-Related Imaging Abnormalities-Edema (ARIA-E) AEs[6]

End point description:

Safety evaluable population included all the participants who received at least one dose of gantenerumab.

End point type	Primary

End point timeframe:

Baseline [Day 1] up to 4 weeks after the last dose of study drug (Up to Week 133)

Notes:

[6] - 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 comparison was planned.

End point values	SCarlet RoAD	Marguerite RoAD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	56		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Amyloid-Related Imaging Abnormalities-Haemosiderin deposition (ARIA-H) AEs

End point title	Number of Participants with Amyloid-Related Imaging Abnormalities-Haemosiderin deposition (ARIA-H) AEs[7]

End point description:

Safety evaluable population included all the participants who received at least one dose of gantenerumab.

End point type	Primary

End point timeframe:

Baseline [Day 1] up to 4 weeks after the last dose of study drug (Up to Week 133)

Notes:

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

End point values	SCarlet RoAD	Marguerite RoAD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	56		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline [Day 1] up to 4 weeks after the last dose of study drug (Up to Week 133)

Adverse event reporting additional description:

Safety evaluable population included all the participants who received at least one dose of gantenerumab.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Marguerite RoAD

Reporting group description:

Participants enrolled from the OLE part of parent study WN28745, received gantenerumab, up to 1200 mg, SC injection, Q4W for up to 129 weeks.

Reporting group title	SCarlet RoAD

Reporting group description:

Participants enrolled from the OLE part of parent study WN25203, received gantenerumab, up to 1200 mg, SC injection, Q4W for up to 129 weeks.

Serious adverse events	Marguerite RoAD	SCarlet RoAD	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 56 (17.86%)	11 / 59 (18.64%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer stage I			
subjects affected / exposed	0 / 56 (0.00%)	1 / 59 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	0 / 56 (0.00%)	1 / 59 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	0 / 56 (0.00%)	1 / 59 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Rectal cancer			
subjects affected / exposed	1 / 56 (1.79%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 56 (0.00%)	1 / 59 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 56 (0.00%)	1 / 59 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 56 (1.79%)	1 / 59 (1.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 56 (1.79%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 56 (1.79%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 56 (1.79%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Seizure			

subjects affected / exposed	1 / 56 (1.79%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	0 / 56 (0.00%)	1 / 59 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 56 (0.00%)	1 / 59 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myoclonus			
subjects affected / exposed	1 / 56 (1.79%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 56 (0.00%)	2 / 59 (3.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Gastrointestinal disorders			
Acute abdomen			
subjects affected / exposed	1 / 56 (1.79%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 56 (0.00%)	1 / 59 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	1 / 56 (1.79%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 56 (0.00%)	1 / 59 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Neuropsychiatric symptoms			
subjects affected / exposed	1 / 56 (1.79%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 56 (1.79%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 56 (3.57%)	1 / 59 (1.69%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 56 (1.79%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Marguerite RoAD	SCarlet RoAD	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 56 (69.64%)	43 / 59 (72.88%)	
Injury, poisoning and procedural complications			
Vaccination complication			
subjects affected / exposed	4 / 56 (7.14%)	0 / 59 (0.00%)	
occurrences (all)	4	0	

Rib fracture			
subjects affected / exposed	3 / 56 (5.36%)	0 / 59 (0.00%)	
occurrences (all)	3	0	
Fall			
subjects affected / exposed	8 / 56 (14.29%)	13 / 59 (22.03%)	
occurrences (all)	15	20	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 56 (1.79%)	4 / 59 (6.78%)	
occurrences (all)	1	4	
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	7 / 56 (12.50%)	14 / 59 (23.73%)	
occurrences (all)	34	183	
Pyrexia			
subjects affected / exposed	3 / 56 (5.36%)	1 / 59 (1.69%)	
occurrences (all)	4	1	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	5 / 56 (8.93%)	3 / 59 (5.08%)	
occurrences (all)	5	3	
Diarrhoea			
subjects affected / exposed	3 / 56 (5.36%)	2 / 59 (3.39%)	
occurrences (all)	5	4	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 56 (0.00%)	3 / 59 (5.08%)	
occurrences (all)	0	4	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 56 (7.14%)	1 / 59 (1.69%)	
occurrences (all)	5	1	
Agitation			
subjects affected / exposed	3 / 56 (5.36%)	5 / 59 (8.47%)	
occurrences (all)	3	6	
Anxiety			

subjects affected / exposed	4 / 56 (7.14%)	4 / 59 (6.78%)	
occurrences (all)	4	4	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 56 (8.93%)	2 / 59 (3.39%)	
occurrences (all)	5	2	
Arthralgia			
subjects affected / exposed	3 / 56 (5.36%)	1 / 59 (1.69%)	
occurrences (all)	5	1	
Infections and infestations			
COVID-19			
subjects affected / exposed	10 / 56 (17.86%)	13 / 59 (22.03%)	
occurrences (all)	10	14	
Urinary tract infection			
subjects affected / exposed	7 / 56 (12.50%)	8 / 59 (13.56%)	
occurrences (all)	10	12	
Upper respiratory tract infection			
subjects affected / exposed	3 / 56 (5.36%)	0 / 59 (0.00%)	
occurrences (all)	3	0	
Nasopharyngitis			
subjects affected / exposed	0 / 56 (0.00%)	4 / 59 (6.78%)	
occurrences (all)	0	5	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 56 (7.14%)	1 / 59 (1.69%)	
occurrences (all)	4	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 January 2022	Protocol was amended to allow participants who completed dosing visit (Week 104) to continue participation in the study for an additional 2 years. Changes to the protocol, along with a rationale for each change, are summarized below: - The study was accordingly divided into two parts. Part 1 reflected the initial study period of 2 years and Part 2 reflected the study period of additional 2 years beyond the initial 2 years because the safety profile combined with the potential benefit indicates that a longer period of treatment is justified. The protocol body was updated accordingly to clarify Part 1 from Part 2. Text from Part 1 was also updated from present to past tense to reflect the completion of Part 1, where applicable. - Sections were updated to reflect the recent study status in alignment with the Gantenerumab Investigator's Brochure v17. - Benefit-risk assessment on concomitant administration of severe acute respiratory syndrome coronavirus 2 vaccines with gantenerumab was added to address a Health Authority request. - The sample size for Part 1 of the study was not available at the time of writing the protocol, as it was going to be determined by the number of participants who completed OLE part of Studies WN25203 and WN28745. As this number was determined. Section 3 was updated accordingly. - Section was revised to clarify the Medical Monitor's responsibility to review and support participant cohort management and other protocol activities. Any reference to approval by the Medical Monitor with regards to medical decisions following enrollment was removed from the protocol. This means that the Principal Investigator (PI) may consult with the Medical Monitor/Sponsor for advice or clarification and may share risk factor information pertinent to the participant, but the medical decisions for the study participants are the responsibility of the PI.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

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

Notes:

Limitations and caveats

None reported