



Clinical trial results:

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

Summary

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

Results information

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

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | WN42171 |
|-----------------------|---------|

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|---------------|
| Analysis stage | Final |
| Date of interim/final analysis | 06 March 2023 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|---------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 06 March 2023 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the safety and tolerability of long-term gantenerumab administered by subcutaneous (SC) injection.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

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

Notes:

Population of trial subjects

Subjects enrolled per country

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

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

Notes:

| Subjects enrolled per age group | |
|---|------|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 186 |
| From 65 to 84 years | 1116 |
| 85 years and over | 79 |

Subject disposition

Recruitment

Recruitment details:

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

Pre-assignment

Screening details:

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

Period 1

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

Arms

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

Arm description:

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

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

Dosage and administration details:

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

| | |
|------------------|---|
| Arm title | Placebo: No Participation in Graduate OLE |
|------------------|---|

Arm description:

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

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

Dosage and administration details:

Gantenerumab administered as SC injections with gradual up titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and then at a dose of 510 mg, Q4W up 3 doses before receiving open label gantenerumab, 510 mg SC injections, Q2W. To maintain the blind to previous treatment assignment, participants received Q2W, SC injections, with alternate doses

containing gantenerumab matching placebo.

| | |
|------------------|--|
| Arm title | Gantenerumab: Participated in Graduate OLE |
|------------------|--|

Arm description:

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

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

Dosage and administration details:

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

| | |
|------------------|--|
| Arm title | Gantenerumab: No Participation in Graduate OLE |
|------------------|--|

Arm description:

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

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

Dosage and administration details:

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

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

| | | | |
|------------------|---|---|---|
| Lack of efficacy | - | - | - |
|------------------|---|---|---|

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

Baseline characteristics

Reporting groups

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

| Reporting group values | Placebo: Participated in Graduate OLE | Placebo: No Participation in Graduate OLE | Gantenerumab: Participated in Graduate OLE |
|------------------------|---------------------------------------|---|--|
| Number of subjects | 15 | 696 | 28 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|-------|-------|-------|
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 76.7 | 73.6 | 74.1 |
| standard deviation | ± 7.8 | ± 7.4 | ± 8.0 |
| Sex: Female, Male | | | |
| Units: participants | | | |
| Female | 11 | 387 | 14 |
| Male | 4 | 309 | 14 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 25 | 4 |
| Asian | 1 | 104 | 1 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 6 | 0 |
| White | 14 | 549 | 22 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 12 | 1 |
| Ethnicity (NIH/OMB) | | | |

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

| | | | |
|-------------------------------|--|-------|--|
| Reporting group values | Gantenerumab: No Participation in Graduate OLE | Total | |
| Number of subjects | 642 | 1381 | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|-------|------|--|
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 73.0 | | |
| standard deviation | ± 7.7 | - | |
| Sex: Female, Male | | | |
| Units: participants | | | |
| Female | 382 | 794 | |
| Male | 260 | 587 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 18 | 47 | |
| Asian | 87 | 193 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 4 | 10 | |
| White | 518 | 1103 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 15 | 28 | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 89 | 225 | |
| Not Hispanic or Latino | 548 | 1147 | |
| Unknown or Not Reported | 5 | 9 | |

End points

End points reporting groups

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

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

| | |
|--|---|
| End point title | Number of Participants With at Least One Adverse Event (AE) and Serious Adverse Event (SAE) ^{[1][2]} |
| End point description: AE is any untoward medical occurrence in clinical investigation participant administered a pharmaceutical product, regardless of casual attribution. SAE is any fatal AE, life threatening, requires or prolongs inpatient hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect in a neonate/infant born to a mother exposed to study drug or a significant medical event in investigator's judgment. Safety evaluable (SE) analysis set included all participants enrolled who received at least one dose of study drug in this study or in OLE part of parent studies (GRADUATE I or GRADUATE II). 6 participants randomized to placebo arm during double-blind treatment in parent studies received at least one dose of gantenerumab and were considered in gantenerumab arm for safety evaluable set. First dosing visit in OLE (first dosing in current study or first dosing in OLE period of parent GRADUATE studies) was considered as baseline (OLE Day 1). | |
| End point type | Primary |
| End point timeframe: From Baseline (OLE Day 1) up to 14 weeks after the last dose (up to 134 weeks) | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics was planned for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

Justification: Only descriptive statistics was planned for this endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

ARIA are an identified risk with anti-amyloid antibodies, including gantenerumab. These changes can be identified on brain MRI. In ARIA-E, (E for oedema or effusion), oedema can be seen in different areas of the brain on MRI, representing fluid leakage into the brain parenchyma or sulcal spaces. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1). M-SE analysis set included all participants in the SE analysis set who had at least one post-baseline safety MRI scan.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics was planned for this endpoint.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

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

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

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|---|
| End point title | Number of Participants with Injection-Site Reactions (ISRs) ^{[7][8]} |
|-----------------|---|

End point description:

An AE is any unfavorable and unintended sign, symptom, or disease temporally associated with the use of an investigational product or other protocol-imposed intervention, regardless of attribution. Local injection reactions (or injection site reactions) are defined as AEs related to the injection site that occur during or within 24 hours after study drug administration that are judged to be related to the study drug injection. SE analysis set included all participants enrolled who received at least one dose of study drug in this study or in the OLE part of the parent studies (GRADUATE I or GRADUATE II). Six participants randomized to placebo arm during the double-blind treatment in the parent studies received at least one dose of gantenerumab and were considered in the gantenerumab arm for safety evaluable set. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

Justification: Only descriptive statistics was planned for this endpoint.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

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

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

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|--|
| End point title | Number of Participants with at Least One Amyloid-Related |
|-----------------|--|

End point description:

ARIA are an identified risk with anti-amyloid antibodies, including gantenerumab. These changes can be identified on brain MRI. ARIA-H (H for hemosiderosis) are small foci of signal loss observed on MRI sequences sensitive for paramagnetic tissue properties and comprise cerebral microbleeds (small foci of bleeding in the brain parenchyma) and leptomeningeal hemosiderosis (small foci of bleeding on the surface of the brain). These changes also occur sporadically in AD. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1). M-SE analysis set included all participants in the SE analysis set who had at least one post-baseline safety MRI scan.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics was planned for this endpoint.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics was planned for this endpoint.

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

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

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

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|---|
| End point title | Number of Participants With at Least One Adverse Event of Special Interest (AESI) ^{[13][14]} |
|-----------------|---|

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics was planned for this endpoint.

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

CDR was derived through semi-structured interview with participant and an appropriate informant, and it rated impairment across 6 domains: memory, orientation, judgment, and problem solving, community affairs, home and hobbies, and personal care on a 5-point scale for which 0=normal, 0.5=very mild dementia, 1=mild dementia, 2=moderate dementia, and 3= severe dementia. Score range for CDR-GS is from 0 to 3 and a high score on the CDR-GS would indicate a high disease severity. A negative change from baseline indicates improvement. Participants in ITT analysis set were analysed. Overall number analyzed is number of participants with data available for analyses. Number of participants analyzed indicates number of participants with data available for analyses at specified timepoint. First dosing visit in OLE (first dosing in current study or first dosing in OLE period of parent GRADUATE studies) was considered as baseline (OLE Day 1).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

CDR rated impairment across 6 domains: memory, orientation, judgment, and problem solving, community affairs, home and hobbies, and personal care on a 5-point scale for which 0=no impairment, 0.5=questionable impairment, and 1, 2, and 3=mild, moderate, and severe impairment, respectively. CDR-SB is based on summing each of domain box scores with total score ranging from 0-18 with higher scores reflecting greater cognitive and functional impairment. A negative change from baseline indicates improvement. ITT analysis set. Overall number analyzed is the number of participants with data available for analyses. The number of participants analyzed indicates the number of participants with data available for analyses at the specified timepoint. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

MMSE is a rater-administered performance-based outcome (PerfO) that includes a set of standardized questions used to evaluate possible cognitive impairment and help stage the severity level of this impairment. The questions target six areas: orientation, registration, attention, short-term recall, language, and constructional praxis/visuospatial abilities. Total score ranges from 0-30, with lower scores indicating greater impairment. A positive change from baseline indicates improvement. ITT analysis set. Overall number analyzed is the number of participants with data available for analyses. The number of participants analyzed indicates the number of participants with data available for analyses at

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The ADAS-Cog13 total score includes all of the items in the ADAS-Cog11 in addition to delayed word recall and the number cancellation. For the ADAS-cog 13 the range is 0-85 (score range for Delayed Word Recall [DWR] score is 0-10 and for Number Cancellation [NC] is 0-5, thus the score is ADAS-cog 11[0-70] plus the scores for DWR and NC). A higher score indicates worse performance. A negative change from baseline indicates improvement in cognitive function. ITT analysis set. Overall number analyzed is the number of participants with data available for analyses. The number of participants analyzed indicates the number of participants with data available for analyses at the specified timepoint. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

VFT is a rater administered PerfO that measures speed and flexibility of verbal thought with a total score that ranges from 0-99 (lower scores indicating lower performance). A positive change from baseline indicates improvement. ITT analysis set included all enrolled participants, who received at least one dose of study drug. Participants will be analyzed by the treatment they were randomized to in the parent studies (GRADUATE I or GRADUATE II). Overall number analyzed is the number of participants with data available for analyses. The number of participants analyzed indicates the number of participants with data available for analyses at the specified timepoint. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

No statistical analyses for this end point

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

| | |
|---|---|
| End point title | Change From Baseline Over Time in Coding (Digit Symbol Substitution Test [DSST]) Subset |
| End point description: Coding, also called DSST is a rater administered PerFO that measures speed of processing and associative memory with a total score that ranges from 0-135 (lower scores indicating lower performance). The DSST was adapted from the Wechsler Adult Intelligence Scale. The 120-second version of the test was used in this study. Positive change from baseline indicates improvement. ITT analysis set included all enrolled participants, who received at least one dose of study drug. Participants will be analyzed by the treatment they were randomized to in the parent studies (GRADUATE I or GRADUATE II). Overall number analyzed is the number of participants with data available for analyses. The number of participants analyzed indicates the number of participants with data available for analyses at the specified timepoint. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1). | |
| End point type | Secondary |
| End point timeframe: Baseline (OLE Day 1), Weeks 24, 36, 52, 76 and 104 | |

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

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Functional Activities Questionnaire (FAQ) Score

| | |
|--|---|
| End point title | Change in Functional Activities Questionnaire (FAQ) Score |
| End point description: FAQ is a rater-administered observer-reported outcomes (ObsRO) (informant-based measure) that measures a participant's functional ability to perform complex higher-order activities. The observer provides performance ratings of the target person on ten complex higher-order activities. Total score that ranges from 0-30, with higher scores reflecting greater functional impairment. A negative change from baseline indicates improvement. ITT analysis set. Overall number analyzed is the number of participants with data available for analyses. The number of participants analyzed indicates the number of participants with data available for analyses at the specified timepoint. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1). | |

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (OLE Day 1), Weeks 24, 36, 52, 76 and 104 | |

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

ADCS-ADL is a 23-item rater-administered, ObsRO that captures a participant's ability to perform basic activities of daily living (e.g., eating and toileting) and more complex ADL or instrumental activities of daily living (iADL, e.g., using the telephone, managing finances, preparing a meal). Total score ranges from 0-78, with higher scores reflecting better functioning. A positive change from baseline indicates improvement. ITT analysis set. Overall number analyzed is the number of participants with data available for analyses. The number of participants analyzed indicates the number of participants with data available for analyses at the specified timepoint. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The number of participants with positive results for ADA against gantenerumab at any of the post-baseline assessment time-points were reported. Evaluable participant during OLE was participant with an ADA assay result from at least one sample during OLE. Treatment Emergent ADA = A participant with a negative or missing baseline ADA result(s) and at least one positive post-baseline ADA result. SE analysis set included all participants enrolled who received at least one dose of study drug in this study or in the OLE part of the parent studies (GRADUATE I or GRADUATE II). Six participants randomized to placebo arm during the double-blind treatment in the parent studies received at least one dose of gantenerumab and were considered in the gantenerumab arm for safety evaluable set. The first dosing visit in the OLE (first dosing in current study or first dosing in the OLE period of the parent GRADUATE studies) was considered as baseline (OLE Day 1).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

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

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

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Adverse event reporting additional description:

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

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Placebo: Participated in Graduate OLE |
|-----------------------|---------------------------------------|

Reporting group description:

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

| | |
|-----------------------|--|
| Reporting group title | Gantenerumab: Participated in Graduate OLE |
|-----------------------|--|

Reporting group description:

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

| | |
|-----------------------|--|
| Reporting group title | Gantenerumab: No Participation in Graduate OLE |
|-----------------------|--|

Reporting group description:

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

| | |
|-----------------------|---|
| Reporting group title | Placebo: No Participation in Graduate OLE |
|-----------------------|---|

Reporting group description:

Participants treated with placebo in the DB part and who did not enter the OLE part of Study WN29922 or WN39658, were enrolled in this arm to receive gantenerumab SC injections with gradual up titration starting at a dose of 120 mg, Q4W for 3 doses, followed by 255 mg, Q4W for 3 doses, and then at a dose of 510 mg, 510 mg Q4W for 3 doses before receiving open-label gantenerumab, 510 mg SC injections, Q2W. To maintain the blind to previous treatment assignment, participants received Q2W, SC injections, with alternate doses containing gantenerumab matching placebo.

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

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

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

| | | | |
|--|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 1 / 647 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 0 / 647 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 0 / 647 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 0 / 647 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic dissection | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 0 / 647 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 0 / 647 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 0 / 647 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 0 / 647 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Generalised oedema | | | |

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

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

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

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

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

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

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

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 0 / 647 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural hygroma | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 0 / 647 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Motor dysfunction | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 0 / 647 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysstasia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 1 / 647 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 1 / 647 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Meniere's disease | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 0 / 647 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 0 / 647 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Small intestinal obstruction | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 0 / 647 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal ulcer | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 0 / 647 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 1 / 647 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 1 / 647 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 0 / 647 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 1 / 647 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 1 / 647 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal fistula | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 29 (0.00%) | 1 / 647 (0.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |

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

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

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

| | | | |
|-------------------------------|-------------|--|--|
| Serious adverse events | Placebo: No | | |
|-------------------------------|-------------|--|--|

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

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

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

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

Notes:

Limitations and caveats

None reported