



Clinical trial results:

A Phase 3 Randomized, Double-Blind, Placebo-Controlled Study of LY2951742 with a Long-Term Open-Label Extension in Patients with Chronic Cluster Headache

Summary

| | |
|--------------------------|-------------------------------|
| EudraCT number | 2014-005429-11 |
| Trial protocol | GB DE ES DK FI BE FR NL GR IT |
| Global end of trial date | 14 August 2019 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 30 August 2020 |
| First version publication date | 30 August 2020 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | I5Q-MC-CGAM |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|---------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02438826 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Trial Number: 15781 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Eli Lilly and Company |
| Sponsor organisation address | Lilly Corporate Center, Indianapolis, IN, United States, 46285 |
| Public contact | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877CTLilly, |
| Scientific contact | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 8772854559, |

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 | 14 August 2019 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|----------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 14 August 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the efficacy of the study drug known as galcanezumab in participants with chronic cluster headache.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 18 June 2015 |
| 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 | Greece: 1 |
| Country: Number of subjects enrolled | Canada: 8 |
| Country: Number of subjects enrolled | Netherlands: 10 |
| Country: Number of subjects enrolled | Belgium: 32 |
| Country: Number of subjects enrolled | United States: 33 |
| Country: Number of subjects enrolled | Finland: 4 |
| Country: Number of subjects enrolled | Denmark: 9 |
| Country: Number of subjects enrolled | Italy: 31 |
| Country: Number of subjects enrolled | United Kingdom: 16 |
| Country: Number of subjects enrolled | France: 40 |
| Country: Number of subjects enrolled | Germany: 42 |
| Country: Number of subjects enrolled | Spain: 11 |
| Worldwide total number of subjects | 237 |
| EEA total number of subjects | 196 |

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) | 236 |
| From 65 to 84 years | 1 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

No Text Available

Pre-assignment

Screening details:

Study consists of a 12-week double-blind treatment phase; an optional 1-year open-label treatment phase; and a 16-week post-treatment phase (washout).

Period 1

| | |
|------------------------------|------------------------------------|
| Period 1 title | Double-Blind Treatment (DBT) Phase |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Participants received placebo once a month by subcutaneous (SC) injection for 3 months.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

3 subcutaneous injections of placebo administered once a month for 3 months.

| | |
|------------------|---------------------|
| Arm title | Galcanezumab 300 mg |
|------------------|---------------------|

Arm description:

Participants received galcanezumab 300 mg once a month by subcutaneous (SC) injection for 3 months.

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Galcanezumab 300 mg |
| Investigational medicinal product code | |
| Other name | LY2951742 |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

300 mg of galcanezumab administered as subcutaneous injection for 3 months.

| Number of subjects in period 1 | Placebo | Galcanezumab 300 mg |
|--|---------|---------------------|
| Started | 123 | 117 |
| Received at Least 1 Dose of Study Drug | 120 | 117 |
| Completed | 117 | 113 |
| Not completed | 6 | 4 |
| Consent withdrawn by subject | 1 | 1 |
| Screen Failure | 2 | - |
| Adverse event, non-fatal | 1 | 1 |
| Protocol deviation | 1 | 2 |
| Lack of efficacy | 1 | - |

Period 2

| | |
|------------------------------|--|
| Period 2 title | Received at least 1 dose (DBT) - Period1 |
| Is this the baseline period? | Yes ^[1] |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | No |
| Arm title | Placebo |

Arm description:

Participants received placebo once a month by subcutaneous (SC) injection for 3 months.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

3 subcutaneous injections of placebo administered once a month for 3 months.

| | |
|------------------|---------------------|
| Arm title | Galcanezumab 300 mg |
|------------------|---------------------|

Arm description:

Participants received galcanezumab 300 mg once a month by subcutaneous (SC) injection for 3 months.

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Galcanezumab 300 mg |
| Investigational medicinal product code | |
| Other name | LY2951742 |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

300 mg of galcanezumab administered as subcutaneous injection for 3 months.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Participants must have completed the double-blind phase to enter the optional open-label phase. One placebo treated participant chose not to enter the open-label phase.

| Number of subjects in period 2 | Placebo | Galcanezumab 300 mg |
|--------------------------------|---------|---------------------|
| Started | 120 | 117 |
| Completed | 117 | 113 |
| Not completed | 3 | 4 |
| Consent withdrawn by subject | 1 | 1 |
| Adverse event, non-fatal | 1 | 1 |
| Lack of efficacy | 1 | - |
| Protocol deviation | - | 2 |

Period 3

| | |
|------------------------------|-------------------------------------|
| Period 3 title | Open-Label Treatment Phase-Period 2 |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|--------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo/GMB 300 mg |

Arm description:

Participants from placebo group received 300 mg of galcanezumab (GMB) by subcutaneous injection every 30 days, for up to a total of 12 administrations.

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Galcanezumab 300 mg |
| Investigational medicinal product code | |
| Other name | LY2951742 |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

300 mg of galcanezumab administered as subcutaneous injections every 30 days, for up to a total of 12 administrations.

| | |
|-----------|-----------------------|
| Arm title | GMB 300 mg/GMB 300 mg |
|-----------|-----------------------|

Arm description:

Participants from galcanezumab group received 300 mg of galcanezumab by subcutaneous injection every 30 days, for up to a total of 12 administrations.

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Galcanezumab 300 mg |
| Investigational medicinal product code | |
| Other name | LY2951742 |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

300 mg of galcanezumab administered as subcutaneous injections every 30 days, for up to a total of 12

| Number of subjects in period 3 | Placebo/GMB 300 mg | GMB 300 mg/GMB 300 mg |
|---------------------------------------|--------------------|-----------------------|
| Started | 116 | 113 |
| Completed | 72 | 80 |
| Not completed | 44 | 33 |
| Consent withdrawn by subject | 6 | 7 |
| Adverse event, non-fatal | 11 | 6 |
| Lost to follow-up | - | 2 |
| Lack of efficacy | 27 | 18 |

Period 4

| | |
|------------------------------|-------------------------------|
| Period 4 title | Post-Treatment Phase-Period 3 |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | No |
| Arm title | Placebo/GMB 300 mg (Open-Label Treatment Phase) |

Arm description:

Participants from Open-Label Treatment Phase entered this phase, they have not received any intervention during this post-treatment period.

| | |
|---|-----------------|
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| | |
|------------------|--|
| Arm title | GMB 300 mg/GMB 300 mg (Open-Label Treatment Phase) |
|------------------|--|

Arm description:

Participants from Open-Label Treatment Phase entered this phase, they have not received any intervention during this post-treatment period.

| | |
|---|-----------------|
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| | |
|------------------|--|
| Arm title | Placebo (Double-Blind Treatment Phase) |
|------------------|--|

Arm description:

Participants from double blind treatment group entered this phase, they have not received any intervention during this post-treatment period.

| | |
|---|-----------------|
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| | |
|---|--|
| Arm title | Galcanezumab 300 mg (Double-Blind Treatment Phase) |
| Arm description: Participants from double blind treatment group entered this phase, they have not received any intervention during this post-treatment period. | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 4 | Placebo/GMB 300 mg (Open-Label Treatment Phase) | GMB 300 mg/GMB 300 mg (Open-Label Treatment Phase) | Placebo (Double-Blind Treatment Phase) |
|---------------------------------------|---|--|--|
| Started | 93 | 93 | 2 |
| Completed | 84 | 92 | 2 |
| Not completed | 9 | 1 | 0 |
| Physician decision | 1 | - | - |
| Consent withdrawn by subject | 1 | 1 | - |
| Adverse event, non-fatal | 3 | - | - |
| Lack of efficacy | 4 | - | - |

| Number of subjects in period 4 | Galcanezumab 300 mg (Double-Blind Treatment Phase) |
|---------------------------------------|--|
| Started | 4 |
| Completed | 4 |
| Not completed | 0 |
| Physician decision | - |
| Consent withdrawn by subject | - |
| Adverse event, non-fatal | - |
| Lack of efficacy | - |

Baseline characteristics

Reporting groups

| | |
|---|---------------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received placebo once a month by subcutaneous (SC) injection for 3 months. | |
| Reporting group title | Galcanezumab 300 mg |
| Reporting group description: | |
| Participants received galcanezumab 300 mg once a month by subcutaneous (SC) injection for 3 months. | |

| Reporting group values | Placebo | Galcanezumab 300 mg | Total |
|---|---------|---------------------|-------|
| Number of subjects | 120 | 117 | 237 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: years | | | |
| arithmetic mean | 44.38 | 45.62 | |
| standard deviation | ± 10.81 | ± 11.03 | - |
| Gender categorical Units: Subjects | | | |
| Female | 34 | 31 | 65 |
| Male | 86 | 86 | 172 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 15 | 18 | 33 |
| Not Hispanic or Latino | 87 | 81 | 168 |
| Unknown or Not Reported | 18 | 18 | 36 |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 1 | 1 | 2 |
| White | 101 | 99 | 200 |
| More than one race | 18 | 17 | 35 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Region of Enrollment | | | |

| | | | |
|--|---------|--------|----|
| Units: Subjects | | | |
| Greece | 0 | 1 | 1 |
| Canada | 4 | 4 | 8 |
| Netherlands | 5 | 5 | 10 |
| Belgium | 16 | 16 | 32 |
| United States | 15 | 18 | 33 |
| Finland | 2 | 2 | 4 |
| Denmark | 5 | 4 | 9 |
| Italy | 17 | 14 | 31 |
| United Kingdom | 8 | 8 | 16 |
| France | 20 | 20 | 40 |
| Germany | 22 | 20 | 42 |
| Spain | 6 | 5 | 11 |
| Weekly Cluster Headache Attacks | | | |
| Units: cluster headache attacks per week | | | |
| arithmetic mean | 18.47 | 19.18 | |
| standard deviation | ± 10.66 | ± 9.82 | - |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Placebo |
| Reporting group description: Participants received placebo once a month by subcutaneous (SC) injection for 3 months. | |
| Reporting group title | Galcanezumab 300 mg |
| Reporting group description: Participants received galcanezumab 300 mg once a month by subcutaneous (SC) injection for 3 months. | |
| Reporting group title | Placebo |
| Reporting group description: Participants received placebo once a month by subcutaneous (SC) injection for 3 months. | |
| Reporting group title | Galcanezumab 300 mg |
| Reporting group description: Participants received galcanezumab 300 mg once a month by subcutaneous (SC) injection for 3 months. | |
| Reporting group title | Placebo/GMB 300 mg |
| Reporting group description: Participants from placebo group received 300 mg of galcanezumab (GMB) by subcutaneous injection every 30 days, for up to a total of 12 administrations. | |
| Reporting group title | GMB 300 mg/GMB 300 mg |
| Reporting group description: Participants from galcanezumab group received 300 mg of galcanezumab by subcutaneous injection every 30 days, for up to a total of 12 administrations. | |
| Reporting group title | Placebo/GMB 300 mg (Open-Label Treatment Phase) |
| Reporting group description: Participants from Open-Label Treatment Phase entered this phase, they have not received any intervention during this post-treatment period. | |
| Reporting group title | GMB 300 mg/GMB 300 mg (Open-Label Treatment Phase) |
| Reporting group description: Participants from Open-Label Treatment Phase entered this phase, they have not received any intervention during this post-treatment period. | |
| Reporting group title | Placebo (Double-Blind Treatment Phase) |
| Reporting group description: Participants from double blind treatment group entered this phase, they have not received any intervention during this post-treatment period. | |
| Reporting group title | Galcanezumab 300 mg (Double-Blind Treatment Phase) |
| Reporting group description: Participants from double blind treatment group entered this phase, they have not received any intervention during this post-treatment period. | |

Primary: Overall Mean Change from Baseline in Weekly Cluster Headache Attack Frequency

| | |
|--|---|
| End point title | Overall Mean Change from Baseline in Weekly Cluster Headache Attack Frequency |
| End point description: Number of cluster headache attacks was recorded daily by study participants in their ePRO Diary, Baseline and 12 weeks of daily data during double-blind treatment phase will be converted into 14-calendar day intervals: the baseline 14-day interval, Weeks 1/2, 3/4, 5/6, 7/8, 9/10, and 11/12. Next, the biweekly interval results were adjusted to 7-day (weekly) interval in order to report the outcome as weekly frequency. Overall mean change from baseline is derived from mixed model repeated measures (MMRM) analysis. Least Square (LS) means were calculated using MMRM model with treatment, sex, verapamil use, pooled investigative site, week, baseline, and treatment by week as fixed effects. Analysis Population Description: All randomized participants who received at least 1 dose of study drug, | |

and had baseline and at least one post baseline value.

| | |
|----------------------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Baseline, Week 1 through Week 12 | |

| End point values | Placebo | Galcanezumab 300 mg | | |
|--|-----------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 117 | | |
| Units: cluster headache attacks per week | | | | |
| least squares mean (standard error) | -4.59 (± 0.79) | -5.38 (± 0.81) | | |

Statistical analyses

| | |
|---|-----------------------------------|
| Statistical analysis title | Cluster Headache Attack Frequency |
| Comparison groups | Placebo v Galcanezumab 300 mg |
| Number of subjects included in analysis | 237 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.334 ^[1] |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.77 |
| upper limit | 1.17 |

Notes:

[1] - Cui, Hung, Wang (CHW) procedure applied

Secondary: Percentage of Participants with a 50% or Greater Reduction from Baseline in the Weekly Number of Cluster Headache Attacks

| | |
|-----------------|---|
| End point title | Percentage of Participants with a 50% or Greater Reduction from Baseline in the Weekly Number of Cluster Headache Attacks |
|-----------------|---|

End point description:

A 50% responder is any participant who has a $\geq 50\%$ reduction from baseline in the weekly number of cluster headache attacks in a 14-day interval: Weeks 1/2, Weeks 3/4, Weeks 5/6, Weeks 7/8, Weeks 9/10, and Weeks 11/12. Mean percentage of participants is derived from the average of weeks 1/2 to weeks 11/12 from generalized linear mixed model repeated measures method with treatment, sex, verapamil use, week, treatment by week, and baseline as fixed effects.

APD: All randomized participants who received at least 1 dose of study drug, and had baseline and at least 1 post baseline value.

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

End point timeframe:

Baseline, Week 1 through Week 12

| End point values | Placebo | Galcanezumab 300 mg | | |
|-----------------------------------|-----------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 117 | | |
| Units: percentage of participants | | | | |
| arithmetic mean (standard error) | 27.1 (± 3.5) | 32.6 (± 3.8) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | 50% Greater Reduction in Cluster Headache Attacks |
| Comparison groups | Placebo v Galcanezumab 300 mg |
| Number of subjects included in analysis | 237 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.17 [2] |
| Method | Mixed models analysis |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.297 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.83 |
| upper limit | 2.028 |

Notes:

[2] - Cui, Hung, Wang (CHW) procedure applied

Secondary: Percentage of Participants With a Sustained Response of 50% or Greater Reduction From Baseline in the Weekly Number of Cluster Headache Attacks

| | |
|-----------------|---|
| End point title | Percentage of Participants With a Sustained Response of 50% or Greater Reduction From Baseline in the Weekly Number of Cluster Headache Attacks |
|-----------------|---|

End point description:

Sustained Response is defined as a 50% or greater reduction in the weekly cluster attack frequency from baseline to Weeks 3/4 and maintained at Weeks 5/6, Weeks 7/8, Weeks 9/10, and Weeks 11/12. Percentage of participants with a sustained response was analyzed using Koch's nonparametric randomization-based analysis of covariance method. This method adjusted for pooled investigative site by including it as a stratification variable. It also adjusted for sex, verapamil use and baseline value. APD: All randomized participants who received at least 1 dose of study drug, had a baseline, and at least one post baseline value.

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

End point timeframe:

Baseline, Week 3 through Week 12

| End point values | Placebo | Galcanzumab 300 mg | | |
|-----------------------------------|-----------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 117 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 17.50 | 16.24 | | |

Statistical analyses

| Statistical analysis title | Sustained Response of Cluster Headache Attacks |
|---|--|
| Comparison groups | Placebo v Galcanzumab 300 mg |
| Number of subjects included in analysis | 237 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.946 ^[3] |
| Method | Mixed models analysis |

Notes:

[3] - Chui, Hung, Wang (CHW) procedure applied)

Secondary: Percentage of Participants with a 30% Reduction in the Weekly Number of Cluster Headache Attacks

| | |
|-----------------|--|
| End point title | Percentage of Participants with a 30% Reduction in the Weekly Number of Cluster Headache Attacks |
|-----------------|--|

End point description:

A 30% responder is any participant who has a $\geq 30\%$ reduction from baseline in the weekly number of cluster headache attacks in a 14-day interval. Weeks 1/2, 3/4, 5/6, 7/8, 9/10, and 11/12. Mean percentage of participants is derived from the average of weeks 1/2 to weeks 11/12 from generalized linear mixed model repeated measures method with treatment, sex, verapamil use, week, treatment by week, and baseline as fixed effects.

APD: All randomized participants who received at least 1 dose of study drug, and had baseline and at least 1 post baseline value.

| | |
|----------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 1 through Week 12 | |

| End point values | Placebo | Galcanzumab 300 mg | | |
|-----------------------------------|-----------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 117 | | |
| Units: percentage of participants | | | | |
| arithmetic mean (standard error) | 39.0 (± 3.9) | 49.1 (± 4.1) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | 30% Reduction in Weekly Cluster Headache Attacks |
| Comparison groups | Placebo v Galcanezumab 300 mg |
| Number of subjects included in analysis | 237 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.057 |
| Method | Mixed models analysis |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.51 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.987 |
| upper limit | 2.309 |

Secondary: Percentage of Participants Reporting a Score of 1 or 2 on the Patient Global Impression of Improvement (PGI-I)

| | |
|-----------------|--|
| End point title | Percentage of Participants Reporting a Score of 1 or 2 on the Patient Global Impression of Improvement (PGI-I) |
|-----------------|--|

End point description:

PGI-I requests participants to mark the box that best describes their cluster headache condition since they started taking the medicine. The options in the displayed boxes are represented on a 7-point scale, with 1 = very much better, 2 = much better, 3 = a little better, 4 = no change, 5 = a little worse, 6 = much worse, and 7 = very much worse. Percentage of participants were derived with a generalized linear mixed model repeated measures method with treatment, sex, verapamil use, baseline cluster headache attack category, month, and treatment by month as fixed effects.

APD: All randomized participants who received at least one dose of study drug and had PGI-I measurement at Week 4.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 4 | |

| | | | | |
|-----------------------------------|-----------------|---------------------|--|--|
| End point values | Placebo | Galcanezumab 300 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 88 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 19.4 | 21.5 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Patient Global Impression of Improvement (PGI-I) |
| Comparison groups | Placebo v Galcanezumab 300 mg |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.713 |
| Method | Mixed models analysis |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.141 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.563 |
| upper limit | 2.314 |

Secondary: Percentage of Participants Reporting a Score of 1 or 2 on the Patient Global Impression of Improvement (PGI-I)

| | |
|-----------------|--|
| End point title | Percentage of Participants Reporting a Score of 1 or 2 on the Patient Global Impression of Improvement (PGI-I) |
|-----------------|--|

End point description:

PGI-I requests participants to mark the box that best describes their cluster headache condition since they started taking the medicine. The options in the displayed boxes are represented on a 7-point scale, with 1 = very much better, 2 = much better, 3 = a little better, 4 = no change, 5 = a little worse, 6 = much worse, and 7 = very much worse. Percentage of participants were derived with a generalized linear mixed model repeated measures method with treatment, sex, verapamil use, baseline cluster headache attack category, month, and treatment by month as fixed effects.

APD: All randomized participants who received at least one dose of study drug and had PGI-I measurement at Week 8.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 8 | |

| | | | | |
|-----------------------------------|-----------------|---------------------|--|--|
| End point values | Placebo | Galcanezumab 300 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 97 | 86 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 32.0 | 32.1 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Patient Global Impression of Improvement (PGI-I) |
| Comparison groups | Placebo v Galcanezumab 300 mg |
| Number of subjects included in analysis | 183 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.979 |
| Method | Mixed models analysis |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.008 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.548 |
| upper limit | 1.856 |

Secondary: Percentage of Participants Reporting a Score of 1 or 2 on the Patient Global Impression of Improvement (PGI-I)

| | |
|-----------------|--|
| End point title | Percentage of Participants Reporting a Score of 1 or 2 on the Patient Global Impression of Improvement (PGI-I) |
|-----------------|--|

End point description:

PGI-I requests participants to mark the box that best describes their cluster headache condition since they started taking the medicine. The options in the displayed boxes are represented on a 7-point scale, with 1 = very much better, 2 = much better, 3 = a little better, 4 = no change, 5 = a little worse, 6 = much worse, and 7 = very much worse. Percentage of participants were derived with a generalized linear mixed model repeated measures method with treatment, sex, verapamil use, baseline cluster headache attack category, month, and treatment by month as fixed effects.

APD: All randomized participants who received at least one dose of study drug and had PGI-I measurement at week 12.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 12 | |

| | | | | |
|-----------------------------------|-----------------|---------------------|--|--|
| End point values | Placebo | Galcanezumab 300 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 95 | 95 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 35.6 | 30.4 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Patient Global Impression of Improvement (PGI-I) |
| Comparison groups | Placebo v Galcanezumab 300 mg |
| Number of subjects included in analysis | 190 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.437 |
| Method | Mixed models analysis |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.788 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.431 |
| upper limit | 1.44 |

Secondary: Percentage of Participants With Suicidal Ideation Assessed by Columbia - Suicide Severity Rating Scale (C-SSRS)

| | |
|-----------------|---|
| End point title | Percentage of Participants With Suicidal Ideation Assessed by Columbia - Suicide Severity Rating Scale (C-SSRS) |
|-----------------|---|

End point description:

C-SSRS captures the occurrence, severity, and frequency of suicide-related thoughts and behaviors during the assessment period. The scale includes suggested questions to solicit the type of information needed to determine if a suicide-related thought or behavior occurred. Some questions are binary responses (yes/no) and some are on a scale of 1 (low severity) to 5 (high severity). Suicidal ideation: a "yes" answer to any of 5 suicidal ideation questions: wish to be dead, non-specific active suicidal thoughts, active suicidal ideation with any methods without intent to act, active suicidal ideation with some intent to act without specific plan, active suicidal ideation with specific plan and intent.

APD: All randomized participants who received at least one dose of study drug and had at least one post baseline C-SSRS assessment.

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

End point timeframe:

Week 1 through Week 12

| | | | | |
|-----------------------------------|-----------------|---------------------|--|--|
| End point values | Placebo | Galcanezumab 300 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 116 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 5.04 | 4.31 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Suicidal Behaviors Assessed by Columbia - Suicide Severity Rating Scale (C-SSRS)

| | |
|-----------------|--|
| End point title | Percentage of Participants With Suicidal Behaviors Assessed by Columbia - Suicide Severity Rating Scale (C-SSRS) |
|-----------------|--|

End point description:

C-SSRS captures the occurrence, severity, and frequency of suicide-related thoughts and behaviors during the assessment period. The scale includes suggested questions to solicit the type of information needed to determine if a suicide-related thought or behavior occurred. Some questions are binary responses (yes/no) and some are on a scale of 1 (low severity) to 5 (high severity). Suicidal behavior: a "yes" answer to any of 5 suicidal behavior questions: preparatory acts or behavior, aborted attempt, interrupted attempt, actual attempt, and completed suicide.

APD: All randomized participants who received at least one dose of study drug and had at least one post baseline C-SSRS assessment.

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

End point timeframe:

Week 1 through Week 12

| End point values | Placebo | Galcanezumab 300 mg | | |
|-----------------------------------|-----------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 116 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Developing Anti-Drug Antibodies (ADA) to Galcanezumab (LY2951742)

| | |
|-----------------|--|
| End point title | Percentage of Participants Developing Anti-Drug Antibodies (ADA) to Galcanezumab (LY2951742) |
|-----------------|--|

End point description:

Treatment emergent (TE) ADA evaluable participant is considered to be TE ADA+ if the subject has at least one post-baseline titer that is a 4-fold or greater increase in titer from baseline measurement. If baseline result is ADA Not Present, then the participant is TE ADA+ if there is at least one post-baseline result of ADA present with titer $\geq 1:20$.

APD: All randomized participants who received at least one dose of study drug and had non-missing baseline ADA result, and at least one non-missing post baseline ADA result.

| | |
|----------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 1 through Week 12 | |

| End point values | Placebo | Galcanezumab 300 mg | | |
|-----------------------------------|-----------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 115 | 113 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 0 | 0.88 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Serum Concentration of Galcanezumab

| | |
|-----------------|--|
| End point title | Pharmacokinetics (PK): Serum Concentration of Galcanezumab |
|-----------------|--|

End point description:

Pharmacokinetics (PK): Serum Concentration of Galcanezumab

APD: All randomized participants who received at least 1 dose of study drug and had evaluable galcanezumab PK samples at Week 2.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 2 | |

| End point values | Galcanezumab 300 mg | | | |
|--------------------------------------|-------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 90 | | | |
| Units: nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | 30600 (\pm 10700) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Serum Concentration of Galcanezumab

| | |
|-----------------|--|
| End point title | Pharmacokinetics (PK): Serum Concentration of Galcanezumab |
|-----------------|--|

End point description:

Pharmacokinetics (PK): Serum Concentration of Galcanezumab

APD: All randomized participants who received at least 1 dose of study drug and had evaluable galcanezumab PK samples at Week 4.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 4 | |

| | | | | |
|--------------------------------------|------------------------|--|--|--|
| End point values | Galcanezumab 300 mg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 96 | | | |
| Units: nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | 20200 (\pm 6780) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Serum Concentration of Galcanezumab

| | |
|-----------------|--|
| End point title | Pharmacokinetics (PK): Serum Concentration of Galcanezumab |
|-----------------|--|

End point description:

Pharmacokinetics (PK): Serum Concentration of Galcanezumab

APD: All randomized participants who received at least 1 dose of study drug and had evaluable galcanezumab PK samples at Week 8.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 8 | |

| | | | | |
|--------------------------------------|-------------------------|--|--|--|
| End point values | Galcanezumab 300 mg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 94 | | | |
| Units: nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | 29700 (\pm 11500) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Serum Concentration of Galcanezumab

| | |
|-----------------|--|
| End point title | Pharmacokinetics (PK): Serum Concentration of Galcanezumab |
|-----------------|--|

End point description:

Pharmacokinetics (PK): Serum Concentration of Galcanezumab

APD: All randomized participants who received at least 1 dose of study drug and had evaluable galcanezumab PK samples at Week 12.

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

End point timeframe:

Week 12

| | | | | |
|--------------------------------------|------------------------|--|--|--|
| End point values | Galcanezumab 300 mg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 96 | | | |
| Units: nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | 31100 (± 11900) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 1 Year 7 Months

Adverse event reporting additional description:

All randomized participants who received at least 1 dose of study drug.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Placebo - Double-Blind Treatment Phase |
|-----------------------|--|

Reporting group description:

Participants received placebo once a month by subcutaneous (SC) injection for 3 months.

| | |
|-----------------------|---|
| Reporting group title | Galcanezumab 300mg - Double-Blind Treatment Phase |
|-----------------------|---|

Reporting group description:

Participants received galcanezumab 300 mg once a month by subcutaneous (SC) injection for 3 months.

| | |
|-----------------------|---|
| Reporting group title | Placebo/Galcanezumab 300mg - Open-Label Treatment Phase |
|-----------------------|---|

Reporting group description:

Participants from placebo group received galcanezumab (GMB) as three 100 mg subcutaneous injections every 30 days, for up to a total of 12 administrations.

| | |
|-----------------------|--|
| Reporting group title | Galcanezumab 300mg/Galcanezumab 300mg - Open-Label Treatment |
|-----------------------|--|

Reporting group description:

Participants from galcanezumab group received galcanezumab as three 100 mg subcutaneous injections every 30 days, for up to a total of 12 administrations.

| | |
|-----------------------|---------------------------|
| Reporting group title | Placebo - Follow-up Phase |
|-----------------------|---------------------------|

Reporting group description:

Participants from double blind treatment group entered this phase, they have not received any intervention during this post-treatment period.

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Galcanezumab 300mg - Follow-up Phase |
|-----------------------|--------------------------------------|

Reporting group description:

Participants from double blind treatment group entered this phase, they have not received any intervention during this post-treatment period.

| | |
|-----------------------|--|
| Reporting group title | Placebo/Galcanezumab 300mg - Follow-up Phase |
|-----------------------|--|

Reporting group description:

Participants from Open-Label Treatment Phase entered this phase, they have not received any intervention during this post-treatment period.

| | |
|-----------------------|---|
| Reporting group title | Galcanezumab 300mg/Galcanezumab 300mg - Follow-up Phase |
|-----------------------|---|

Reporting group description:

Participants from Open-Label Treatment Phase entered this phase, they have not received any intervention during this post-treatment period.

| Serious adverse events | Placebo - Double-Blind Treatment Phase | Galcanezumab 300mg - Double-Blind Treatment Phase | Placebo/Galcanezumab 300mg - Open-Label Treatment Phase |
|---|--|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 120 (2.50%) | 2 / 117 (1.71%) | 11 / 116 (9.48%) |

| | | | |
|---|-----------------|-----------------|-----------------|
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| breast cancer stage iii | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 1 / 116 (0.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| colon neoplasm | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 0 / 116 (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 |
| metastasis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 1 / 116 (0.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pituitary tumour | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 0 / 116 (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 |
| Surgical and medical procedures | | | |
| arthrodesis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 0 / 116 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| chest pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 1 / 116 (0.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| injection site urticaria alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 1 / 116 (0.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| non-cardiac chest pain alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | 0 / 117 (0.00%) | 0 / 116 (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 |
| Social circumstances pregnancy of partner alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 0 / 116 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders anxiety alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 1 / 116 (0.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| depression alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | 0 / 117 (0.00%) | 0 / 116 (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 |
| Injury, poisoning and procedural complications extradural haematoma alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 1 / 116 (0.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| kidney rupture | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 0 / 116 (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 |
| road traffic accident | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 1 / 116 (0.86%) |
| 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 | | | |
| atrial fibrillation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 1 / 117 (0.85%) | 0 / 116 (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 |
| palpitations | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 0 / 116 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| cerebral ischaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 1 / 116 (0.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cluster headache | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 1 / 116 (0.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| reversible cerebral vasoconstriction syndrome | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 0 / 116 (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 | | | |
| amaurosis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 0 / 116 (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 | | | |
| constipation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 1 / 117 (0.85%) | 0 / 116 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| melaena | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | 0 / 117 (0.00%) | 0 / 116 (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 |
| small intestinal obstruction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 0 / 116 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| ureterolithiasis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 0 / 116 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| rhabdomyolysis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 1 / 116 (0.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| appendicitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 0 / 116 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| diverticulitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 1 / 116 (0.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastroenteritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 0 / 116 (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 |
| helicobacter gastritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 1 / 116 (0.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| rectal abscess | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 0 / 116 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| urinary tract infection bacterial | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 0 / 116 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Galcanezumab 300mg/Galcanezumab 300mg - Open-Label Treatment | Placebo - Follow-up Phase | Galcanezumab 300mg - Follow-up Phase |
|---|--|---------------------------|--------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 10 / 113 (8.85%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| breast cancer stage iii | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (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 neoplasm | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 113 (0.88%) | 0 / 2 (0.00%) | 0 / 4 (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 |
| metastasis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (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 |
| pituitary tumour | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|--|-----------------|---------------|---------------|
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (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 |
| Surgical and medical procedures | | | |
| arthrodesis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 113 (0.88%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| chest pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (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 |
| injection site urticaria | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (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 |
| non-cardiac chest pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (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 |
| Social circumstances | | | |
| pregnancy of partner | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| anxiety | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|---------------|---------------|
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (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 |
| depression | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| extradural haematoma | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (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 |
| kidney rupture | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (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 |
| road traffic accident | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| atrial fibrillation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (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 |
| palpitations | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|---------------|---------------|
| subjects affected / exposed | 1 / 113 (0.88%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| cerebral ischaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (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 |
| cluster headache | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 113 (1.77%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| reversible cerebral vasoconstriction syndrome | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 113 (0.88%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| amaurosis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 113 (0.88%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| constipation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (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 |
| melaena | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|---------------|---------------|
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (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 |
| small intestinal obstruction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| ureterolithiasis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| rhabdomyolysis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (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 | | | |
| appendicitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 113 (0.88%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| diverticulitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastroenteritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|---------------|---------------|
| subjects affected / exposed | 1 / 113 (0.88%) | 0 / 2 (0.00%) | 0 / 4 (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 |
| helicobacter gastritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (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 |
| rectal abscess | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 113 (0.88%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| urinary tract infection bacterial | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 113 (0.88%) | 0 / 2 (0.00%) | 0 / 4 (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 |

| Serious adverse events | Placebo/Galcanezumab 300mg - Follow-up Phase | Galcanezumab 300mg/Galcanezumab 300mg - Follow-up Phase | |
|---|--|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 5 / 93 (5.38%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| breast cancer stage iii | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| colon neoplasm | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| metastasis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| pituitary tumour | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 93 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| arthrodesis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| chest pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| injection site urticaria | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| non-cardiac chest pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Social circumstances | | | |
| pregnancy of partner | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 93 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| anxiety | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| depression | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| extradural haematoma | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| kidney rupture | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 93 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| road traffic accident | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| atrial fibrillation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| palpitations | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| cerebral ischaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| cluster headache | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| reversible cerebral vasoconstriction syndrome | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| amaurosis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| constipation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| melaena | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| small intestinal obstruction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 93 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| ureterolithiasis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 93 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| rhabdomyolysis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| appendicitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| diverticulitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| gastroenteritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| helicobacter gastritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| rectal abscess | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| urinary tract infection bacterial | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 2 %

| Non-serious adverse events | Placebo - Double-Blind Treatment Phase | Galcanzumab 300mg - Double-Blind Treatment Phase | Placebo/Galcanzumab 300mg - Open-Label Treatment Phase |
|--|--|--|---|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 60 / 120 (50.00%) | 68 / 117 (58.12%) | 69 / 116 (59.48%) |
| Vascular disorders hypertension alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 3 / 120 (2.50%) 3 | 2 / 117 (1.71%) 2 | 2 / 116 (1.72%) 2 |
| General disorders and administration site conditions asthenia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) chest pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) fatigue alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) influenza like illness alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) injection site erythema alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) injection site pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) injection site pruritus | 1 / 120 (0.83%) 1 2 / 120 (1.67%) 2 7 / 120 (5.83%) 9 1 / 120 (0.83%) 1 1 / 120 (0.83%) 1 11 / 120 (9.17%) 15 | 1 / 117 (0.85%) 4 0 / 117 (0.00%) 0 5 / 117 (4.27%) 5 5 / 117 (4.27%) 8 8 / 117 (6.84%) 11 14 / 117 (11.97%) 32 | 2 / 116 (1.72%) 2 0 / 116 (0.00%) 0 6 / 116 (5.17%) 6 4 / 116 (3.45%) 4 5 / 116 (4.31%) 6 16 / 116 (13.79%) 32 |

| | | | |
|---|----------------------|-----------------------|-----------------------|
| alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 120 (0.83%) 1 | 7 / 117 (5.98%) 10 | 5 / 116 (4.31%) 7 |
| injection site reaction alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 120 (0.00%) 0 | 1 / 117 (0.85%) 2 | 8 / 116 (6.90%) 20 |
| injection site swelling alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 120 (0.83%) 1 | 1 / 117 (0.85%) 1 | 1 / 116 (0.86%) 1 |
| non-cardiac chest pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 120 (0.00%) 0 | 2 / 117 (1.71%) 7 | 1 / 116 (0.86%) 1 |
| pyrexia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 120 (0.83%) 1 | 3 / 117 (2.56%) 3 | 2 / 116 (1.72%) 2 |
| Immune system disorders seasonal allergy alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 120 (0.00%) 0 | 0 / 117 (0.00%) 0 | 1 / 116 (0.86%) 1 |
| Reproductive system and breast disorders dysmenorrhoea alternative dictionary used: MedDRA 22.0 subjects affected / exposed ^[1] occurrences (all) | 0 / 34 (0.00%) 0 | 1 / 31 (3.23%) 1 | 1 / 33 (3.03%) 1 |
| menstrual disorder alternative dictionary used: MedDRA 22.0 subjects affected / exposed ^[2] occurrences (all) | 0 / 34 (0.00%) 0 | 1 / 31 (3.23%) 1 | 0 / 33 (0.00%) 0 |
| ovarian cyst alternative dictionary used: | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| MedDRA 22.0 | | | |
| subjects affected / exposed ^[3] | 0 / 34 (0.00%) | 0 / 31 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| uterine haemorrhage | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed ^[4] | 0 / 34 (0.00%) | 0 / 31 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| anxiety | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | 0 / 117 (0.00%) | 1 / 116 (0.86%) |
| occurrences (all) | 1 | 0 | 1 |
| depression | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 117 (0.00%) | 5 / 116 (4.31%) |
| occurrences (all) | 0 | 0 | 6 |
| insomnia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 120 (3.33%) | 1 / 117 (0.85%) | 2 / 116 (1.72%) |
| occurrences (all) | 4 | 1 | 4 |
| Investigations | | | |
| weight increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | 1 / 117 (0.85%) | 3 / 116 (2.59%) |
| occurrences (all) | 1 | 1 | 3 |
| Injury, poisoning and procedural complications | | | |
| fall | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 120 (1.67%) | 0 / 117 (0.00%) | 0 / 116 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| ligament sprain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | 0 / 117 (0.00%) | 1 / 116 (0.86%) |
| occurrences (all) | 1 | 0 | 1 |
| Cardiac disorders | | | |

| | | | |
|--|--|--|--|
| palpitations alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 3 / 120 (2.50%) 3 | 0 / 117 (0.00%) 0 | 0 / 116 (0.00%) 0 |
| Nervous system disorders dizziness alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) headache alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 6 / 120 (5.00%) 7 4 / 120 (3.33%) 5 | 5 / 117 (4.27%) 5 2 / 117 (1.71%) 3 | 4 / 116 (3.45%) 5 2 / 116 (1.72%) 2 |
| Ear and labyrinth disorders tinnitus alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) vertigo alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 120 (0.83%) 1 3 / 120 (2.50%) 4 | 3 / 117 (2.56%) 3 1 / 117 (0.85%) 1 | 1 / 116 (0.86%) 1 0 / 116 (0.00%) 0 |
| Eye disorders visual impairment alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 120 (0.83%) 1 | 0 / 117 (0.00%) 0 | 3 / 116 (2.59%) 3 |
| Gastrointestinal disorders abdominal pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) constipation alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 3 / 120 (2.50%) 3 2 / 120 (1.67%) 2 | 2 / 117 (1.71%) 2 2 / 117 (1.71%) 2 | 2 / 116 (1.72%) 2 6 / 116 (5.17%) 8 |

| | | | |
|--|----------------------|----------------------|----------------------|
| diarrhoea alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 6 / 120 (5.00%) 6 | 1 / 117 (0.85%) 1 | 5 / 116 (4.31%) 6 |
| nausea alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 6 / 120 (5.00%) 8 | 6 / 117 (5.13%) 7 | 3 / 116 (2.59%) 3 |
| vomiting alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 3 / 120 (2.50%) 4 | 3 / 117 (2.56%) 3 | 2 / 116 (1.72%) 2 |
| Renal and urinary disorders haematuria alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 120 (0.00%) 0 | 0 / 117 (0.00%) 0 | 0 / 116 (0.00%) 0 |
| nephrolithiasis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 120 (0.83%) 1 | 0 / 117 (0.00%) 0 | 1 / 116 (0.86%) 1 |
| Endocrine disorders thyroid mass alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 120 (0.00%) 0 | 0 / 117 (0.00%) 0 | 0 / 116 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders arthralgia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 4 / 120 (3.33%) 4 | 0 / 117 (0.00%) 0 | 5 / 116 (4.31%) 6 |
| back pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 120 (0.83%) 1 | 5 / 117 (4.27%) 5 | 4 / 116 (3.45%) 4 |

| | | | |
|--|-------------------------|-------------------------|-------------------------|
| bursitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 120 (0.00%) 0 | 0 / 117 (0.00%) 0 | 0 / 116 (0.00%) 0 |
| myalgia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 3 / 120 (2.50%) 3 | 3 / 117 (2.56%) 3 | 4 / 116 (3.45%) 5 |
| neck pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 120 (0.83%) 1 | 0 / 117 (0.00%) 0 | 2 / 116 (1.72%) 2 |
| pain in extremity alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 120 (0.83%) 2 | 4 / 117 (3.42%) 4 | 3 / 116 (2.59%) 3 |
| Infections and infestations bronchitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 120 (0.83%) 1 | 2 / 117 (1.71%) 2 | 4 / 116 (3.45%) 5 |
| gastroenteritis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 120 (0.83%) 1 | 3 / 117 (2.56%) 3 | 3 / 116 (2.59%) 3 |
| influenza alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 3 / 120 (2.50%) 4 | 2 / 117 (1.71%) 2 | 8 / 116 (6.90%) 8 |
| nasopharyngitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 15 / 120 (12.50%) 16 | 12 / 117 (10.26%) 13 | 14 / 116 (12.07%) 19 |
| sinusitis alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 120 (1.67%) | 1 / 117 (0.85%) | 3 / 116 (2.59%) |
| occurrences (all) | 2 | 1 | 3 |
| tracheitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 1 / 117 (0.85%) | 3 / 116 (2.59%) |
| occurrences (all) | 0 | 1 | 4 |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 120 (1.67%) | 1 / 117 (0.85%) | 2 / 116 (1.72%) |
| occurrences (all) | 2 | 1 | 2 |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 2 / 117 (1.71%) | 1 / 116 (0.86%) |
| occurrences (all) | 0 | 2 | 1 |
| vulvovaginal mycotic infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed ^[5] | 0 / 34 (0.00%) | 0 / 31 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |

| Non-serious adverse events | Galcanezumab 300mg/Galcanezumab 300mg - Open- Label Treatment | Placebo - Follow-up Phase | Galcanezumab 300mg - Follow-up Phase |
|--|--|------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 72 / 113 (63.72%) | 1 / 2 (50.00%) | 2 / 4 (50.00%) |
| Vascular disorders | | | |
| hypertension | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 113 (3.54%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| General disorders and administration site conditions | | | |
| asthenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 113 (1.77%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| chest pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|---------------|---------------|
| subjects affected / exposed | 3 / 113 (2.65%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| fatigue | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 113 (2.65%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| influenza like illness | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 113 (3.54%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| injection site erythema | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 113 (1.77%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 7 | 0 | 0 |
| injection site pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 8 / 113 (7.08%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 14 | 0 | 0 |
| injection site pruritus | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 113 (1.77%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 10 | 0 | 0 |
| injection site reaction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 113 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| injection site swelling | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 113 (2.65%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| non-cardiac chest pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 113 (2.65%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |

| | | | |
|--|--|--|--|
| pyrexia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 3 / 113 (2.65%) 4 | 0 / 2 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Immune system disorders seasonal allergy alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 3 / 113 (2.65%) 4 | 0 / 2 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Reproductive system and breast disorders dysmenorrhoea alternative dictionary used: MedDRA 22.0 subjects affected / exposed ^[1] occurrences (all) menstrual disorder alternative dictionary used: MedDRA 22.0 subjects affected / exposed ^[2] occurrences (all) ovarian cyst alternative dictionary used: MedDRA 22.0 subjects affected / exposed ^[3] occurrences (all) uterine haemorrhage alternative dictionary used: MedDRA 22.0 subjects affected / exposed ^[4] occurrences (all) | 0 / 29 (0.00%) 0 0 / 29 (0.00%) 0 1 / 29 (3.45%) 1 0 / 29 (0.00%) 0 | 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 | 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 |
| Psychiatric disorders anxiety alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) depression alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 4 / 113 (3.54%) 4 2 / 113 (1.77%) 2 | 0 / 2 (0.00%) 0 1 / 2 (50.00%) 1 | 1 / 4 (25.00%) 1 0 / 4 (0.00%) 0 |

| | | | |
|---|--|--|--|
| insomnia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 6 / 113 (5.31%) 6 | 0 / 2 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Investigations weight increased alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 113 (0.88%) 1 | 0 / 2 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Injury, poisoning and procedural complications fall alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) ligament sprain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 3 / 113 (2.65%) 3 3 / 113 (2.65%) 3 | 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 | 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 |
| Cardiac disorders palpitations alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 2 / 113 (1.77%) 2 | 0 / 2 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Nervous system disorders dizziness alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) headache alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 3 / 113 (2.65%) 4 3 / 113 (2.65%) 6 | 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 | 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 |
| Ear and labyrinth disorders tinnitus alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) vertigo alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 113 (0.88%) 1 1 / 113 (0.88%) 1 | 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 | 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 |
| Eye disorders visual impairment alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 113 (0.88%) 1 | 0 / 2 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Gastrointestinal disorders abdominal pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) constipation alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) diarrhoea alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) nausea alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) vomiting alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 4 / 113 (3.54%) 4 4 / 113 (3.54%) 4 4 / 113 (3.54%) 4 2 / 113 (1.77%) 2 1 / 113 (0.88%) 1 | 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 | 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 |
| Renal and urinary disorders haematuria alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|--|------------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 113 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| nephrolithiasis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 113 (0.88%) 1 | 0 / 2 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| Endocrine disorders thyroid mass alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 113 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| Musculoskeletal and connective tissue disorders arthralgia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 6 / 113 (5.31%) 6 | 0 / 2 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| back pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 10 / 113 (8.85%) 12 | 0 / 2 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| bursitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 3 / 113 (2.65%) 3 | 0 / 2 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| myalgia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 113 (0.88%) 1 | 0 / 2 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| neck pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 2 / 113 (1.77%) 2 | 0 / 2 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| pain in extremity alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-------------------|---------------|---------------|
| subjects affected / exposed | 2 / 113 (1.77%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Infections and infestations | | | |
| bronchitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 113 (2.65%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| gastroenteritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 113 (0.88%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| influenza | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 5 / 113 (4.42%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| nasopharyngitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 17 / 113 (15.04%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 24 | 0 | 0 |
| sinusitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 6 / 113 (5.31%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| tracheitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 113 (0.88%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 5 / 113 (4.42%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|---------------|---------------|
| subjects affected / exposed | 3 / 113 (2.65%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| vulvovaginal mycotic infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed ^[5] | 0 / 29 (0.00%) | 0 / 1 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Placebo/Galcanezumab 300mg - Follow-up Phase | Galcanezumab 300mg/Galcanezumab 300mg - Follow-up Phase | |
|---|--|---|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 18 / 93 (19.35%) | 16 / 93 (17.20%) | |
| Vascular disorders | | | |
| hypertension | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 93 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |
| asthenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 93 (2.15%) | 1 / 93 (1.08%) | |
| occurrences (all) | 2 | 1 | |
| chest pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| fatigue | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| influenza like illness | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 93 (1.08%) | |
| occurrences (all) | 0 | 1 | |
| injection site erythema | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| injection site pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| injection site pruritus | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| injection site reaction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| injection site swelling | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| non-cardiac chest pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 93 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| pyrexia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Immune system disorders | | | |
| seasonal allergy | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Reproductive system and breast disorders | | | |
| dysmenorrhoea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|--|--|--|--|
| <p>subjects affected / exposed^[1]</p> <p>0 / 25 (0.00%)</p> <p>0 / 25 (0.00%)</p> <p>0</p> <p>0</p> <p>menstrual disorder</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed^[2]</p> <p>0 / 25 (0.00%)</p> <p>0 / 25 (0.00%)</p> <p>0</p> <p>0</p> <p>ovarian cyst</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed^[3]</p> <p>0 / 25 (0.00%)</p> <p>0 / 25 (0.00%)</p> <p>0</p> <p>0</p> <p>uterine haemorrhage</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed^[4]</p> <p>1 / 25 (4.00%)</p> <p>0 / 25 (0.00%)</p> <p>3</p> <p>0</p> | | | |
| <p>Psychiatric disorders</p> <p>anxiety</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>2 / 93 (2.15%)</p> <p>1 / 93 (1.08%)</p> <p>2</p> <p>1</p> <p>depression</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>2 / 93 (2.15%)</p> <p>0 / 93 (0.00%)</p> <p>2</p> <p>0</p> <p>insomnia</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>1 / 93 (1.08%)</p> <p>0 / 93 (0.00%)</p> <p>1</p> <p>0</p> | | | |
| <p>Investigations</p> <p>weight increased</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>2 / 93 (2.15%)</p> <p>0 / 93 (0.00%)</p> <p>2</p> <p>0</p> | | | |
| <p>Injury, poisoning and procedural complications</p> | | | |

| | | | |
|--|---------------------|---------------------|--|
| fall alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 93 (0.00%) 0 | 0 / 93 (0.00%) 0 | |
| ligament sprain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 93 (0.00%) 0 | 0 / 93 (0.00%) 0 | |
| Cardiac disorders palpitations alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 93 (1.08%) 1 | 0 / 93 (0.00%) 0 | |
| Nervous system disorders dizziness alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 93 (1.08%) 1 | 0 / 93 (0.00%) 0 | |
| headache alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 2 / 93 (2.15%) 2 | 0 / 93 (0.00%) 0 | |
| Ear and labyrinth disorders tinnitus alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 93 (0.00%) 0 | 0 / 93 (0.00%) 0 | |
| vertigo alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 93 (0.00%) 0 | 0 / 93 (0.00%) 0 | |
| Eye disorders visual impairment alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 93 (0.00%) 0 | 0 / 93 (0.00%) 0 | |

| | | | |
|--|---|--|--|
| Gastrointestinal disorders abdominal pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) constipation alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) diarrhoea alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) nausea alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) vomiting alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 93 (0.00%) 0 1 / 93 (1.08%) 1 0 / 93 (0.00%) 0 1 / 93 (1.08%) 4 0 / 93 (0.00%) 0 | 0 / 93 (0.00%) 0 2 / 93 (2.15%) 2 2 / 93 (2.15%) 2 0 / 93 (0.00%) 0 1 / 93 (1.08%) 0 1 / 93 (1.08%) 1 | |
| Renal and urinary disorders haematuria alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) nephrolithiasis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 93 (0.00%) 0 0 / 93 (0.00%) 0 | 0 / 93 (0.00%) 0 0 / 93 (0.00%) 0 | |
| Endocrine disorders thyroid mass alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 93 (0.00%) 0 | 0 / 93 (0.00%) 0 | |
| Musculoskeletal and connective tissue | | | |

| | | | |
|---|----------------|----------------|--|
| disorders | | | |
| arthralgia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 1 / 93 (1.08%) | |
| occurrences (all) | 1 | 1 | |
| back pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 2 / 93 (2.15%) | |
| occurrences (all) | 0 | 2 | |
| bursitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| myalgia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| neck pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 93 (2.15%) | 2 / 93 (2.15%) | |
| occurrences (all) | 2 | 2 | |
| pain in extremity | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 93 (1.08%) | |
| occurrences (all) | 0 | 1 | |
| Infections and infestations | | | |
| bronchitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 1 / 93 (1.08%) | |
| occurrences (all) | 1 | 1 | |
| gastroenteritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 93 (2.15%) | 1 / 93 (1.08%) | |
| occurrences (all) | 2 | 1 | |
| influenza | | | |

| | | | |
|---|----------------|----------------|--|
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 93 (4.30%) | 0 / 93 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| nasopharyngitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 2 / 93 (2.15%) | |
| occurrences (all) | 3 | 2 | |
| sinusitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| tracheitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 93 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| vulvovaginal mycotic infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed ^[5] | 0 / 25 (0.00%) | 0 / 25 (0.00%) | |
| occurrences (all) | 0 | 0 | |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events occurring only in male or female participants have had the number

of participants at risk adjusted accordingly.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 27 March 2015 | Protocol (a) 1) Updated planned duration of treatment. 2) Updated primary endpoint duration. 3) Updated Inclusion and Exclusion Criteria. |
| 22 December 2015 | Protocol (b) -Added rescreening details (Inclusion Criteria 3). |
| 10 February 2017 | Protocol (c) -Updated rescreening details (Inclusion Criterion 3b and Exclusion Criterion 24d). |
| 28 March 2018 | Protocol (d): 1) Duration of primary analysis was changed from Week 3/4 to 12-Week. 2) Updated blinding information. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported