



Clinical trial results:

A Randomized, Double-Blind, Placebo-Controlled Study of Galcanezumab in Adults with Treatment-Resistant Migraine - The CONQUER Study

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2018-000600-42 |
| Trial protocol | FR DE ES CZ BE NL HU DK GB |
| Global end of trial date | 19 September 2019 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 05 July 2020 |
| First version publication date | 05 July 2020 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | I5Q-MC-CGAW |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|---------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03559257 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Trial Number: 16670 |

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 | 19 September 2019 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 19 September 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to assess the safety and efficacy of galcanezumab in people with treatment-resistant episodic or chronic migraine.

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 | 31 July 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--|
| Country: Number of subjects enrolled | Spain: 56 |
| Country: Number of subjects enrolled | United Kingdom: 7 |
| Country: Number of subjects enrolled | United States: 90 |
| Country: Number of subjects enrolled | Belgium: 27 |
| Country: Number of subjects enrolled | Canada: 11 |
| Country: Number of subjects enrolled | Czech Republic: 109 |
| Country: Number of subjects enrolled | France: 30 |
| Country: Number of subjects enrolled | Germany: 26 |
| Country: Number of subjects enrolled | Hungary: 16 |
| Country: Number of subjects enrolled | Japan: 42 |
| Country: Number of subjects enrolled | Korea, Democratic People's Republic of: 28 |
| Country: Number of subjects enrolled | Netherlands: 20 |
| Worldwide total number of subjects | 462 |
| EEA total number of subjects | 291 |

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) | 433 |
| From 65 to 84 years | 29 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Total 463 participants were randomized and 462 participants received at least one dose of study drug. one participant was screen failure.

Pre-assignment

Screening details:

NA

Period 1

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

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

Participants received matching placebo every month for three months by subcutaneous (SC) injection.

| | |
|--|--|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received matching placebo every month for three months by SC injection.

| | |
|------------------|--------------------|
| Arm title | Galcanezumab 120mg |
|------------------|--------------------|

Arm description:

Participants received initial loading dose of 240 milligrams (mg) of galcanezumab followed by 120mg galcanezumab every month for two months by SC injection.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Galcanezumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received initial loading dose of 240 milligrams (mg) of Galcanezumab followed by 120mg Galcanezumab every month for two months by SC injection.

| Number of subjects in period 1 | Placebo | Galcanezumab 120mg |
|--------------------------------|---------|--------------------|
| Started | 230 | 232 |
| Completed | 226 | 225 |
| Not completed | 4 | 7 |
| Consent withdrawn by subject | 2 | 1 |
| Adverse event, non-fatal | - | 1 |
| Lack of efficacy | 1 | 1 |
| Protocol deviation | 1 | 4 |

Period 2

| | |
|------------------------------|-----------------------------|
| Period 2 title | Open-label Treatment Period |
| 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 | Galcanezumab 120mg |

Arm description:

Participants received initial loading dose of 240mg galcanezumab followed by 120mg every month for two months during open label treatment phase.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Galcanezumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received initial loading dose of 240mg Galcanezumab followed by 120mg every month for two months during open label treatment phase by subcutaneous injection.

| | |
|------------------|--------------------|
| Arm title | Galcanezumab 120mg |
|------------------|--------------------|

Arm description:

Participants received 120mg of galcanezumab every month for three months by subcutaneous injection.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Galcanezumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received 120mg of Galcanezumab every month for three months during open label treatment period by subcutaneous injection.

| Number of subjects in period 2^[1] | Galcanezumab 120mg | Galcanezumab 120mg |
|---|---------------------------|---------------------------|
| Started | 225 | 224 |
| Completed | 215 | 217 |
| Not completed | 10 | 7 |
| Consent withdrawn by subject | 3 | - |
| Physician decision | - | 1 |
| Adverse event, non-fatal | 1 | 4 |
| Lost to follow-up | 1 | - |
| Lack of efficacy | 3 | 2 |
| Protocol deviation | 2 | - |

Notes:

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

Justification: One participant in placebo group who completed double blind period has withdrawn from the study.

One participant in Galcanezumab group who completed double blind period had discontinued due to AE.

Baseline characteristics

Reporting groups

| | |
|--|--------------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received matching placebo every month for three months by subcutaneous (SC) injection. | |
| Reporting group title | Galcanezumab 120mg |
| Reporting group description: | |
| Participants received initial loading dose of 240 milligrams (mg) of galcanezumab followed by 120mg galcanezumab every month for two months by SC injection. | |

| Reporting group values | Placebo | Galcanezumab 120mg | Total |
|--|---------|--------------------|-------|
| Number of subjects | 230 | 232 | 462 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 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) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 45.67 | 45.87 | |
| standard deviation | ± 12.33 | ± 11.34 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 202 | 195 | 397 |
| Male | 28 | 37 | 65 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 16 | 15 | 31 |
| Not Hispanic or Latino | 174 | 172 | 346 |
| Unknown or Not Reported | 40 | 45 | 85 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 1 | 0 | 1 |
| Asian | 35 | 37 | 72 |
| Native Hawaiian or Other Pacific Islander | 0 | 1 | 1 |
| Black or African American | 2 | 3 | 5 |
| White | 182 | 183 | 365 |
| More than one race | 3 | 0 | 3 |
| Unknown or Not Reported | 7 | 8 | 15 |

| | | | |
|--------------------------------|--------|--------|---|
| Monthly Migraine Headache Days | | | |
| Units: Days | | | |
| arithmetic mean | 13.01 | 13.44 | |
| standard deviation | ± 5.73 | ± 6.08 | - |

End points

End points reporting groups

| | |
|--|--------------------|
| Reporting group title | Placebo |
| Reporting group description: Participants received matching placebo every month for three months by subcutaneous (SC) injection. | |
| Reporting group title | Galcanezumab 120mg |
| Reporting group description: Participants received initial loading dose of 240 milligrams (mg) of galcanezumab followed by 120mg galcanezumab every month for two months by SC injection. | |
| Reporting group title | Galcanezumab 120mg |
| Reporting group description: Participants received initial loading dose of 240mg galcanezumab followed by 120mg every month for two months during open label treatment phase. | |
| Reporting group title | Galcanezumab 120mg |
| Reporting group description: Participants received 120mg of galcanezumab every month for three months by subcutaneous injection. | |

Primary: Overall Mean Change from Baseline in the Number of Monthly Migraine Headache Days

| | |
|---|---|
| End point title | Overall Mean Change from Baseline in the Number of Monthly Migraine Headache Days |
| End point description: Migraine Headache Day (MHD): A calendar day on which a migraine headache or probable migraine headache occurred. Overall mean is derived from the average of months 1 to 3 from mixed model repeated measures (MMRM) model. Least square (LS) Mean was calculated using MMRM model with treatment, pooled country, month, treatment by month, baseline, and baseline by month as fixed effects. All randomized participants who received at least one dose of study drug and had baseline and at least one post baseline value. | |
| End point type | Primary |
| End point timeframe: Baseline, Month 1 through Month 3 | |

| End point values | Placebo | Galcanezumab 120mg | | |
|-------------------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 228 | 230 | | |
| Units: Days | | | | |
| least squares mean (standard error) | -1.02 (± 0.32) | -4.14 (± 0.32) | | |

Statistical analyses

| | |
|----------------------------|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Galcanezumab 120mg v Placebo |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 458 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -3.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.92 |
| upper limit | -2.32 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.41 |

Secondary: Overall Mean Change from Baseline in the Number of Monthly Migraine Headache Days in Participants with Episodic Migraine

| | |
|---|--|
| End point title | Overall Mean Change from Baseline in the Number of Monthly Migraine Headache Days in Participants with Episodic Migraine |
| End point description: | |
| <p>MHD: A calendar day on which a migraine headache or probable migraine headache occurred.</p> <p>Overall mean is derived from the average of months 1 to 3 from MMRM model. Least square (LS) Mean was calculated using MMRM model with treatment, pooled country, month, treatment by month, baseline, and baseline by month as fixed effects.</p> <p>APD: All randomized episodic migraine participants who received at least one dose of study drug and had baseline and at least one post baseline value.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Month 1 through Month 3 | |

| End point values | Placebo | Galcanezumab 120mg | | |
|-------------------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 132 | 137 | | |
| Units: Days | | | | |
| least squares mean (standard error) | -0.31 (± 0.34) | -2.88 (± 0.34) | | |

Statistical analyses

| | |
|----------------------------|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Galcanezumab 120mg |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 269 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -2.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.41 |
| upper limit | -1.72 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.43 |

Secondary: Percentage of Participants with $\geq 50\%$ Reduction from Baseline in Monthly Migraine Headache Days

| | |
|-----------------|---|
| End point title | Percentage of Participants with $\geq 50\%$ Reduction from Baseline in Monthly Migraine Headache Days |
|-----------------|---|

End point description:

MHD: A calendar day on which a migraine headache or probable migraine headache occurred.

Overall mean percentage across months 1 through 3 of patients with at least a 50% reduction in monthly MHDs from baseline using a categorical pseudo likelihood-based repeated measures model for binary responder indicator with fixed, categorical effects of treatment, month, treatment by month, and continuous, fixed covariate of baseline monthly MHD.

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

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

End point timeframe:

Baseline, Month 1 through Month 3

| End point values | Placebo | Galcanezumab 120mg | | |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 228 | 230 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 13.3 (10.2 to 17.3) | 37.7 (32.9 to 42.8) | | |

Statistical analyses

| | |
|----------------------------|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Galcanezumab 120mg |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 458 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Mixed models analysis |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.935 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.719 |
| upper limit | 5.693 |

Secondary: Percentage of Participants With Episodic Migraine With $\geq 50\%$ Reduction From Baseline in Monthly Migraine Headache Days

| | |
|-----------------|--|
| End point title | Percentage of Participants With Episodic Migraine With $\geq 50\%$ Reduction From Baseline in Monthly Migraine Headache Days |
|-----------------|--|

End point description:

MHD: A calendar day on which a migraine headache or probable migraine headache occurred.

Overall mean percentage across months 1 through 3 of patients with at least a 50% reduction in monthly MHDs from baseline using a categorical pseudo likelihood-based repeated measures model for binary responder indicator with fixed, categorical effects of treatment, month, treatment by month, and continuous, fixed covariate of baseline monthly MHD.

APD: All randomized episodic migraine participants who received at least one dose of study drug and had baseline and at least one post baseline value.

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

End point timeframe:

Baseline, Month 1 through Month 3

| End point values | Placebo | Galcanezumab 120mg | | |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 132 | 137 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 17.1 (12.7 to 22.7) | 41.8 (35.7 to 48.1) | | |

Statistical analyses

| | |
|----------------------------|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Galcanezumab 120mg |

| | |
|---|--|
| Number of subjects included in analysis | 269 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Pseudo likelihood-based repeated measure |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.481 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.252 |
| upper limit | 5.381 |

Secondary: Mean Change from Baseline in the Role Function-Restrictive Domain Score of the Migraine-Specific Quality of Life Questionnaire Version 2.1 (MSQ v2.1)

| | |
|-----------------|---|
| End point title | Mean Change from Baseline in the Role Function-Restrictive Domain Score of the Migraine-Specific Quality of Life Questionnaire Version 2.1 (MSQ v2.1) |
|-----------------|---|

End point description:

MSQ v2.1 is a health status instrument, with a 4-week recall period, developed to address physical and emotional limitations of specific concern to individuals with migraine. Addressing the impact of migraine on work or daily activities, relationships with family & friends, leisure time, productivity, concentration, energy, tiredness & feelings. It consists of 14 items that address 3 domains: (1) Role Function-Restrictive (items 1-7); (2) Role Function- Preventive (items 8-11); & (3) Emotional Function (items 12-14). Response options range from "none of the time" (value 1) to "all of the time" (value 6), & are reverse-recoded (value 6 to 1) before the domain scores are calculated. Total raw scores for each domain is the sum of the final item value for all of the items in that domain. After the total raw score is computed for each domain, they are transformed to a 0-100 scale with higher scores indicating a better health status & a positive change in scores reflecting functional improvement.

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

End point timeframe:

Baseline, Month 3

APD: All randomized participants who received at least one dose of study drug and had a post baseline value at Month 3.

| End point values | Placebo | Galcanezumab 120mg | | |
|-------------------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 222 | 223 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | 10.86 (± 1.34) | 23.21 (± 1.35) | | |

Statistical analyses

| | |
|----------------------------|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Galcanezumab 120mg |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 445 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 ^[1] |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 12.53 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 9.19 |
| upper limit | 15.87 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.7 |

Notes:

[1] - LS Mean was calculated using MMRM model with treatment, pooled country, month, treatment by month, baseline, and baseline by month as fixed effects.

Secondary: Mean Change from Baseline in the Role Function-Restrictive Domain Score of the Migraine-Specific Quality of Life Questionnaire Version 2.1 (MSQ v2.1) in Participants with Episodic Migraine

| | |
|-----------------|--|
| End point title | Mean Change from Baseline in the Role Function-Restrictive Domain Score of the Migraine-Specific Quality of Life Questionnaire Version 2.1 (MSQ v2.1) in Participants with Episodic Migraine |
|-----------------|--|

End point description:

MSQ v2.1 is a health status instrument, with a 4-week recall period, developed to address physical and emotional limitations of specific concern to individuals with migraine. Addressing the impact of migraine on work or daily activities, relationships with family & friends, leisure time, productivity, concentration, energy, tiredness & feelings. It consists of 14 items that address 3 domains: (1) Role Function-Restrictive (items 1-7); (2) Role Function- Preventive (items 8-11); & (3) Emotional Function (items 12-14). Response options range from "none of the time" (value 1) to "all of the time" (value 6), & are reverse-recoded (value 6 to 1) before the domain scores are calculated. Total raw scores for each domain is the sum of the final item value for all of the items in that domain. After the total raw score is computed for each domain, they are transformed to a 0-100 scale with higher scores indicating a better health status & a positive change in scores reflecting functional improvement.

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

End point timeframe:

Baseline, Month 3

APD: All randomized episodic migraine participants who received at least one dose of study drug and had a post baseline value at Month 3.

| End point values | Placebo | Galcanezumab 120mg | | |
|-------------------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 127 | 135 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | 11.88 (± 1.80) | 23.39 (± 1.79) | | |

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Galcanezumab 120mg |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 ^[2] |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 11.51 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 7.14 |
| upper limit | 15.89 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.22 |

Notes:

[2] - LS Mean was calculated using MMRM model with treatment, pooled country, month, treatment by month, baseline, and baseline by month as fixed effects.

Secondary: Percentage of Participants With Episodic Migraine with $\geq 75\%$ Reduction from Baseline in Monthly Migraine Headache Days

| | |
|-----------------|--|
| End point title | Percentage of Participants With Episodic Migraine with $\geq 75\%$ Reduction from Baseline in Monthly Migraine Headache Days |
|-----------------|--|

End point description:

MHD: A calendar day on which a migraine headache or probable migraine headache occurred.

Overall mean percentage across months 1 through 3 of patients with at least a 75% reduction in monthly MHDs from baseline using a categorical pseudo likelihood-based repeated measures model for binary responder indicator with fixed, categorical effects of treatment, month, treatment by month, and continuous, fixed covariate of baseline monthly MHD.

APD: All randomized episodic migraine participants who received at least one dose of study drug and had baseline and at least one post baseline value.

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

End point timeframe:

Baseline, Month 1 through Month 3

| End point values | Placebo | Galcanezumab 120mg | | |
|-----------------------------------|------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 132 | 137 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 3.7 (1.6 to 8.2) | 18.4 (13.9 to 23.9) | | |

Statistical analyses

| | |
|-----------------------------------|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Galcanezumab 120mg |

| | |
|---|--|
| Number of subjects included in analysis | 269 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0001 |
| Method | Pseudo likelihood-based repeated measure |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 5.878 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.374 |
| upper limit | 14.554 |

Secondary: Percentage of Participants With Episodic Migraine With 100% Reduction From Baseline in Monthly Migraine Headache Days

| | |
|-----------------|---|
| End point title | Percentage of Participants With Episodic Migraine With 100% Reduction From Baseline in Monthly Migraine Headache Days |
|-----------------|---|

End point description:

MHD: A calendar day on which a migraine headache or probable migraine headache occurred.

Overall mean percentage across months 1 through 3 of patients with 100% reduction in monthly MHDs from baseline using a categorical pseudo likelihood-based repeated measures model for binary responder indicator with fixed, categorical effects of treatment, month, treatment by month, and continuous, fixed covariate of baseline monthly MHD.

APD: All randomized episodic migraine participants who received at least one dose of study drug and had baseline and at least one post baseline value.

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

End point timeframe:

Baseline, Month 1 through Month 3

| End point values | Placebo | Galcanezumab 120mg | | |
|-----------------------------------|---------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 132 | 137 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 0.00 (0.00 to 0.00) | 7.7 (4.7 to 12.3) | | |

Statistical analyses

| | |
|----------------------------|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Galcanezumab 120mg |

| | |
|---|--|
| Number of subjects included in analysis | 269 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 ^[3] |
| Method | Pseudo likelihood-based repeated measure |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 999.999 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 548.706 |
| upper limit | 999.999 |

Notes:

[3] - Estimated value and upper bound are >999.999

Secondary: Percentage of Participants with ≥75% Reduction from Baseline in Monthly Migraine Headache Days

| | |
|-----------------|--|
| End point title | Percentage of Participants with ≥75% Reduction from Baseline in Monthly Migraine Headache Days |
|-----------------|--|

End point description:

MHD: A calendar day on which a migraine headache or probable migraine headache occurred.

Overall mean percentage across months 1 through 3 of patients with at least a 75% reduction in monthly MHDs from baseline using a categorical pseudo likelihood-based repeated measures model for binary responder indicator with fixed, categorical effects of treatment, month, treatment by month, and continuous, fixed covariate of baseline monthly MHD.

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

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

End point timeframe:

Baseline, Month 1 through Month 3

| End point values | Placebo | Galcanezumab 120mg | | |
|-----------------------------------|------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 228 | 230 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 3.3 (1.7 to 6.3) | 14.5 (10.9 to 19.0) | | |

Statistical analyses

| | |
|----------------------------|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Galcanezumab 120mg |

| | |
|---|--|
| Number of subjects included in analysis | 458 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | pseudo likelihood-based repeated measure |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 5.012 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.352 |
| upper limit | 10.679 |

Secondary: Percentage of Participants with 100% Reduction from Baseline in Monthly Migraine Headache Days

| | |
|-----------------|--|
| End point title | Percentage of Participants with 100% Reduction from Baseline in Monthly Migraine Headache Days |
|-----------------|--|

End point description:

MHD: A calendar day on which a migraine headache or probable migraine headache occurred.

Overall mean percentage across months 1 through 3 of patients with 100% reduction in monthly MHDs from baseline using a categorical pseudo likelihood-based repeated measures model for binary responder indicator with fixed, categorical effects of treatment, month, treatment by month, and continuous, fixed covariate of baseline monthly MHD

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

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

End point timeframe:

Baseline, Month 1 through Month 3

| End point values | Placebo | Galcanezumab 120mg | | |
|-----------------------------------|------------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 228 | 230 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 0.000 (0.000 to 0.000) | 4.9 (2.8 to 8.6) | | |

Statistical analyses

| | |
|----------------------------|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Galcanezumab 120mg |

| | |
|---|--|
| Number of subjects included in analysis | 458 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [4] |
| Method | Pseudo likelihood-based repeated measure |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 999.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 999.99 |
| upper limit | 999.99 |

Notes:

[4] - Point estimate, upper limit and lower limit are >999.99

Secondary: Overall Mean Change from Baseline in the Number of Monthly Days with Acute Headache Medication Use

| | |
|-----------------|--|
| End point title | Overall Mean Change from Baseline in the Number of Monthly Days with Acute Headache Medication Use |
|-----------------|--|

End point description:

Overall mean is derived from the average of months 1 to 3 from Mixed model repeated measures (MMRM) model. Least square (LS) Mean was calculated using MMRM model with treatment, pooled country, month, treatment by month, baseline, and baseline by month as fixed effects.

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

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

End point timeframe:

Baseline, Month 1 through Month 3

| End point values | Placebo | Galcanezumab 120mg | | |
|-------------------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 228 | 230 | | |
| Units: Days | | | | |
| least squares mean (standard error) | -0.80 (± 0.31) | -4.19 (± 0.32) | | |

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Galcanezumab 120mg |
| Number of subjects included in analysis | 458 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -3.4 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.14 |
| upper limit | -2.65 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.38 |

Secondary: Overall Mean Change from Baseline in the Number of Monthly Headache Days

| | |
|-----------------|--|
| End point title | Overall Mean Change from Baseline in the Number of Monthly Headache Days |
|-----------------|--|

End point description:

Headache Day: A calendar day on which any type of headache occurred (including migraine, probable migraine, and non-migraine headache).

Overall mean is derived from the average of months 1 to 3 from MMRM model. Least square (LS) Mean was calculated using MMRM model with treatment, pooled country, month, treatment by month, baseline, and baseline by month as fixed effects.

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

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

End point timeframe:

Baseline, Month 1 through Month 3

| End point values | Placebo | Galcanezumab 120mg | | |
|-------------------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 228 | 230 | | |
| Units: Days | | | | |
| least squares mean (standard error) | -1.05 (± 0.36) | -4.18 (± 0.35) | | |

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Galcanezumab 120mg |
| Number of subjects included in analysis | 458 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -3.13 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.96 |
| upper limit | -2.29 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.42 |

Secondary: Mean Change from Baseline in the Migraine Disability Assessment Test (MIDAS) Total Score

| | |
|-----------------|--|
| End point title | Mean Change from Baseline in the Migraine Disability Assessment Test (MIDAS) Total Score |
|-----------------|--|

End point description:

The MIDAS is a participant-rated scale which was designed to quantify headache-related disability over a 3-month period. This instrument consists of five items that reflect the number of days reported as missed or with reduced productivity at work or home, and the number of days of missed social events. Each item has a numeric response range from 0 to 90 days, if days are missed from work or home they are not counted as days with reduced productivity at work or home. The numeric responses are summed to produce a total score ranging from 0 to 270, in which a higher value is indicative of more disability. LS mean was calculated using analysis of covariance (ANCOVA) with last observation carried forward (LOCF), with baseline, pooled country, baseline migraine frequency category, and treatment as fixed effects.

APD: All randomized participants who received at least one dose of study drug and had a post baseline value at Month 3.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Month 3 | |

| End point values | Placebo | Galcanezumab 120mg | | |
|-------------------------------------|------------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 225 | 228 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -3.295 (\pm 3.2834) | -21.097 (\pm 3.3164) | | |

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Galcanezumab 120mg |
| Number of subjects included in analysis | 453 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |

Secondary: Mean Change from Baseline in the 4-item Migraine Interictal Burden Scale (MIBS-4)

| | |
|-----------------|---|
| End point title | Mean Change from Baseline in the 4-item Migraine Interictal Burden Scale (MIBS-4) |
|-----------------|---|

End point description:

MIBS-4 is a self-administered scale that measures the burden related to headache in the time between attacks. The instrument consists of 4 items that address disruption at work and school, diminished family and social life, difficulty planning, and emotional difficulty. The questionnaire specifically asks about the effect of the disease over the past 4 weeks on days without a headache attack. Response options include: don't know/not applicable (0), never (0), rarely (1), some of the time (2), much of the time (3), or most or all of the time (3). Each responses associated numerical score are summed across all 4 items resulting in a total score ranging from 0 to 12, and the level of interictal burden being categorized into the following: 0 for none, 1-2 mild, 3-4 moderate, and >5 severe. LS mean was calculated using MMRM model with fixed effects of treatment, pooled country, baseline migraine frequency category, month, treatment by month as fixed effects.

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

End point timeframe:

Baseline, Month 3

APD: All randomized participants who received at least one dose of study drug and had a post baseline value at Month 3.

| End point values | Placebo | Galcanezumab 120mg | | |
|-------------------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 222 | 223 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -0.78 (± 0.21) | -1.83 (± 0.21) | | |

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Galcanezumab 120mg |
| Number of subjects included in analysis | 445 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -1.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.58 |
| upper limit | -0.54 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.27 |

Secondary: Mean Change from Baseline in the Work Productivity and Activity Impairment Questionnaire (WPAI)

| | |
|-----------------|---|
| End point title | Mean Change from Baseline in the Work Productivity and Activity Impairment Questionnaire (WPAI) |
|-----------------|---|

End point description:

The WPAI Questionnaire is a patient-reported instrument developed to measure the impact on work productivity and regular activities attributable to a specific health problem (migraine). Recall period is the past 7 days. It contains 6 items that measure: 1) employment status, 2) hours missed from work due to the specific health problem, 3) hours missed from work for other reasons, 4) hours actually worked, 5) degree health affected productivity while working, and 6) degree health affected productivity in regular unpaid activities. Four scores are calculated from the responses to these 6 items: absenteeism, presenteeism, work productivity loss, and activity impairment. Scores are calculated as impairment percentages (0-100%), with higher numbers indicating greater impairment and less productivity, i.e, worse outcomes. LS mean was calculated using ANCOVA with LOCF with baseline, pooled country, baseline migraine frequency category, and treatment as fixed effects.

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

End point timeframe:

Baseline, Month 3

APD: All randomized participants who received at least one dose of study drug and had a post baseline value at Month 3.

| End point values | Placebo | Galcanezumab 120mg | | |
|-------------------------------------|-------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 225 | 227 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Activity Impairment (n = 225,227) | -8.644 (± 1.9195) | -20.713 (± 1.9537) | | |
| Absenteeism (n = 145, 148) | -2.900 (± 1.2436) | -4.224 (± 1.2929) | | |
| Presenteeism (n = 141, 147) | -2.564 (± 2.3222) | -12.504 (± 2.3705) | | |
| Work Impairment (n = 145, 148) | -3.457 (± 2.4098) | -14.307 (± 2.5148) | | |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Activity Impairment.

| | |
|-------------------|------------------------------|
| Comparison groups | Placebo v Galcanezumab 120mg |
|-------------------|------------------------------|

| | |
|---|----------------------------|
| Number of subjects included in analysis | 452 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[5] |
| P-value | < 0.0001 |
| Method | ANCOVA |

Notes:

[5] - Activity Impairment.

| | |
|---|------------------------------|
| Statistical analysis title | Statistical Analysis 2 |
| Statistical analysis description: Absenteeism. | |
| Comparison groups | Placebo v Galcanezumab 120mg |
| Number of subjects included in analysis | 452 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[6] |
| P-value | = 0.388 |
| Method | ANCOVA |

Notes:

[6] - Absenteeism.

| | |
|--|------------------------------|
| Statistical analysis title | Statistical Analysis 3 |
| Statistical analysis description: Presenteeism. | |
| Comparison groups | Placebo v Galcanezumab 120mg |
| Number of subjects included in analysis | 452 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[7] |
| P-value | = 0.0004 |
| Method | ANCOVA |

Notes:

[7] - Presenteeism.

| | |
|---|------------------------------|
| Statistical analysis title | Statistical Analysis 4 |
| Statistical analysis description: Work Impairment. | |
| Comparison groups | Placebo v Galcanezumab 120mg |
| Number of subjects included in analysis | 452 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[8] |
| P-value | = 0.0003 |
| Method | ANCOVA |

Notes:

[8] - Work Impairment.

Secondary: Mean Change from Baseline in the Patient Global Impression of Severity (PGI-S)

| | |
|-----------------|--|
| End point title | Mean Change from Baseline in the Patient Global Impression of Severity (PGI-S) |
|-----------------|--|

End point description:

The PGI-S is a patient-rated instrument that measures illness severity. For this study, the patient was instructed as follows: "Considering migraine as a chronic condition, how would you rate your level of illness?" The PGI-S includes a range of possible responses, from 1 ("normal, not at all ill") to 7 ("extremely ill"). LS mean was calculated using ANCOVA with LOCF with baseline, pooled country, baseline migraine frequency category, and treatment as fixed effects.

APD: All randomized participants who received at least one dose of study drug and had a post baseline value at Month 3.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Month 3 | |

| End point values | Placebo | Galcanezumab 120mg | | |
|-------------------------------------|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 225 | 228 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -0.283 (\pm 0.0863) | -0.664 (\pm 0.0873) | | |

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Galcanezumab 120mg |
| Number of subjects included in analysis | 453 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0003 |
| Method | ANCOVA |

Secondary: Mean Change from Baseline in the European Quality of Life Questionnaire 5 Dimensions 5 Levels (EQ-5D-5L) - Health State Index (US)

| | |
|-----------------|--|
| End point title | Mean Change from Baseline in the European Quality of Life Questionnaire 5 Dimensions 5 Levels (EQ-5D-5L) - Health State Index (US) |
|-----------------|--|

End point description:

EQ-5D-5L is a 2-part questionnaire that assesses general health status for 'today'. The first part is comprised of the following 5 participant-reported dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. The responses are used to derive the health state index scores using country-specific algorithms, with scores ranging from less than 0 (where zero is a health state equivalent to death; negative values are valued as worse than dead) to 1 (perfect health). Index values were calculated using the US algorithm (-0.109 to 1). A higher score indicates better health state. LS mean was calculated using ANCOVA with LOCF with baseline, pooled country, baseline migraine frequency category, and treatment as fixed effects.

APD: All randomized participants who received at least one dose of study drug and had a post baseline value at Month 3.

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

End point timeframe:

Baseline, Month 3

| End point values | Placebo | Galcanezumab 120mg | | |
|-------------------------------------|------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 225 | 227 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -0.002 (\pm 0.0079) | 0.013 (\pm 0.0080) | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|------------------------------|
| Comparison groups | Placebo v Galcanezumab 120mg |
| Number of subjects included in analysis | 452 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1267 |
| Method | ANCOVA |

Secondary: Mean Change from Baseline in the European Quality of Life Questionnaire 5 Dimensions 5 Levels (EQ-5D-5L) - Health State Index (UK)

| | |
|-----------------|--|
| End point title | Mean Change from Baseline in the European Quality of Life Questionnaire 5 Dimensions 5 Levels (EQ-5D-5L) - Health State Index (UK) |
|-----------------|--|

End point description:

EQ-5D-5L is a 2-part questionnaire that assesses general health status for 'today'. The first part is comprised of the following 5 participant-reported dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. The responses are used to derive the health state index scores using country-specific algorithms, with scores ranging from less than 0 (where zero is a health state equivalent to death; negative values are valued as worse than dead) to 1 (perfect health). Index values were calculated using the UK algorithm (-0.594 to 1). LS mean was calculated using ANCOVA with LOCF with baseline, pooled country, baseline migraine frequency category, and treatment as fixed effects.

APD: All randomized participants who received at least one dose of study drug and had a post baseline value at Month 3.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Month 3 | |

| End point values | Placebo | Galcanezumab 120mg | | |
|-------------------------------------|------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 225 | 227 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -0.001 (\pm 0.0109) | 0.017 (\pm 0.0110) | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|------------------------------|
| Comparison groups | Placebo v Galcanezumab 120mg |
| Number of subjects included in analysis | 452 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.163 |
| Method | ANCOVA |

Secondary: Mean Change from Baseline in the European Quality of Life Questionnaire 5 Dimensions 5 Levels (EQ-5D-5L) - VAS Score

| | |
|-----------------|--|
| End point title | Mean Change from Baseline in the European Quality of Life Questionnaire 5 Dimensions 5 Levels (EQ-5D-5L) - VAS Score |
|-----------------|--|

End point description:

EQ-5D-5L is a 2-part questionnaire that assesses general health status 'today'. . The second part is assessed using a visual analog scale (VAS) on which the patient rates their perceived health state, ranging from 0 (the worst health you can imagine) to 100 (the best health you can imagine). LS mean was calculated using ANCOVA with LOCF with baseline, pooled country, baseline migraine frequency category, and treatment as fixed effects.

APD: All randomized participants who received at least one dose of study drug and had a post baseline value at Month 3.

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

End point timeframe:

Baseline, Month 3

| End point values | Placebo | Galcanezumab 120mg | | |
|-------------------------------------|------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 225 | 227 | | |
| Units: mm | | | | |
| least squares mean (standard error) | -0.086 (\pm 1.2916) | 3.376 (\pm 1.3080) | | |

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Galcanezumab 120mg |
| Number of subjects included in analysis | 452 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0277 |
| Method | ANCOVA |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

I5Q-MC-CGAW

| | |
|-----------------|------------|
| 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: -

| | |
|-----------------------|---|
| Reporting group title | Galcanezumab 120mg - Double-Blind Treatment Phase |
|-----------------------|---|

Reporting group description: -

| | |
|-----------------------|---|
| Reporting group title | Placebo/Galcanezumab 120mg - Open-Label Treatment Phase |
|-----------------------|---|

Reporting group description: -

| | |
|-----------------------|--|
| Reporting group title | Galcanezumab 120mg/Galcanezumab 120mg - Open-Label Treatment |
|-----------------------|--|

Reporting group description: -

| Serious adverse events | Placebo - Double-Blind Treatment Phase | Galcanezumab 120mg - Double-Blind Treatment Phase | Placebo/Galcanezumab 120mg - Open-Label Treatment Phase |
|---|--|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 230 (0.87%) | 2 / 232 (0.86%) | 6 / 225 (2.67%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| arthropod bite | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 230 (0.00%) | 0 / 232 (0.00%) | 1 / 225 (0.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| injury | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 230 (0.00%) | 0 / 232 (0.00%) | 1 / 225 (0.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-----------------------------------|-----------------------------------|-----------------------------------|
| lower limb fracture alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 230 (0.43%) 0 / 1 0 / 0 | 0 / 232 (0.00%) 0 / 0 0 / 0 | 0 / 225 (0.00%) 0 / 0 0 / 0 |
| Vascular disorders behcet's syndrome alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 230 (0.43%) 0 / 1 0 / 0 | 0 / 232 (0.00%) 0 / 0 0 / 0 | 0 / 225 (0.00%) 0 / 0 0 / 0 |
| Nervous system disorders hemiplegia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 230 (0.00%) 0 / 0 0 / 0 | 0 / 232 (0.00%) 0 / 0 0 / 0 | 1 / 225 (0.44%) 0 / 1 0 / 0 |
| General disorders and administration site conditions asthenia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 230 (0.00%) 0 / 0 0 / 0 | 0 / 232 (0.00%) 0 / 0 0 / 0 | 0 / 225 (0.00%) 0 / 0 0 / 0 |
| pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 230 (0.00%) 0 / 0 0 / 0 | 0 / 232 (0.00%) 0 / 0 0 / 0 | 1 / 225 (0.44%) 0 / 1 0 / 0 |
| Gastrointestinal disorders haemorrhoids alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 230 (0.00%) 0 / 0 0 / 0 | 1 / 232 (0.43%) 0 / 1 0 / 0 | 0 / 225 (0.00%) 0 / 0 0 / 0 |

| | | | |
|--|---|-----------------------------------|-----------------------------------|
| inguinal hernia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 230 (0.00%) 0 / 0 0 / 0 | 0 / 232 (0.00%) 0 / 0 0 / 0 | 1 / 225 (0.44%) 0 / 1 0 / 0 |
| Reproductive system and breast disorders ovarian cyst ruptured alternative dictionary used: MedDRA 22.0 subjects affected / exposed ^[1] occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 202 (0.00%) 0 / 0 0 / 0 | 0 / 195 (0.00%) 0 / 0 0 / 0 | 0 / 197 (0.00%) 0 / 0 0 / 0 |
| Respiratory, thoracic and mediastinal disorders pulmonary embolism alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 230 (0.00%) 0 / 0 0 / 0 | 0 / 232 (0.00%) 0 / 0 0 / 0 | 1 / 225 (0.44%) 0 / 1 0 / 0 |
| Infections and infestations pneumonia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 230 (0.00%) 0 / 0 0 / 0 | 0 / 232 (0.00%) 0 / 0 0 / 0 | 0 / 225 (0.00%) 0 / 0 0 / 0 |
| tonsillitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 230 (0.00%) 0 / 0 0 / 0 | 1 / 232 (0.43%) 0 / 1 0 / 0 | 0 / 225 (0.00%) 0 / 0 0 / 0 |
| Serious adverse events | Galcanezumab 120mg/Galcanezumab 120mg - Open- Label Treatment | | |
| Total subjects affected by serious adverse events subjects affected / exposed number of deaths (all causes) | 3 / 224 (1.34%) 0 | | |

| | | | |
|--|-----------------|--|--|
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| arthropod bite | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 224 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| injury | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 224 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| lower limb fracture | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 224 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| behcet's syndrome | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 224 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| hemiplegia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 224 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| asthenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 224 (0.45%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 224 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| haemorrhoids | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 224 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| inguinal hernia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 224 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| ovarian cyst ruptured | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed ^[1] | 1 / 187 (0.53%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| pulmonary embolism | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 224 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| pneumonia | | | |

| | | | |
|--|-----------------|--|--|
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 224 (0.45%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| tonsillitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 224 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Notes:

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

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

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

| Non-serious adverse events | Placebo - Double- Blind Treatment Phase | Galcanezumab 120mg - Double- Blind Treatment Phase | Placebo/Galcanezumab 120mg - Open- Label Treatment Phase |
|--|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 31 / 230 (13.48%) | 21 / 232 (9.05%) | 19 / 225 (8.44%) |
| General disorders and administration site conditions | | | |
| injection site pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 13 / 230 (5.65%) | 5 / 232 (2.16%) | 11 / 225 (4.89%) |
| occurrences (all) | 30 | 7 | 19 |
| Infections and infestations | | | |
| nasopharyngitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 21 / 230 (9.13%) | 16 / 232 (6.90%) | 11 / 225 (4.89%) |
| occurrences (all) | 24 | 17 | 11 |

| Non-serious adverse events | Galcanezumab 120mg/Galcanezumab 120mg - Open- Label Treatment | | |
|--|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 13 / 224 (5.80%) | | |
| General disorders and administration site conditions | | | |

| | | | |
|---|----------------------|--|--|
| injection site pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 5 / 224 (2.23%) 7 | | |
| Infections and infestations nasopharyngitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 8 / 224 (3.57%) 9 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported