



Clinical trial results:

Interventional, randomized, double-blind, parallel-group, placebo-controlled delayed-start study to evaluate the efficacy and safety of eptinezumab in patients with episodic Cluster Headache

Summary

| | |
|--------------------------|-------------------------------------|
| EudraCT number | 2020-001969-37 |
| Trial protocol | NO DK DE SE CZ PT FR BE NL FI GR IT |
| Global end of trial date | 05 October 2023 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v1 (current) |
| This version publication date | 29 September 2024 |
| First version publication date | 29 September 2024 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 19386A |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04688775 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | H. Lundbeck A/S |
| Sponsor organisation address | Ottiliavej 9, Valby, Denmark, 2500 |
| Public contact | Email contact via H. Lundbeck A/S, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@Lundbeck.com |
| Scientific contact | Email contact via H. Lundbeck A/S, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@Lundbeck.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 05 October 2023 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 05 October 2023 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the efficacy of eptinezumab in participants with episodic Cluster Headache (eCH).

Protection of trial subjects:

This trial was conducted in compliance with Good Clinical Practice and in accordance with the ethical principles described in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 23 December 2020 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Belgium: 4 |
| Country: Number of subjects enrolled | Czechia: 29 |
| Country: Number of subjects enrolled | Germany: 6 |
| Country: Number of subjects enrolled | Denmark: 18 |
| Country: Number of subjects enrolled | Spain: 19 |
| Country: Number of subjects enrolled | Finland: 6 |
| Country: Number of subjects enrolled | France: 17 |
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | Georgia: 27 |
| Country: Number of subjects enrolled | Greece: 10 |
| Country: Number of subjects enrolled | Italy: 48 |
| Country: Number of subjects enrolled | Japan: 5 |
| Country: Number of subjects enrolled | Netherlands: 1 |
| Country: Number of subjects enrolled | Norway: 2 |
| Country: Number of subjects enrolled | Portugal: 13 |
| Country: Number of subjects enrolled | Russian Federation: 6 |
| Country: Number of subjects enrolled | Sweden: 4 |
| Country: Number of subjects enrolled | United States: 14 |
| Worldwide total number of subjects | 231 |
| EEA total number of subjects | 177 |

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) | 223 |
| From 65 to 84 years | 8 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 231 participants were enrolled in 18 countries.

Period 1

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

Arms

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

| | |
|------------------|-------------|
| Arm title | Eptinezumab |
|------------------|-------------|

Arm description:

Participants received a single intravenous (IV) infusion of eptinezumab 400 milligrams (mg) in 100 milliliters (mL) 0.9% saline solution.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Eptinezumab |
| Investigational medicinal product code | |
| Other name | Vyepti |
| Pharmaceutical forms | Solution for infusion, Solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Eptinezumab was administered per schedule specified in the arm description.

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

Arm description:

Participants received a single IV infusion of 0.9% saline solution as matching placebo for eptinezumab.

| | |
|--|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Placebo was administered per schedule specified in the arm description.

| Number of subjects in period 1 | Eptinezumab | Placebo |
|--|-------------|---------|
| Started | 113 | 118 |
| Received at least 1 dose of study drug | 112 | 117 |
| Completed | 108 | 107 |
| Not completed | 5 | 11 |

| | | |
|------------------------------|---|---|
| Consent withdrawn by subject | 1 | 6 |
| Adverse event, non-fatal | 2 | - |
| Other reasons | - | 1 |
| Randomized, not treated | 1 | 1 |
| Lack of efficacy | 1 | 2 |
| Protocol deviation | - | 1 |

Period 2

| | |
|------------------------------|-----------------------------|
| Period 2 title | Delayed start period |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Delayed Start Period: Placebo to Eptinezumab |

Arm description:

Participants who received placebo in the placebo-controlled period received a single IV infusion of eptinezumab 400mg in 100 mL 0.9% saline solution.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Eptinezumab |
| Investigational medicinal product code | |
| Other name | Vyepti |
| Pharmaceutical forms | Solution for infusion, Solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Eptinezumab was administered per schedule specified in the arm description.

| | |
|------------------|--|
| Arm title | Delayed Start Period: Eptinezumab to Placebo |
|------------------|--|

Arm description:

Participants who received eptinezumab in the placebo-controlled period received a single IV infusion of 0.9% saline solution as matching placebo for eptinezumab.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Placebo was administered per schedule specified in the arm description.

| Number of subjects in period 2 | Delayed Start Period: Placebo to Eptinezumab | Delayed Start Period: Eptinezumab to Placebo |
|--|--|--|
| Started | 107 | 108 |
| Received at least 1 dose of study drug | 107 | 108 |
| Completed | 101 | 100 |
| Not completed | 6 | 8 |
| Consent withdrawn by subject | 2 | 4 |
| Adverse event, non-fatal | 1 | - |
| Other reasons | 1 | - |
| Lost to follow-up | 2 | 1 |
| Lack of efficacy | - | 3 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------------------|
| Reporting group title | Placebo-controlled period |
|-----------------------|---------------------------|

Reporting group description: -

| Reporting group values | Placebo-controlled period | Total | |
|--|---------------------------|-------|--|
| Number of subjects | 231 | 231 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 223 | 223 | |
| From 65-84 years | 8 | 8 | |
| 85 years and over | 0 | 0 | |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 51 | 51 | |
| Male | 180 | 180 | |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 8 | 8 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 1 | 1 | |
| White | 202 | 202 | |
| Other | 3 | 3 | |
| Unknown or Not Reported | 17 | 17 | |
| Number of Weekly Cluster Headache (CH) Attacks | | | |
| Units: Number of Weekly Attacks | | | |
| arithmetic mean | 15.4 | | |
| standard deviation | ± 8.17 | - | |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Eptinezumab |
| Reporting group description: Participants received a single intravenous (IV) infusion of eptinezumab 400 milligrams (mg) in 100 milliliters (mL) 0.9% saline solution. | |
| Reporting group title | Placebo |
| Reporting group description: Participants received a single IV infusion of 0.9% saline solution as matching placebo for eptinezumab. | |
| Reporting group title | Delayed Start Period: Placebo to Eptinezumab |
| Reporting group description: Participants who received placebo in the placebo-controlled period received a single IV infusion of eptinezumab 400mg in 100 mL 0.9% saline solution. | |
| Reporting group title | Delayed Start Period: Eptinezumab to Placebo |
| Reporting group description: Participants who received eptinezumab in the placebo-controlled period received a single IV infusion of 0.9% saline solution as matching placebo for eptinezumab. | |

Primary: Change From Baseline in the Number of Weekly Cluster Headache (CH) Attacks, Averaged Over Weeks 1-2

| | |
|--|---|
| End point title | Change From Baseline in the Number of Weekly Cluster Headache (CH) Attacks, Averaged Over Weeks 1-2 |
| End point description: The participant completed a CH eDiary, daily, and recorded for each day/week whether he/she had any CH attacks. For each CH attack, the start date and time was collected. The participant recorded further daily information regarding CH characteristics and intake of acute medication for CH. CH items were assessed with a yes/no response. The APRS included all randomized participants. | |
| End point type | Primary |
| End point timeframe: Baseline (Week 0), Weeks 1-2 | |

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 113 | 118 | | |
| Units: Number of Weekly Attacks | | | | |
| least squares mean (standard error) | -4.0 (\pm 0.93) | -4.6 (\pm 0.89) | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Number of Weekly Attacks: Eptinezumab vs. Placebo |
| Comparison groups | Eptinezumab v Placebo |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 231 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.5048 |
| Method | Mixed Models Repeated Measures |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 2.6 |

Secondary: Change From Baseline in the Number of Weekly Times an Abortive Medication Was Used, Averaged Over Weeks 1-2

| | |
|-----------------|---|
| End point title | Change From Baseline in the Number of Weekly Times an Abortive Medication Was Used, Averaged Over Weeks 1-2 |
|-----------------|---|

End point description:

Abortive medications included the use of triptans or oxygen (O2).

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure.

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

End point timeframe:

Baseline (Week 0), Weeks 1-2

| End point values | Eptinezumab | Placebo | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 109 | 116 | | |
| Units: Abortive therapy use per week | | | | |
| least squares mean (standard error) | -2.54 (± 0.98) | -3.55 (± 0.93) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With ≥50% Reduction From Baseline in Number of Weekly Attacks Over Weeks 1-2

| | |
|-----------------|---|
| End point title | Number of Participants With ≥50% Reduction From Baseline in Number of Weekly Attacks Over Weeks 1-2 |
|-----------------|---|

End point description:

The APRS included all randomized participants.

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

End point timeframe:

Baseline (Week 0), Weeks 1-2

| End point values | Eptinezumab | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 113 | 118 | | |
| Units: participants | 44 | 37 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Number of Daily Attacks, Averaged Over Days 1-3

| | |
|-----------------|---|
| End point title | Change From Baseline in the Number of Daily Attacks, Averaged Over Days 1-3 |
|-----------------|---|

End point description:

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure.

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

End point timeframe:

Baseline (Week 0), Days 1-3

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 110 | 115 | | |
| Units: Attacks per day | | | | |
| least squares mean (standard error) | -0.22 (± 0.16) | -0.35 (± 0.15) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Number of Days With <3 Attacks Per Day, Averaged Over Weeks 1-2

| | |
|-----------------|---|
| End point title | Change From Baseline in the Number of Days With <3 Attacks Per Day, Averaged Over Weeks 1-2 |
|-----------------|---|

End point description:

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure.

| | |
|------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Week 0), Weeks 1-2 | |

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 109 | 116 | | |
| Units: Days | | | | |
| least squares mean (standard error) | 0.60 (\pm 0.20) | 0.82 (\pm 0.19) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Number of Attacks Starting \leq 24 Hours After the Start of the First Infusion of IMP

| | |
|-----------------|---|
| End point title | Change from Baseline in Number of Attacks Starting \leq 24 Hours After the Start of the First Infusion of IMP |
|-----------------|---|

End point description:

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure.

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

End point timeframe:

From first infusion in the placebo-controlled period (Baseline, Day 0) to 24-hours after the first infusion in the placebo-controlled period

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 104 | 110 | | |
| Units: Number of attacks | | | | |
| least squares mean (standard error) | 2.07 (\pm 0.18) | 1.96 (\pm 0.17) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time From First Infusion of IMP to Resolution of Cluster Headache Bout Within the First 4 Weeks

| | |
|-----------------|---|
| End point title | Time From First Infusion of IMP to Resolution of Cluster Headache Bout Within the First 4 Weeks |
|-----------------|---|

End point description:

Presented here is the result of the analysis of time from first infusion of IMP to resolution of cluster headache bout. The hazard ratio estimate is an estimate from the Cox model of time to resolution.

The APRS included all randomized participants.

"99999" = Data Not Reported. Median and 95% CI could not be calculated due to insufficient number of events.

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

End point timeframe:

From first infusion (Baseline, Day 0) to 4 weeks

| End point values | Eptinezumab | Placebo | | |
|----------------------------------|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 112 | 117 | | |
| Units: days | | | | |
| median (confidence interval 95%) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | | |

Statistical analyses

| Statistical analysis title | Time From First Infusion to Resolution |
|---|--|
| Comparison groups | Eptinezumab v Placebo |
| Number of subjects included in analysis | 229 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0772 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.45 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.96 |
| upper limit | 2.17 |

Secondary: Change From Baseline to Week 1 in the Number of Weekly Attacks

| | |
|-----------------|--|
| End point title | Change From Baseline to Week 1 in the Number of Weekly Attacks |
|-----------------|--|

End point description:

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure.

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

End point timeframe:

Baseline (Week 0), Week 1

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 109 | 116 | | |
| Units: Attacks per week | | | | |
| least squares mean (standard error) | -2.62 (\pm 0.95) | -3.71 (\pm 0.90) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Daily Mean Score on 5-Point Self-Rating Pain Severity Scale, Averaged Over Days 1-3

| | |
|-----------------|---|
| End point title | Change From Baseline in the Daily Mean Score on 5-Point Self-Rating Pain Severity Scale, Averaged Over Days 1-3 |
|-----------------|---|

End point description:

The severity of pain was rated on an ordinal scale that ranged from 0 to 4 with higher scores indicating more headache pain (headache pain ratings: 0 = none/barely any pain; 1 = mild; 2 = moderate; 3 = severe; 4 = excruciating).

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure.

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

End point timeframe:

Baseline (Week 0), Days 1-3

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 99 | 112 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -0.30 (\pm 0.10) | -0.18 (\pm 0.09) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Week 2 in the Number of Weekly Attacks

| | |
|-----------------|--|
| End point title | Change From Baseline to Week 2 in the Number of Weekly Attacks |
|-----------------|--|

End point description:

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome

measure.

| | |
|---------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Week 0), Week 2 | |

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 106 | 110 | | |
| Units: Attacks per week | | | | |
| least squares mean (standard error) | -5.44 (± 1.00) | -5.64 (± 0.96) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With ≥50% Reduction From Baseline in Number of Weekly Attacks in Week 1

| | |
|-----------------|--|
| End point title | Number of Participants With ≥50% Reduction From Baseline in Number of Weekly Attacks in Week 1 |
|-----------------|--|

End point description:

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure.

| | |
|---------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Week 0), Week 1 | |

| End point values | Eptinezumab | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 109 | 116 | | |
| Units: participants | 36 | 28 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With ≥30% Reduction From Baseline in Number of Weekly Attacks in Week 1

| | |
|-----------------|--|
| End point title | Number of Participants With ≥30% Reduction From Baseline in Number of Weekly Attacks in Week 1 |
|-----------------|--|

End point description:

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the

number of participants evaluable for this outcome measure.

| | |
|---------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Week 0), Week 1 | |

| End point values | Eptinezumab | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 109 | 116 | | |
| Units: participants | 48 | 50 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Week 1 in Weekly Integrated Measure of Frequency and Intensity of Pain

| | |
|-----------------|--|
| End point title | Change From Baseline to Week 1 in Weekly Integrated Measure of Frequency and Intensity of Pain |
|-----------------|--|

End point description:

The weekly integrated measure of frequency and intensity of pain calculates a singular numerical value for frequency and intensity of pain by adding the intensity rating (Worst pain on a 5-point Self-rating pain severity scale) for each attack during that week. The intensity of pain for each attack was rated on an ordinal scale that ranged from 0 to 4 with higher scores indicating more headache pain (0 = none/barely any pain; 1 = mild; 2 = moderate; 3 = severe; 4 = excruciating). The total weekly score could range from 0 (no attacks and/or no pain) to no specified upper limit, with lower scores representing better outcomes.

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure.

| | |
|---------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Week 0), Week 1 | |

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 109 | 116 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -10.58 (± 2.55) | -11.96 (± 2.42) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weekly Integrated Measure of Frequency and Intensity of pain, Averaged Over Weeks 1-2

| | |
|-----------------|---|
| End point title | Change From Baseline in Weekly Integrated Measure of Frequency and Intensity of pain, Averaged Over Weeks 1-2 |
|-----------------|---|

End point description:

The weekly integrated measure of frequency and intensity of pain calculates a singular numerical value for frequency and intensity of pain by adding the intensity rating (Worst pain on a 5-point Self-rating pain severity scale) for each attack during that week. The intensity of pain for each attack was rated on an ordinal scale that ranged from 0 to 4 with higher scores indicating more headache pain (0 = none/barely any pain; 1 = mild; 2 = moderate; 3 = severe; 4 = excruciating). The total weekly score could range from 0 (no attacks and/or no pain) to no specified upper limit, with lower scores representing better outcomes.

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure.

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

End point timeframe:

Baseline (Week 0), Weeks 1-2

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 109 | 116 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -13.39 (± 2.56) | -14.46 (± 2.43) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With ≥30% Reduction from Baseline in Number of Weekly Attacks Over Weeks 1-2

| | |
|-----------------|---|
| End point title | Number of Participants With ≥30% Reduction from Baseline in Number of Weekly Attacks Over Weeks 1-2 |
|-----------------|---|

End point description:

The APRS included all randomized participants.

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

End point timeframe:

Baseline (Week 0), Weeks 1-2

| End point values | Eptinezumab | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 113 | 118 | | |
| Units: participants | 59 | 53 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Week 2 in Weekly Integrated Measure of Frequency and Intensity of Pain

| | |
|-----------------|--|
| End point title | Change From Baseline to Week 2 in Weekly Integrated Measure of Frequency and Intensity of Pain |
|-----------------|--|

End point description:

The weekly integrated measure of frequency and intensity of pain calculates a singular numerical value for frequency and intensity of pain by adding the intensity rating (Worst pain on a 5-point Self-rating pain severity scale) for each attack during that week. The intensity of pain for each attack was rated on an ordinal scale that ranged from 0 to 4 with higher scores indicating more headache pain (0 = none/barely any pain; 1 = mild; 2 = moderate; 3 = severe; 4 = excruciating). The total weekly score could range from 0 (no attacks and/or no pain) to no specified upper limit, with lower scores representing better outcomes.

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure.

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

End point timeframe:

Baseline (Week 0), Week 2

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 106 | 110 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -16.20 (\pm 2.73) | -16.95 (\pm 2.61) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Mean Score on 5-Point Self-Rating Pain Severity Scale (Average Per Attack Over a Week) for Weeks 1, 2, 3, and 4

| | |
|-----------------|---|
| End point title | Change From Baseline in the Mean Score on 5-Point Self-Rating Pain Severity Scale (Average Per Attack Over a Week) for Weeks 1, 2, 3, and 4 |
|-----------------|---|

End point description:

The severity of pain for each attack was rated on an ordinal scale that ranged from 0 to 4 with higher scores indicating more headache pain (headache pain ratings: 0 = none/barely any pain; 1 = mild; 2 =

moderate; 3 = severe; 4 = excruciating).

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure and "Number Analyzed" is the number of participants evaluable at the specified time point.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Week 0), Weeks 1, 2, 3, and 4 | |

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 101 | 116 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 1 (n=101,116) | -0.33 (± 0.09) | -0.24 (± 0.08) | | |
| Week 2 (n=91,100) | -0.46 (± 0.10) | -0.35 (± 0.09) | | |
| Week 3 (n=80,97) | -0.56 (± 0.11) | -0.31 (± 0.10) | | |
| Week 4 (n=70,86) | -0.51 (± 0.11) | -0.42 (± 0.10) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weekly Integrated Measure of Frequency and Intensity of Pain, Averaged Over Weeks 1-4

| | |
|-----------------|---|
| End point title | Change From Baseline in Weekly Integrated Measure of Frequency and Intensity of Pain, Averaged Over Weeks 1-4 |
|-----------------|---|

End point description:

The weekly integrated measure of frequency and intensity of pain score calculates a singular numerical value for frequency and intensity of pain by adding the intensity rating (Worst pain on a 5-point Self-rating pain severity scale) for each attack during that week. The intensity of pain for each attack was rated on an ordinal scale that ranged from 0 to 4 with higher scores indicating more headache pain (0 = none/barely any pain; 1 = mild; 2 = moderate; 3 = severe; 4 = excruciating). The total weekly score could range from 0 (no attacks and/or no pain) to no specified upper limit, with lower scores representing better outcomes.

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure.

| | |
|------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Week 0), Weeks 1-4 | |

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 109 | 116 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -17.81 (\pm 2.50) | -16.81 (\pm 2.37) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Number of Weekly Attacks, Averaged Over Weeks 1-4

| | |
|-----------------|---|
| End point title | Change From Baseline in the Number of Weekly Attacks, Averaged Over Weeks 1-4 |
|-----------------|---|

End point description:

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure.

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

End point timeframe:

Baseline (Week 0), Weeks 1-4

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 109 | 116 | | |
| Units: Attacks per week | | | | |
| least squares mean (standard error) | -5.95 (\pm 0.92) | -5.78 (\pm 0.88) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Number of Weekly Attacks for Each of Weeks 3 and 4

| | |
|-----------------|--|
| End point title | Change from Baseline in the Number of Weekly Attacks for Each of Weeks 3 and 4 |
|-----------------|--|

End point description:

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure and "Number Analyzed" is the number of participants evaluable at the specified time point.

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

End point timeframe:

Baseline (Week 0), Weeks 3-4

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 104 | 112 | | |
| Units: Attacks per week | | | | |
| least squares mean (standard error) | | | | |
| Week 3 (n=104,112) | -7.35 (\pm 0.98) | -6.60 (\pm 0.94) | | |
| Week 4 (n=102,107) | -8.37 (\pm 1.11) | -7.15 (\pm 1.07) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Impression of Change (PGIC) Score at Weeks 1, 2, and 4

| | |
|-----------------|---|
| End point title | Patient Global Impression of Change (PGIC) Score at Weeks 1, 2, and 4 |
|-----------------|---|

End point description:

The PGIC is a patient-reported measure of improvement in pain sensation and quality of life scored on a scale from 1 (very much improved) to 7 (very much worse). Lower scores indicate better health status.

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure and "Number Analyzed" is the number of participants evaluable at the specified time point.

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

End point timeframe:

Weeks 1, 2, and 4

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 104 | 106 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 1 (n=102,96) | 3.19 (\pm 0.16) | 3.55 (\pm 0.15) | | |
| Week 2 (n=95,93) | 2.92 (\pm 0.17) | 3.44 (\pm 0.16) | | |
| Week 4 (n=104,106) | 2.85 (\pm 0.18) | 3.23 (\pm 0.17) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Sleep Impact Scale (SIS) Domain Scores at Weeks 2 and 4

| | |
|--|---|
| End point title | Change From Baseline in Sleep Impact Scale (SIS) Domain Scores at Weeks 2 and 4 |
| End point description: | |
| The SIS is a patient-reported clinical outcome assessment used to assess quality of life resulting from sleep disturbance. The SIS questionnaire includes 35 items belonging to 7 domains to assess sleep impact on: daily activities; emotional well-being; emotional impact; energy/fatigue; social well-being; mental fatigue; and satisfaction with sleep. Each item, for 6 out of the 7 domains, is rated on a 5-point scale ranging from 1 (always or all of the time) to 5 (never or none of the time), whereas satisfaction with sleep is rated on a 5-point scale ranging from 1 (very satisfied) to 5 (very dissatisfied). Each domain yields a score ranging from 0 to 100, which is presented here. A higher score for Daily Activities, Emotional Well-being, Emotional Impact, Energy/Fatigue, Social Well-being, and Mental Fatigue indicates better quality of life. A lower score for Satisfaction with Sleep indicates a higher quality of life. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Week 0), Weeks 2 and 4 | |

| End point values | Eptinezumab | Placebo | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 102 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Daily Activities - Week 2 (n=91,84) | 16.83 (± 3.08) | 8.93 (± 3.06) | | |
| Daily Activities - Week 4 (n=100,102) | 24.82 (± 3.19) | 13.97 (± 3.08) | | |
| Emotional Well-being - Week 2 (n=91,84) | 14.85 (± 2.84) | 6.04 (± 2.81) | | |
| Emotional Well-being - Week 4 (n=100,102) | 22.77 (± 3.07) | 12.22 (± 2.97) | | |
| Energy/Fatigue - Week 2 (n=91,84) | 18.16 (± 3.23) | 8.03 (± 3.19) | | |
| Energy/Fatigue - Week 4 (n=100,102) | 24.16 (± 3.47) | 14.68 (± 3.36) | | |
| Mental Fatigue - Week 2 (n=91,84) | 9.04 (± 2.66) | 4.15 (± 2.64) | | |
| Mental Fatigue - Week 4 (n=100,102) | 15.15 (± 2.91) | 8.00 (± 2.81) | | |
| Emotional Impact - Week 2 (n=91,84) | 14.39 (± 3.02) | 6.00 (± 3.00) | | |
| Emotional Impact - Week 4 (n=100,102) | 23.09 (± 3.29) | 13.36 (± 3.18) | | |
| Social Well-being - Week 2 (n=91,84) | 15.22 (± 3.37) | 6.92 (± 3.35) | | |
| Social Well-being - Week 4 (n=100,102) | 23.74 (± 3.46) | 13.91 (± 3.35) | | |
| Satisfaction with Sleep - Week 2 (n=91,84) | -11.41 (± 2.75) | -6.06 (± 2.73) | | |
| Satisfaction with Sleep - Week 4 (n=100,102) | -19.60 (± 2.88) | -9.63 (± 2.78) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Euroqol 5-Dimension 5-Levels (EQ-5D-5L) Visual Analogue Scale (VAS) at Weeks 2 and 4

| | |
|-----------------|--|
| End point title | Change From Baseline in Euroqol 5-Dimension 5-Levels (EQ-5D-5L) Visual Analogue Scale (VAS) at Weeks 2 and 4 |
|-----------------|--|

End point description:

The EQ-5D-5L VAS is a participant-reported assessment designed to measure the participant's well-

being and ranges from 0 (worst imaginable health state) to 100 (best imaginable health state).

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure and "Number Analyzed" is the number of participants evaluable at the specified time point.

| | |
|----------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Week 0), Weeks 2 and 4 | |

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|---------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 76 | 80 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 2 (n=70,63) | 8.21 (\pm 2.79) | 3.47 (\pm 2.86) | | |
| Week 4 (n=76,80) | 13.49 (\pm 2.80) | 5.73 (\pm 2.77) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Resource Utilization (HCRU) Score: Number of Visits to a Family Doctor/General Practitioner

| | |
|-----------------|---|
| End point title | Health Care Resource Utilization (HCRU) Score: Number of Visits to a Family Doctor/General Practitioner |
|-----------------|---|

End point description:

Number of participants who visited a family doctor/general practitioner has been reported.

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure at the specified time point.

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

| End point values | Eptinezumab | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 104 | | |
| Units: participants | | | | |
| 0 visits | 85 | 85 | | |
| 1 visit | 9 | 10 | | |
| 2 visits | 1 | 6 | | |
| 3 visits | 3 | 1 | | |
| 5 visits | 1 | 1 | | |
| 6 visits | 1 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: HCRU Score: Number of Visits to a Specialist

| | |
|-----------------|--|
| End point title | HCRU Score: Number of Visits to a Specialist |
|-----------------|--|

End point description:

Number of participants who visited a specialist has been reported.

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure at the specified time point.

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

End point timeframe:

Week 4

| End point values | Eptinezumab | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 104 | | |
| Units: participants | | | | |
| 0 visits | 77 | 68 | | |
| 1 visit | 11 | 18 | | |
| 2 visits | 6 | 14 | | |
| 3 visits | 4 | 2 | | |
| 4 visits | 2 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: HCRU Score: Number of Emergency Department Visits Due to Cluster Headache

| | |
|-----------------|---|
| End point title | HCRU Score: Number of Emergency Department Visits Due to Cluster Headache |
|-----------------|---|

End point description:

Number of participants who visited an emergency department due to CH was reported.

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure at the specified time point.

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

End point timeframe:

Week 4

| End point values | Eptinezumab | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 104 | | |
| Units: participants | | | | |
| 0 visits | 98 | 99 | | |
| 1 visit | 1 | 2 | | |
| 2 visits | 1 | 2 | | |
| 3 visits | 0 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: HCRU Score: Number of Hospital Admissions Due to Cluster Headache

| | |
|-----------------|---|
| End point title | HCRU Score: Number of Hospital Admissions Due to Cluster Headache |
|-----------------|---|

End point description:

Number of participants who were admitted to a hospital due to CH was reported.

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure at the specified time point.

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

End point timeframe:

Week 4

| End point values | Eptinezumab | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 104 | | |
| Units: participants | | | | |
| 0 admissions | 97 | 102 | | |
| 1 admission | 1 | 0 | | |
| 2 admissions | 2 | 1 | | |
| 3 admissions | 0 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: HCRU Score: Number of Overnight Hospital Stays Due to Cluster Headache

| | |
|-----------------|--|
| End point title | HCRU Score: Number of Overnight Hospital Stays Due to Cluster Headache |
|-----------------|--|

End point description:

Number of participants who stayed overnight in a hospital due to CH was reported.

The APRS included all randomized participants. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure at the specified time point.

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

End point timeframe:

Week 4

| End point values | Eptinezumab | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 104 | | |
| Units: participants | | | | |
| 0 overnight hospital stays | 99 | 104 | | |
| 5 overnight hospital stays | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Work Productivity Activity Impairment (WPAI) Questionnaire Subscores at Week 4

| | |
|-----------------|--|
| End point title | Change From Baseline in the Work Productivity Activity Impairment (WPAI) Questionnaire Subscores at Week 4 |
|-----------------|--|

End point description:

The WPAI:GH2.0 is a patient self-rated clinical outcome assessment designed to provide a quantitative measure of the work productivity and activity impairment due to a health condition. The WPAI:GH2.0 assesses activities over the preceding 7 days and consists of 6 items: 1 item assesses employment (yes/no); 3 items assess the number of hours worked, the number of hours missed from work due to the participant's condition, or due to other reasons; and 2 visual numerical scales assess how much the participant's condition affects his/her productivity at work and his/her ability to complete normal daily activities. Each item (Absenteeism, Presenteeism, Work Productivity Loss, Activity Impairment) was calculated into an impairment percentage ranging from 0 to 100%, with higher numbers indicating greater impairment and less productivity (i.e. worse outcomes). Change from baseline for each item is shown here.

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

End point timeframe:

Baseline (Week 0), Week 4

| End point values | Eptinezumab | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 95 | 95 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Absenteeism | -13.71 (± 3.95) | -4.37 (± 3.74) | | |
| Presenteeism | -19.29 (± 4.81) | -11.03 (± 4.68) | | |
| Work productivity loss | -23.59 (± 5.34) | -13.68 (± 5.20) | | |
| Activity impairment | -25.84 (± 3.70) | -15.82 (± 3.58) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From date of first dose of IMP to 20 weeks after last dose (up to 24 weeks)

Adverse event reporting additional description:

The APTS included all randomized participants in the who received infusion with double-blind IMP.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Placebo-controlled Period: Eptinezumab |
|-----------------------|--|

Reporting group description:

Participants received a single IV infusion of eptinezumab 400mg in 100 mL 0.9% saline solution.

| | |
|-----------------------|--|
| Reporting group title | Delayed Start Period: Placebo to Eptinezumab |
|-----------------------|--|

Reporting group description:

Participants who received placebo in the placebo-controlled period received a single IV infusion of eptinezumab 400mg in 100 mL 0.9% saline solution.

| | |
|-----------------------|--|
| Reporting group title | Delayed Start Period: Eptinezumab to Placebo |
|-----------------------|--|

Reporting group description:

Participants who received eptinezumab in the placebo-controlled period received a single IV infusion of 0.9% saline solution as matching placebo for eptinezumab.

| | |
|-----------------------|------------------------------------|
| Reporting group title | Placebo-controlled Period: Placebo |
|-----------------------|------------------------------------|

Reporting group description:

Participants received a single IV infusion of 0.9% saline solution as matching placebo for eptinezumab.

| Serious adverse events | Placebo-controlled Period: Eptinezumab | Delayed Start Period: Placebo to Eptinezumab | Delayed Start Period: Eptinezumab to Placebo |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 112 (1.79%) | 1 / 107 (0.93%) | 2 / 108 (1.85%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Bladder cancer | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 107 (0.00%) | 1 / 108 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |

| | | | |
|---|---------------------------------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 107 (0.93%) | 0 / 108 (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 |
| Hypersensitivity | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 107 (0.00%) | 0 / 108 (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 |
| Reproductive system and breast disorders | | | |
| Cystocele | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 107 (0.00%) | 0 / 108 (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 |
| Renal and urinary disorders | | | |
| Urinary incontinence | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 107 (0.00%) | 0 / 108 (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 |
| Infections and infestations | | | |
| Meningitis enteroviral | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 107 (0.00%) | 1 / 108 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Serious adverse events | Placebo-controlled Period: Placebo | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 117 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Bladder cancer | | | |
| subjects affected / exposed | 0 / 117 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |

| | | | |
|---|-----------------|--|--|
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 117 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 117 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Cystocele | | | |
| subjects affected / exposed | 0 / 117 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 117 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Meningitis enteroviral | | | |
| subjects affected / exposed | 0 / 117 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Placebo-controlled Period: Eptinezumab | Delayed Start Period: Placebo to Eptinezumab | Delayed Start Period: Eptinezumab to Placebo |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 10 / 112 (8.93%) | 9 / 107 (8.41%) | 13 / 108 (12.04%) |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 4 / 112 (3.57%) | 1 / 107 (0.93%) | 0 / 108 (0.00%) |
| occurrences (all) | 4 | 1 | 0 |
| Gastrointestinal disorders | | | |

| | | | |
|---|----------------------|----------------------|----------------------|
| Constipation subjects affected / exposed occurrences (all) | 4 / 112 (3.57%) 4 | 0 / 107 (0.00%) 0 | 3 / 108 (2.78%) 4 |
| Infections and infestations COVID-19 subjects affected / exposed occurrences (all) | 1 / 112 (0.89%) 1 | 2 / 107 (1.87%) 3 | 7 / 108 (6.48%) 7 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 2 / 112 (1.79%) 2 | 6 / 107 (5.61%) 6 | 2 / 108 (1.85%) 2 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 112 (0.00%) 0 | 0 / 107 (0.00%) 0 | 3 / 108 (2.78%) 3 |

| | | | |
|--|---------------------------------------|--|--|
| Non-serious adverse events | Placebo-controlled Period: Placebo | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 9 / 117 (7.69%) | | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 1 / 117 (0.85%) 1 | | |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) | 2 / 117 (1.71%) 3 | | |
| Infections and infestations COVID-19 subjects affected / exposed occurrences (all) | 3 / 117 (2.56%) 3 | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 3 / 117 (2.56%) 3 | | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 1 / 117 (0.85%) 1 | | |

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