



Clinical trial results:

A 15 WEEK, RANDOMIZED, DOUBLE BLIND, PARALLEL-GROUP, PLACEBO-CONTROLLED, FLEXIBLE-DOSE, SAFETY AND EFFICACY STUDY OF PREGABALIN IN ADOLESCENTS (12-17 YEARS OLD) WITH FIBROMYALGIA

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2010-019521-34 |
| Trial protocol | CZ |
| Global end of trial date | 08 December 2014 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 08 July 2016 |
| First version publication date | 11 June 2015 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | A0081180 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01020474 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Pfizer Inc |
| Sponsor organisation address | 235 East 42nd Street, New York, United States, NY 10017 |
| Public contact | Clinical Trials.gov Call Center, Pfizer Inc., 1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Clinical Trials.gov Call Center, Pfizer Inc., 1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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 | 08 May 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 08 December 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 December 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and efficacy of pregabalin (75-450 mg/day) compared with placebo in an adolescent fibromyalgia population.

Protection of trial subjects:

The study was conducted in accordance with the protocol, legal and regulatory requirements, as well as the general principles set forth in the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Council for International Organizations of Medical Sciences 2002), Guidelines for Good Clinical Practice (GCP) (International Conference on Harmonization [ICH] 1996), and the Declaration of Helsinki (World Medical Association 1996 and 2008). In addition, the study was conducted in accordance with applicable local regulatory requirements and laws.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 07 May 2010 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Czech Republic: 4 |
| Country: Number of subjects enrolled | India: 35 |
| Country: Number of subjects enrolled | Taiwan: 1 |
| Country: Number of subjects enrolled | United States: 67 |
| Worldwide total number of subjects | 107 |
| EEA total number of subjects | 4 |

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) | 107 |

| | |
|----------------------|---|
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

A total of 147 participants were screened, 107 participants were randomized to treatment. The 107 randomized participants were recruited in 4 countries at 23 study centers: United States (17 centers; 67 participants), India (4 centers; 35 participants), Czech Republic (1 center; 4 participants), and Taiwan (1 center; 1 participant).

Pre-assignment

Screening details:

This study consisted of 4 phases, screening (1 Week), dose optimization (3 Weeks), fixed dose (12 Weeks) and follow-up (1 Week).

Period 1

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

Blinding implementation details:

Participants were assigned a single subject identification number (SSID) which was obtained at the time of screening using the automated telorandomization system and retained throughout the study. Qualified participants were randomized in a 1:1 ratio to receive either pregabalin or placebo according to a computer-generated pseudorandom code using the method of random permuted blocks.

Arms

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

Arm description:

Pregabalin was administered orally, BID (twice a day) for 15 weeks (3 week dose optimization phase and 12 week fixed-dose phase). Participants received 75 milligram per day (mg/day) to 450 mg/day. Dosing was started on Day 1. The dose was optimized over a 3-week period followed by an additional 12 weeks at the optimized dose.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Lyrica |
| Investigational medicinal product code | PD-144,723 |
| Other name | Pregabalin |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Pregabalin was administered BID 75 mg/day to 450 mg/day for 15 weeks.

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

Arm description:

Placebo was administered orally, BID for 15 weeks (3 week dose optimization phase and 12 week fixed-dose phase). Dosing was started on Day 1.

| | |
|--|------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Matching placebo |
| Investigational medicinal product code | |
| Other name | Placebo |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Matching placebo capsules were administered twice daily.

| Number of subjects in period 1 | Pregabalin | Placebo |
|---------------------------------------|------------|---------|
| Started | 54 | 53 |
| Completed | 44 | 36 |
| Not completed | 10 | 17 |
| Consent withdrawn by subject | 5 | 7 |
| Adverse event, non-fatal | 4 | 4 |
| Other Reasons | 1 | 1 |
| Insufficient Clinical Response | - | 3 |
| Protocol Violation | - | 2 |

Baseline characteristics

Reporting groups

| | |
|---|------------|
| Reporting group title | Pregabalin |
| Reporting group description: | |
| Pregabalin was administered orally, BID (twice a day) for 15 weeks (3 week dose optimization phase and 12 week fixed-dose phase). Participants received 75 milligram per day (mg/day) to 450 mg/day. Dosing was started on Day 1. The dose was optimized over a 3-week period followed by an additional 12 weeks at the optimized dose. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Placebo was administered orally, BID for 15 weeks (3 week dose optimization phase and 12 week fixed-dose phase). Dosing was started on Day 1. | |

| Reporting group values | Pregabalin | Placebo | Total |
|---|------------|---------|-------|
| Number of subjects | 54 | 53 | 107 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 54 | 53 | 107 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 14.6 | 14.7 | |
| standard deviation | ± 1.2 | ± 1.2 | - |
| Gender categorical Units: Subjects | | | |
| Female | 48 | 44 | 92 |
| Male | 6 | 9 | 15 |

End points

End points reporting groups

| | |
|---|------------|
| Reporting group title | Pregabalin |
| Reporting group description: Pregabalin was administered orally, BID (twice a day) for 15 weeks (3 week dose optimization phase and 12 week fixed-dose phase). Participants received 75 milligram per day (mg/day) to 450 mg/day. Dosing was started on Day 1. The dose was optimized over a 3-week period followed by an additional 12 weeks at the optimized dose. | |
| Reporting group title | Placebo |
| Reporting group description: Placebo was administered orally, BID for 15 weeks (3 week dose optimization phase and 12 week fixed-dose phase). Dosing was started on Day 1. | |

Primary: Change from Baseline to Week 15 in mean pain diary score

| | |
|--|--|
| End point title | Change from Baseline to Week 15 in mean pain diary score |
| End point description: The Primary Endpoint is based on the daily pain diary, and is defined as change from baseline to Week 15 in mean pain diary score. The daily pain diary consists of an 11-point numeric rating scale ranging from zero (no pain) to 10 (worst possible pain). The participants rate their pain during the past 24 hours by choosing the appropriate number between 0 ("no pain") and 10 ("worst possible pain"). | |
| End point type | Primary |
| End point timeframe: Week 15 | |

| End point values | Pregabalin | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 51 | | |
| Units: participants | | | | |
| least squares mean (standard error) | -1.6 (± 0.32) | -0.94 (± 0.31) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Mean pain diary score from Baseline to Week 15 |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.121 ^[1] |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.66 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.51 |
| upper limit | 0.18 |

Notes:

[1] - Missing data for week 15 mean pain score are imputed based on distribution of baseline pain scores if participants discontinue due to adverse events/ abnormal laboratory test results or lack of efficacy.

Secondary: Change from Baseline to Week 15 in mean sleep quality diary score

| | |
|-----------------|---|
| End point title | Change from Baseline to Week 15 in mean sleep quality diary score |
|-----------------|---|

End point description:

Change from Baseline to endpoint in mean sleep quality score from the daily sleep diary, defined as the mean of the last 7 diary entries prior to Visit 10 in the study while the participant is on study medication. The daily quality of sleep diary consists of an 11-point numeric rating scale with which the patient rates the quality of their sleep during the past 24 hours. Zero indicates "best possible sleep" and 10 indicates "worst possible sleep".

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

End point timeframe:

Week 15

| End point values | Pregabalin | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 50 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | -1.13 (± 0.3) | -0.94 (± 0.31) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Mean sleep quality daily score in Week 15 |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.655 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.18 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 0.63 |

Secondary: Mean Change from Baseline to weekly mean pain score - daily pain numeric rating scale (NRS)

| | |
|-----------------|---|
| End point title | Mean Change from Baseline to weekly mean pain score - daily pain numeric rating scale (NRS) |
|-----------------|---|

End point description:

Mean pain score was calculated for each week during the double-blind treatment phase (Week 1 to Week 15). For each week, only days up to the last day on study medication were considered. A minimum of 4 pain diaries are required to calculate the mean pain score. The pain NRS consists of an 11 point NRS ranging from 0 (no pain) to 10 (worst possible pain).

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

End point timeframe:

Baseline to Week 15

| End point values | Pregabalin | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 51 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 1 (N= 52, 49) | -0.48 (± 0.25) | -0.41 (± 0.26) | | |
| Week 2 (N= 54, 47) | -1.11 (± 0.25) | -0.48 (± 0.26) | | |
| Week 3 (N= 52, 44) | -1.27 (± 0.25) | -0.45 (± 0.26) | | |
| Week 4 (N= 50, 46) | -1.45 (± 0.25) | -0.55 (± 0.26) | | |
| Week 5 (N= 49, 44) | -1.27 (± 0.25) | -0.59 (± 0.26) | | |
| Week 6 (N= 49, 44) | -1.47 (± 0.25) | -0.51 (± 0.27) | | |
| Week 7 (N= 48, 42) | -1.67 (± 0.25) | -0.77 (± 0.27) | | |
| Week 8 (N= 46, 44) | -1.65 (± 0.25) | -0.59 (± 0.27) | | |
| Week 9 (N= 46, 42) | -1.61 (± 0.26) | -0.66 (± 0.27) | | |
| Week 10 (N= 45, 40) | -1.82 (± 0.26) | -0.85 (± 0.27) | | |
| Week 11 (N= 44, 38) | -1.93 (± 0.26) | -1.07 (± 0.28) | | |
| Week 12 (N= 43, 34) | -1.75 (± 0.26) | -0.78 (± 0.28) | | |
| Week 13 (N= 42, 33) | -1.75 (± 0.27) | -1.01 (± 0.29) | | |
| Week 14 (N= 41, 34) | -2.01 (± 0.27) | -1.11 (± 0.29) | | |
| Week 15 (N= 35, 33) | -1.9 (± 0.28) | -1.16 (± 0.3) | | |

Statistical analyses

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 1. |
| Comparison groups | Placebo v Pregabalin |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.842 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.07 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.75 |
| upper limit | 0.61 |

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 2. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.07 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.63 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.32 |
| upper limit | 0.05 |

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 3. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.019 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.83 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.51 |
| upper limit | -0.14 |

| | |
|-----------------------------------|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 4. |
| Comparison groups | Pregabalin v Placebo |

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|---|--------------------------------|
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.011 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.59 |
| upper limit | -0.21 |

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 5. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.056 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.68 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.38 |
| upper limit | 0.02 |

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 6. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.008 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.96 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.66 |
| upper limit | -0.26 |

| | |
|-----------------------------------|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 7. |
|-----------------------------------|---------------------------------|

| | |
|---|--------------------------------|
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.013 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.89 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.6 |
| upper limit | -0.19 |

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 8. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.004 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.77 |
| upper limit | -0.35 |

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 9. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.009 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.95 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.67 |
| upper limit | -0.24 |

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical analysis of Week 10. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.008 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.97 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.69 |
| upper limit | -0.25 |

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical analysis of Week 11. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.021 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.59 |
| upper limit | -0.13 |

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical analysis of Week 12. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.01 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.97 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.71 |
| upper limit | -0.23 |

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical analysis of Week 13. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.051 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.49 |
| upper limit | 0 |

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical analysis of Week 14. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.02 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.66 |
| upper limit | -0.14 |

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical analysis of Week 15. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.06 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.74 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.51 |
| upper limit | 0.03 |

Secondary: Mean change from Baseline to weekly mean sleep quality score (NRS)

| | |
|--|--|
| End point title | Mean change from Baseline to weekly mean sleep quality score (NRS) |
| End point description: | |
| Mean sleep quality score was calculated for each week during the double-blind treatment phase (Week 1 to Week 15). A minimum of 4 sleep diaries are required to calculate the mean pain score. The daily quality of sleep diary consists of an 11-point numeric rating scale with which the patient rates the quality of their sleep during the past 24 hours. Zero indicates "best possible sleep" and 10 indicates "worst possible sleep". | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to Week 15 | |

| End point values | Pregabalin | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 51 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 1 (N= 52, 49) | -0.52 (± 0.25) | -0.3 (± 0.26) | | |
| Week 2 (N= 54, 47) | -0.84 (± 0.25) | -0.65 (± 0.26) | | |
| Week 3 (N= 52, 44) | -0.89 (± 0.25) | -0.44 (± 0.26) | | |
| Week 4 (N= 50, 46) | -1.03 (± 0.25) | -0.54 (± 0.26) | | |
| Week 5 (N= 49, 44) | -0.99 (± 0.25) | -0.61 (± 0.27) | | |
| Week 6 (N= 49, 44) | -1.18 (± 0.25) | -0.54 (± 0.27) | | |
| Week 7 (N= 48, 42) | -1.3 (± 0.25) | -0.81 (± 0.27) | | |
| Week 8 (N= 46, 44) | -1.43 (± 0.25) | -0.42 (± 0.27) | | |
| Week 9 (N= 46, 42) | -1.38 (± 0.26) | -0.81 (± 0.27) | | |
| Week 10 (N= 45, 40) | -1.43 (± 0.26) | -0.66 (± 0.27) | | |
| Week 11 (N= 44, 38) | -1.39 (± 0.26) | -0.95 (± 0.28) | | |
| Week 12 (N= 43, 34) | -1.38 (± 0.26) | -0.77 (± 0.28) | | |
| Week 13 (N= 42, 33) | -1.34 (± 0.27) | -1 (± 0.29) | | |
| Week 14 (N= 41, 34) | -1.36 (± 0.27) | -0.94 (± 0.29) | | |
| Week 15 (N= 35, 33) | -1.25 (± 0.28) | -1.08 (± 0.3) | | |

Statistical analyses

| | |
|----------------------------|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 1. |
| Comparison groups | Pregabalin v Placebo |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.54 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.21 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.9 |
| upper limit | 0.47 |

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 2. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.593 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.19 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.87 |
| upper limit | 0.5 |

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 3. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.206 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.13 |
| upper limit | 0.25 |

| | |
|-----------------------------------|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 4. |
|-----------------------------------|---------------------------------|

| | |
|---|--------------------------------|
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.168 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.49 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.18 |
| upper limit | 0.21 |

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 5. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.28 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.38 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.08 |
| upper limit | 0.32 |

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 6. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.075 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.34 |
| upper limit | 0.06 |

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 7. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.168 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.21 |
| upper limit | 0.21 |

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 8. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.006 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.73 |
| upper limit | -0.3 |

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis of Week 9. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.12 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.29 |
| upper limit | 0.15 |

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical analysis of Week 10. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.037 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.49 |
| upper limit | -0.05 |

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical analysis of Week 11. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.246 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.16 |
| upper limit | 0.3 |

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical analysis of Week 12. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.105 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.61 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.36 |
| upper limit | 0.13 |

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical analysis of Week 13. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.376 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.34 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.09 |
| upper limit | 0.41 |

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical analysis of Week 14. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.285 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.41 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.18 |
| upper limit | 0.35 |

| | |
|-----------------------------------|----------------------------------|
| Statistical analysis title | Statistical analysis of Week 15. |
| Comparison groups | Pregabalin v Placebo |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.663 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.95 |
| upper limit | 0.61 |

Secondary: Proportion of 30% pain responders in weekly mean pain score (NRS) at Week 15

| | |
|---|--|
| End point title | Proportion of 30% pain responders in weekly mean pain score (NRS) at Week 15 |
| End point description: | |
| At each visit, participants with at least 30% reduction from Baseline in mean pain score were defined as a 30% responder at the visit. The pain NRS consists of an 11 point NRS ranging from 0 (no pain) to 10 (worst possible pain). | |
| End point type | Secondary |
| End point timeframe: | |
| Week 15 | |

| End point values | Pregabalin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 49 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 42.6 | 38.8 | | |

Statistical analyses

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis at Week 15 |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.694 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.17 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.53 |
| upper limit | 2.58 |

Secondary: Proportion of 50% pain responders in weekly mean pain score (NRS) at Week 15

| | |
|-----------------|--|
| End point title | Proportion of 50% pain responders in weekly mean pain score (NRS) at Week 15 |
|-----------------|--|

End point description:

At each visit, participants with at least 50% reduction from Baseline in mean pain score were defined as a 50% responder at the visit. The pain NRS consists of an 11 point NRS ranging from 0 (no pain) to 10 (worst possible pain).

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

End point timeframe:

Week 15

| End point values | Pregabalin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 49 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 20.4 | 10.2 | | |

Statistical analyses

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical analysis at Week 15. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.162 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.25 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.72 |
| upper limit | 7.02 |

Secondary: Proportion of Patient Global Impression Change (PGIC) at Week 15

| | |
|---|--|
| End point title | Proportion of Patient Global Impression Change (PGIC) at Week 15 |
| End point description: Responder rates based on PGIC was derived and tabulated by treatment group. A responder was defined as a participant who reports much improved or very much improved. The PGIC is a patient-rated single item that measures patient's perception of change in their overall status since starting study medication on a scale ranging from 1 (very much improved) to 7 (very much worse). | |
| End point type | Secondary |
| End point timeframe: Week 15 | |

| End point values | Pregabalin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 49 | 44 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Very much improved | 16.3 | 2.3 | | |
| Much improved | 36.7 | 27.3 | | |
| Minimally improved | 22.4 | 27.3 | | |
| No change | 18.4 | 38.6 | | |
| Minimally worse | 6.1 | 2.3 | | |
| Much worse | 0 | 2.3 | | |
| Very much worse | 0 | 0 | | |

Statistical analyses

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical analysis at Week 15. |
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 93 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.013 ^[2] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[2] - P-value uses the row mean score statistic based on Cochran Mantel Haenszel (CMH) test with modified rdit transformation.

Secondary: Change from Baseline to Week 15 in mean pain numeric rating scale (1 week recall period)

| | |
|---|--|
| End point title | Change from Baseline to Week 15 in mean pain numeric rating scale (1 week recall period) |
| End point description: The weekly pain numeric rating scale (Weekly Pain NRS) consists of an 11-point NRS ranging from 0 (no pain) to 10 (worst possible pain), where higher scores indicate greater degree of impairment. Participants choose the number that best describes the pain during the last week. | |
| End point type | Secondary |
| End point timeframe: Week 15 | |

| End point values | Pregabalin | Placebo | | |
|-------------------------------------|---------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 53 | | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | -1.64 (\pm 0.31) | -0.77 (\pm 0.3) | | |

Statistical analyses

| Statistical analysis title | Statistical analysis for Week 15 |
|---|----------------------------------|
| Comparison groups | Pregabalin v Placebo |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.037 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.68 |
| upper limit | -0.05 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from signing the informed consent until a follow-up visit (Week 16).

Adverse event reporting additional description:

Participants are only counted once per treatment for each event.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Pregabalin |
|-----------------------|------------|

Reporting group description:

Pregabalin was administered orally, BID for 15 weeks (3 week dose optimization phase and 12 week fixed-dose phase). Participants received 75 mg/day to 450 mg/day. Dosing was started on Day 1. The dose was optimized over a 3-week period followed by an additional 12 weeks at the optimized dose.

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Placebo was administered orally, BID for 15 weeks (3 week dose optimization phase and 12 week fixed-dose phase). Dosing was started on Day 1.

| Serious adverse events | Pregabalin | Placebo | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | 0 / 53 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Major depression | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Pregabalin | Placebo | |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 33 / 54 (61.11%) | 27 / 53 (50.94%) | |
| Investigations | | | |
| Weight increased | | | |
| subjects affected / exposed | 9 / 54 (16.67%) | 0 / 53 (0.00%) | |
| occurrences (all) | 10 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Ligament sprain | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Nervous system disorders | | | |
| Balance disorder | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Dizziness | | | |
| subjects affected / exposed | 16 / 54 (29.63%) | 7 / 53 (13.21%) | |
| occurrences (all) | 19 | 7 | |
| Headache | | | |
| subjects affected / exposed | 10 / 54 (18.52%) | 10 / 53 (18.87%) | |
| occurrences (all) | 10 | 18 | |
| Migraine | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | 3 / 53 (5.66%) | |
| occurrences (all) | 3 | 3 | |
| Somnolence | | | |
| subjects affected / exposed | 5 / 54 (9.26%) | 2 / 53 (3.77%) | |
| occurrences (all) | 6 | 2 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 8 / 54 (14.81%) | 4 / 53 (7.55%) | |
| occurrences (all) | 12 | 6 | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 54 (7.41%) | 3 / 53 (5.66%) | |
| occurrences (all) | 5 | 3 | |
| Gastrointestinal disorders | | | |

| | | | |
|--|------------------------|---------------------|--|
| Abdominal discomfort subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | 3 / 53 (5.66%) 3 | |
| Abdominal pain subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | 1 / 53 (1.89%) 1 | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 0 / 54 (0.00%) 0 | 3 / 53 (5.66%) 3 | |
| Dry mouth subjects affected / exposed occurrences (all) | 2 / 54 (3.70%) 2 | 3 / 53 (5.66%) 3 | |
| Nausea subjects affected / exposed occurrences (all) | 12 / 54 (22.22%) 14 | 5 / 53 (9.43%) 5 | |
| Vomiting subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | 4 / 53 (7.55%) 4 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | 4 / 53 (7.55%) 4 | |
| Nasal congestion subjects affected / exposed occurrences (all) | 2 / 54 (3.70%) 2 | 3 / 53 (5.66%) 3 | |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 4 / 54 (7.41%) 4 | 2 / 53 (3.77%) 2 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | 4 / 53 (7.55%) 8 | |
| Back pain subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 4 | 5 / 53 (9.43%) 6 | |
| Neck pain | | | |

| | | | |
|--|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 54 (0.00%) 0 | 3 / 53 (5.66%) 3 | |
| Pain in extremity subjects affected / exposed occurrences (all) | 4 / 54 (7.41%) 5 | 0 / 53 (0.00%) 0 | |
| Infections and infestations Pharyngitis streptococcal subjects affected / exposed occurrences (all) | 0 / 54 (0.00%) 0 | 4 / 53 (7.55%) 4 | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | 4 / 53 (7.55%) 4 | |
| Metabolism and nutrition disorders Increased appetite subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | 1 / 53 (1.89%) 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