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 telerandomization 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

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 ridit 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 (± 0.31)	-0.77 (± 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	1 / 54 (1.85%)	3 / 53 (5.66%)	
occurrences (all)	1	3	
Abdominal pain			
subjects affected / exposed	3 / 54 (5.56%)	1 / 53 (1.89%)	
occurrences (all)	3	1	
Abdominal pain upper			
subjects affected / exposed	0 / 54 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	3	
Dry mouth			
subjects affected / exposed	2 / 54 (3.70%)	3 / 53 (5.66%)	
occurrences (all)	2	3	
Nausea			
subjects affected / exposed	12 / 54 (22.22%)	5 / 53 (9.43%)	
occurrences (all)	14	5	
Vomiting			
subjects affected / exposed	3 / 54 (5.56%)	4 / 53 (7.55%)	
occurrences (all)	3	4	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 54 (1.85%)	4 / 53 (7.55%)	
occurrences (all)	1	4	
Nasal congestion			
subjects affected / exposed	2 / 54 (3.70%)	3 / 53 (5.66%)	
occurrences (all)	2	3	
Oropharyngeal pain			
subjects affected / exposed	4 / 54 (7.41%)	2 / 53 (3.77%)	
occurrences (all)	4	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 54 (1.85%)	4 / 53 (7.55%)	
occurrences (all)	1	8	
Back pain			
subjects affected / exposed	3 / 54 (5.56%)	5 / 53 (9.43%)	
occurrences (all)	4	6	
Neck pain			

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