



Clinical trial results:

A DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL-GROUP, MULTICENTER STUDY OF THE EFFICACY AND SAFETY OF PREGABALIN AS ADJUNCTIVE THERAPY IN CHILDREN 4 -16 YEARS OF AGE WITH PARTIAL ONSET SEIZURES

Summary

| | |
|--------------------------|---|
| EudraCT number | 2010-020852-79 |
| Trial protocol | CZ LT FI NL FR HU BE EE SE PL AT GR IT BG |
| Global end of trial date | 10 August 2016 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 16 February 2017 |
| First version publication date | 16 February 2017 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | A0081041 |
|-----------------------|----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Pfizer, Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, 110017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, 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 | 10 August 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 August 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of 2 dose levels of pregabalin (Level 1: 2.5 mg/kg/day [maximum 150 mg/day] and Level 2: 10 mg/kg/day [maximum 600 mg/day]) compared to placebo as an adjunctive treatment in reducing the frequency of partial onset seizures in pediatric subjects 4 to 16 years of age.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 27 September 2011 |
| 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 | Belgium: 8 |
| Country: Number of subjects enrolled | Bulgaria: 2 |
| Country: Number of subjects enrolled | Czech Republic: 5 |
| Country: Number of subjects enrolled | France: 6 |
| Country: Number of subjects enrolled | Greece: 4 |
| Country: Number of subjects enrolled | Hungary: 48 |
| Country: Number of subjects enrolled | Israel: 1 |
| Country: Number of subjects enrolled | Italy: 3 |
| Country: Number of subjects enrolled | Korea, Republic of: 7 |
| Country: Number of subjects enrolled | Malaysia: 4 |
| Country: Number of subjects enrolled | Philippines: 64 |
| Country: Number of subjects enrolled | Poland: 13 |
| Country: Number of subjects enrolled | Romania: 27 |
| Country: Number of subjects enrolled | Serbia: 14 |
| Country: Number of subjects enrolled | Singapore: 8 |
| Country: Number of subjects enrolled | Turkey: 6 |
| Country: Number of subjects enrolled | Ukraine: 55 |
| Country: Number of subjects enrolled | United States: 20 |

| | |
|------------------------------------|-----|
| Worldwide total number of subjects | 295 |
| EEA total number of subjects | 116 |

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) | 173 |
| Adolescents (12-17 years) | 122 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The subjects for the study were enrolled from 18 countries. The study start date was 29-Sep-2011 and the study completion date was 10-Aug-2016.

Period 1

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

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day |

Arm description:

Subjects aged 4 to 16 years and less than (<) 30 kilograms (kg) in weight, received pregabalin 3.5 milligram per kilogram per day (mg/kg/day) (up to a maximum of 150 mg/day) oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months). Subjects aged 4 to 16 years and greater than or equal to (\geq) 30 kg in weight, received pregabalin 2.5 mg/kg/day (up to a maximum of 150 mg/day) capsule or oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months).

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Pregabalin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects aged 4 to 16 years and < 30 kilograms (kg) in weight, received pregabalin 3.5 mg/kg/day (up to a maximum of 150 mg/day) oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months). Subjects aged 4 to 16 years and \geq 30 kg in weight, received pregabalin 2.5 mg/kg/day (up to a maximum of 150 mg/day) capsule or oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months).

| | |
|------------------|--|
| Arm title | Pregabalin: 10 mg/kg/day or 14 mg/kg/day |
|------------------|--|

Arm description:

Subjects aged 4 to 16 years and < 30 kg in weight, received pregabalin 14 mg/kg/day (up to a maximum of 600 mg/day) oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months). Subjects aged 4 to 16 years and \geq 30 kg in weight, received pregabalin 10 mg/kg/day (up to a maximum of 600 mg/day) capsule or oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months).

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Pregabalin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects aged 4 to 16 years and < 30 kilograms (kg) in weight, received pregabalin 14 mg/kg/day (up to a maximum of 600 mg/day) oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months). Subjects aged 4 to 16 years and \geq 30 kg in weight,

received pregabalin 10 mg/kg/day (up to a maximum of 600 mg/day) capsule or oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months).

| | |
|---|-----------------|
| Arm title | Placebo |
| Arm description: Subjects aged 4 to 16 years received placebo matched to pregabalin, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months). Subjects <30 kg in weight received placebo in the form of oral solution while subjects ≥30 kg in weight received placebo in the form of oral solution or capsule. | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 1 | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo |
|---------------------------------------|--|--|---------|
| Started | 104 | 97 | 94 |
| Completed | 94 | 81 | 84 |
| Not completed | 10 | 16 | 10 |
| Adverse event, serious fatal | - | 1 | - |
| Consent withdrawn by subject | 1 | 2 | 2 |
| Adverse event, non-fatal | 1 | 4 | - |
| Insufficient Clinical Response | 3 | 4 | 5 |
| Protocol deviation | 3 | 4 | 3 |
| Other Unspecified | 2 | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day |
|-----------------------|--|

Reporting group description:

Subjects aged 4 to 16 years and less than (<) 30 kilograms (kg) in weight, received pregabalin 3.5 milligram per kilogram per day (mg/kg/day) (up to a maximum of 150 mg/day) oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months). Subjects aged 4 to 16 years and greater than or equal to (>=) 30 kg in weight, received pregabalin 2.5 mg/kg/day (up to a maximum of 150 mg/day) capsule or oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months).

| | |
|-----------------------|--|
| Reporting group title | Pregabalin: 10 mg/kg/day or 14 mg/kg/day |
|-----------------------|--|

Reporting group description:

Subjects aged 4 to 16 years and < 30 kg in weight, received pregabalin 14 mg/kg/day (up to a maximum of 600 mg/day) oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months). Subjects aged 4 to 16 years and >= 30 kg in weight, received pregabalin 10 mg/kg/day (up to a maximum of 600 mg/day) capsule or oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months).

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

Reporting group description:

Subjects aged 4 to 16 years received placebo matched to pregabalin, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months). Subjects <30 kg in weight received placebo in the form of oral solution while subjects >=30 kg in weight received placebo in the form of oral solution or capsule.

| Reporting group values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo |
|--|--|--|---------|
| Number of subjects | 104 | 97 | 94 |
| 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) | 62 | 59 | 52 |
| Adolescents (12-17 years) | 42 | 38 | 42 |
| 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 | 10.2 | 10.1 | 10.3 |
| standard deviation | ± 3.9 | ± 3.5 | ± 3.7 |
| Gender, Male/Female Units: Subjects | | | |
| Female | 52 | 41 | 40 |
| Male | 52 | 56 | 54 |

| Reporting group values | Total | | |
|------------------------|-------|--|--|
| Number of subjects | 295 | | |

| | | | |
|---|-----|--|--|
| Age categorical Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 173 | | |
| Adolescents (12-17 years) | 122 | | |
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age Continuous Units: years arithmetic mean standard deviation | - | | |
| Gender, Male/Female Units: Subjects | | | |
| Female | 133 | | |
| Male | 162 | | |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day |
| Reporting group description: Subjects aged 4 to 16 years and less than (<) 30 kilograms (kg) in weight, received pregabalin 3.5 milligram per kilogram per day (mg/kg/day) (up to a maximum of 150 mg/day) oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months). Subjects aged 4 to 16 years and greater than or equal to (>=) 30 kg in weight, received pregabalin 2.5 mg/kg/day (up to a maximum of 150 mg/day) capsule or oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months). | |
| Reporting group title | Pregabalin: 10 mg/kg/day or 14 mg/kg/day |
| Reporting group description: Subjects aged 4 to 16 years and < 30 kg in weight, received pregabalin 14 mg/kg/day (up to a maximum of 600 mg/day) oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months). Subjects aged 4 to 16 years and >= 30 kg in weight, received pregabalin 10 mg/kg/day (up to a maximum of 600 mg/day) capsule or oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months). | |
| Reporting group title | Placebo |
| Reporting group description: Subjects aged 4 to 16 years received placebo matched to pregabalin, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months). Subjects <30 kg in weight received placebo in the form of oral solution while subjects >=30 kg in weight received placebo in the form of oral solution or capsule. | |

Primary: Log-Transformed 28-Day Seizure Rate For All Partial Onset Seizures During Baseline Phase

| | |
|---|---|
| End point title | Log-Transformed 28-Day Seizure Rate For All Partial Onset Seizures During Baseline Phase ^[1] |
| End point description: All partial onset seizures experienced during baseline phase were recorded by the subjects or their parents/legal guardian, in a daily seizure diary. 28-day seizure rate for all partial onset seizures = ([number of seizures in the baseline phase] divided by [number of days in baseline phase minus {-} number of missing diary days in baseline phase])*28. For log-transformation, the quantity 1 was added to the 28-day seizure rate for all subjects to account for any possible "0" seizure incidence. This resulted in final calculation as: log transformed (28-day seizure rate +1). | |
| End point type | Primary |
| End point timeframe: Baseline phase (up to 8 weeks prior to treatment phase [Day 1]) | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: For baseline, Only descriptive data was planned to be analyzed for this endpoint.

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|--------------------------------------|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 | 97 | 93 | |
| Units: Seizures per 28 days | | | | |
| arithmetic mean (standard deviation) | 3.27 (± 1.215) | 3.19 (± 1.269) | 3.18 (± 1.302) | |

Statistical analyses

No statistical analyses for this end point

Primary: Log-Transformed 28-Day Seizure Rate For All Partial Onset Seizures During 12-Week Treatment Phase

| | |
|-----------------|---|
| End point title | Log-Transformed 28-Day Seizure Rate For All Partial Onset Seizures During 12-Week Treatment Phase |
|-----------------|---|

End point description:

All partial onset seizures experienced during treatment phase were recorded by the subjects or their parents/legal guardian in a daily seizure diary. 28-day seizure rate for all partial onset seizures = ([number of seizures in the treatment phase] divided by [number of days in treatment phase minus {-} number of missing diary days in treatment phase])*28. For log-transformation, the quantity 1 was added to the 28-day seizure rate for all subjects to account for any possible "0" seizure incidence. This resulted in final calculation as: log transformed (28-day seizure rate +1).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 1 up to Week 12

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|-------------------------------------|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 103 | 96 | 93 | |
| Units: Seizures per 28 days | | | | |
| least squares mean (standard error) | 2.86 (± 0.07) | 2.74 (± 0.072) | 2.96 (± 0.073) | |

Statistical analyses

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

Statistical analysis description:

Linear Model With Log transformed baseline seizure rate as continuous covariate and geographic regions, treatment groups and weight as fixed effects.

| | |
|---|--|
| Comparison groups | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day v Placebo |
| Number of subjects included in analysis | 196 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2577 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.29 |
| upper limit | 0.08 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.092 |

| | |
|--|--|
| Statistical analysis title | Statistical Analysis 2 |
| Statistical analysis description: Linear Model With Log transformed baseline seizure rate as continuous covariate and geographic regions, treatment groups and weight as fixed effects. | |
| Comparison groups | Pregabalin: 10 mg/kg/day or 14 mg/kg/day v Placebo |
| Number of subjects included in analysis | 189 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0185 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.22 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.41 |
| upper limit | -0.04 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.094 |

Secondary: Percentage of Participants With at Least 50 Percent (%) or Greater Reduction From Baseline in 28-day Seizure Rate During the 12 Week Treatment Phase

| | |
|-----------------|--|
| End point title | Percentage of Participants With at Least 50 Percent (%) or Greater Reduction From Baseline in 28-day Seizure Rate During the 12 Week Treatment Phase |
|-----------------|--|

End point description:

Percentage of subjects with 50 percent (%) or greater reduction from baseline in 28-day seizure rate during the 12 week treatment phase were reported. 28-day seizure rate for all partial onset seizures = ([number of seizures in the treatment phase] divided by [number of days in treatment phase minus {-} number of missing diary days in treatment phase])*28.

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

End point timeframe:

Day 1 up to Week 12

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|-------------------------------|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 | 97 | 93 | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 29.1 | 40.6 | 22.6 | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|--|
| Statistical analysis description: P-values were from a Logistic Regression Model including fixed effects for treatment, weight group, and geographical region. | |
| Comparison groups | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day v Placebo |
| Number of subjects included in analysis | 197 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8024 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.036 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.528 |
| upper limit | 2.03 |

| Statistical analysis title | Statistical Analysis 2 |
|---|--|
| Statistical analysis description: P-values were from a Logistic Regression Model including fixed effects for treatment, weight group, and geographical region. | |
| Comparison groups | Pregabalin: 10 mg/kg/day or 14 mg/kg/day v Placebo |
| Number of subjects included in analysis | 190 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0092 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.636 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.851 |
| upper limit | 3.147 |

Other pre-specified: Number of Subjects With Treatment-Emergent Adverse Events (AEs) or Serious Adverse Events (SAEs)

| | |
|-----------------|--|
| End point title | Number of Subjects With Treatment-Emergent Adverse Events (AEs) or Serious Adverse Events (SAEs) |
|-----------------|--|

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent were events between first dose of study drug and up to 7 days after last dose of study drug (up to 13 weeks) that were absent before treatment or that worsened

relative to pre- treatment state. AEs included both serious and non-serious adverse events.

| | |
|---|---------------------|
| End point type | Other pre-specified |
| End point timeframe: | |
| Day 1 up to 7 days after last dose of study drug (up to 13 weeks) | |

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|-----------------------------|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 | 97 | 94 | |
| Units: subjects | | | | |
| AEs | 67 | 68 | 56 | |
| SAEs | 5 | 10 | 7 | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Treatment Emergent Treatment-Related Adverse Events (AEs) and Serious Adverse Events (SAEs)

| | |
|-----------------|---|
| End point title | Number of Subjects With Treatment Emergent Treatment-Related Adverse Events (AEs) and Serious Adverse Events (SAEs) |
|-----------------|---|

End point description:

Treatment-related AE was any untoward medical occurrence attributed to study drug in a subject who received study drug. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent were events between first dose of study drug and up to 7 days after last dose of study drug (up to 13 weeks) that were absent before treatment or that worsened relative to pre-treatment state. Relatedness to drug was assessed by the investigator. AEs included both serious and non-serious adverse events.

| | |
|---|---------------------|
| End point type | Other pre-specified |
| End point timeframe: | |
| Day 1 up to 7 days after last dose of study drug (up to 13 weeks) | |

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|-----------------------------|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 | 97 | 94 | |
| Units: subjects | | | | |
| AEs | 37 | 46 | 30 | |
| SAEs | 1 | 1 | 1 | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Adverse Events by Severity

| | |
|-----------------|--------------------------------------|
| End point title | Number of Adverse Events by Severity |
|-----------------|--------------------------------------|

End point description:

An AE was any untoward medical occurrence attributed to study drug in a subject who received study drug. AEs were classified according to the severity in 3 categories a) mild: AEs does not interfere with subject's usual function b) moderate: AEs interferes to some extent with subject's usual function c) severe: AEs interferes significantly with subject's usual function.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Day 1 up to 7 days after last dose of study drug (up to 13 weeks)

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|-----------------------------|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 | 97 | 94 | |
| Units: events | | | | |
| Mild | 144 | 162 | 126 | |
| Moderate | 33 | 31 | 21 | |
| Severe | 7 | 3 | 5 | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Child Behaviour Checklist (CBCL): Internalizing Subscale Score in Subjects Less Than 6 Years of Age

| | |
|-----------------|---|
| End point title | Child Behaviour Checklist (CBCL): Internalizing Subscale Score in Subjects Less Than 6 Years of Age |
|-----------------|---|

End point description:

CBCL assessed suicidal behavior in children below 6 years. It is 100-item questionnaire completed by parent/legal guardian, based on subject's behavior in past 2 months. All 100 items rated on 3-point scale: 0=not true for that child; 1=sometimes true; 2=very/often true. Total CBCL score ranges from 0 (not true) to 200 (very/often true). Higher scores=higher levels of problematic behaviors or dysfunction. Scores from all items were used to calculate 3 subscale scores: Withdrawn subscale scores, Internalizing problems subscale scores and total problem subscale scores. All subscale scores reported scaled to T Scores. In this study, a cut-off of ≥ 68 on the T-scores was used for all 3 subscales. If a subject T Score was ≥ 68 in any of the sub-scales, the subject was referred for Mental Health Risk Assessment that included assessment of subject continuation to the study. Safety population. N=subjects evaluable for endpoint, n=number of subjects evaluable for specific categories.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Week -8 (8 weeks prior to Day 1 of treatment), Week -4 (4 weeks prior to Day 1 of treatment), Day 1 (Week 0), Week 1, 2, 3, 6, 9, 12, end of study visit (Week 13)

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|--------------------------------------|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 12 | 14 | 14 | |
| Units: T scores | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week -8 (n= 12, 14, 14) | 48.3 (± 12.12) | 55.1 (± 9.37) | 54.9 (± 11.15) | |
| Week -4 (n= 12, 14, 14) | 48.1 (± 12.12) | 50.9 (± 7.01) | 52.6 (± 9.19) | |
| Week 0 (n= 12, 14, 14) | 46.4 (± 14.14) | 49.1 (± 7.08) | 50.6 (± 9.61) | |
| Week 1 (n= 12, 13, 14) | 46.3 (± 14.47) | 48.7 (± 9.36) | 50.7 (± 9.47) | |
| Week 2 (n= 11, 13, 13) | 46.5 (± 14.45) | 45.6 (± 8.21) | 48.3 (± 10.93) | |
| Week 3 (n= 12, 14, 13) | 45.6 (± 13.33) | 44.2 (± 9.37) | 49.6 (± 10.38) | |
| Week 6 (n= 11, 13, 11) | 45.5 (± 16.73) | 42.1 (± 9.65) | 47.5 (± 15.19) | |
| Week 9 (n= 11, 13, 11) | 46 (± 15.43) | 40.6 (± 10.19) | 51 (± 9.81) | |
| Week 12 (n= 11, 14, 13) | 42.1 (± 11.99) | 40.8 (± 8.95) | 50.5 (± 8.91) | |
| Week 13 (n= 12, 14, 11) | 44.3 (± 13.61) | 39.9 (± 7.77) | 50.8 (± 10.23) | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Child Behaviour Checklist (CBCL): Withdraw Subscale Score in Subjects Less Than 6 Years of Age

| | |
|-----------------|--|
| End point title | Child Behaviour Checklist (CBCL): Withdraw Subscale Score in Subjects Less Than 6 Years of Age |
|-----------------|--|

End point description:

CBCL assessed suicidal behavior in children below 6 years. It is 100-item questionnaire completed by parent/legal guardian, based on subject's behavior in past 2 months. All 100 items rated on 3-point scale: 0=not true for that child; 1=sometimes true; 2=very/often true. Total CBCL score ranges from 0 (not true) to 200 (very/often true). Higher scores=higher levels of problematic behaviors or dysfunction. Scores from all items were used to calculate 3 subscale scores: Withdrawn subscale scores, Internalizing problems subscale scores and total problem subscale scores. All subscale scores reported scaled to T Scores. In this study, a cut-off of ≥ 68 on the T-scores was used for all 3 subscales. If a subject T Score was ≥ 68 in any of the sub-scales, the subject was referred for Mental Health Risk Assessment that included assessment of subject continuation to the study Safety population. N= subjects evaluable for endpoint, n=number of subjects evaluable for specific categories.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Week -8 (8 weeks prior to Day 1 of treatment), Week -4 (4 weeks prior to Day 1 of treatment), Day 1 (Week 0), Week 1, 2, 3, 6, 9, 12, end of study visit (Week 13)

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|--------------------------------------|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 12 | 14 | 14 | |
| Units: T scores | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week -8 (n= 12, 14, 14) | 56.4 (± 6.04) | 64 (± 10.29) | 63.1 (± 10.5) | |
| Week -4 (n= 12, 14, 14) | 55.4 (± 5.43) | 61.3 (± 8.99) | 61.9 (± 10.48) | |
| Week 0 (n= 12, 14, 14) | 56.6 (± 6.68) | 60.6 (± 8.06) | 60.9 (± 10.86) | |
| Week 1 (n= 12, 13, 14) | 56.8 (± 7.12) | 60.9 (± 10.01) | 59.5 (± 10.09) | |
| Week 2 (n= 11, 13, 13) | 56.3 (± 6.17) | 60.2 (± 9.32) | 59.2 (± 11.61) | |
| Week 3 (n= 12, 14, 13) | 54.8 (± 6.8) | 58.6 (± 8.53) | 60.8 (± 11.02) | |
| Week 6 (n= 11, 13, 11) | 55.5 (± 8.29) | 56.6 (± 5.24) | 54.5 (± 20.82) | |
| Week 9 (n= 11, 13, 11) | 56.1 (± 6.99) | 57.1 (± 7.3) | 60 (± 10.64) | |
| Week 12 (n= 11, 14, 13) | 54 (± 5.48) | 57.3 (± 9.53) | 59.6 (± 10.11) | |
| Week 13 (n= 12, 14, 11) | 55.1 (± 6.43) | 56.1 (± 7.21) | 57.9 (± 10.58) | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Child Behaviour Checklist (CBCL): Total Problem Subscale Score in Subjects Less Than 6 Years of Age

| | |
|-----------------|---|
| End point title | Child Behaviour Checklist (CBCL): Total Problem Subscale Score in Subjects Less Than 6 Years of Age |
|-----------------|---|

End point description:

CBCL assessed suicidal behavior in children below 6 years. It is 100-item questionnaire completed by parent/legal guardian, based on subject's behavior in past 2 months. All 100 items rated on 3-point scale: 0=not true for that child; 1=sometimes true; 2=very/often true. Total CBCL score ranges from 0 (not true) to 200 (very/often true). Higher scores=higher levels of problematic behaviors or dysfunction. Scores from all items were used to calculate 3 subscale scores: Withdrawn subscale scores, Internalizing problems subscale scores and total problem subscale scores. All subscale scores reported scaled to T Scores. In this study, a cut-off of ≥ 68 on the T-scores was used for all 3 subscales. If a subject T Score was ≥ 68 in any of the sub-scales, the subject was referred for Mental Health Risk Assessment that included assessment of subject continuation to the study Safety population. N= subjects evaluable for endpoint, n=number of subjects evaluable for specific categories.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Week -8 (8 weeks prior to Day 1 of treatment), Week -4 (4 weeks prior to Day 1 of treatment), Day 1 (Week 0), Week 1, 2, 3, 6, 9, 12, end of study visit (Week 13)

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|--------------------------------------|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 12 | 14 | 14 | |
| Units: T scores | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week -8 (n= 12, 14, 14) | 48 (± 10.84) | 50.7 (± 11.48) | 54.1 (± 10.94) | |
| Week -4 (n= 12, 14, 14) | 47.8 (± 11.04) | 47 (± 8.36) | 52.5 (± 7.35) | |

| | | | | |
|-------------------------|----------------|---------------|---------------|--|
| Week 0 (n= 12, 14, 14) | 46.9 (± 11.75) | 45.2 (± 7.79) | 50.1 (± 8.81) | |
| Week 1 (n= 12, 13, 14) | 46 (± 13.65) | 43.8 (± 9.77) | 50.1 (± 8.4) | |
| Week 2 (n= 11, 13, 13) | 46.5 (± 13.17) | 42.1 (± 7.77) | 48.9 (± 8.95) | |
| Week 3 (n= 12, 14, 13) | 46.4 (± 12.64) | 42.4 (± 9.16) | 49.5 (± 9.81) | |
| Week 6 (n= 11, 13, 11) | 46.7 (± 15.25) | 38.7 (± 5.95) | 50.7 (± 8.86) | |
| Week 9 (n= 11, 13, 11) | 47.6 (± 13.13) | 38.4 (± 5.91) | 51.2 (± 9.12) | |
| Week 12 (n= 11, 14, 13) | 44.3 (± 11.78) | 39 (± 8.94) | 50.2 (± 9.28) | |
| Week 13 (n= 12, 14, 11) | 45.5 (± 13.28) | 37.9 (± 8.45) | 51.6 (± 9.53) | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Cognitive Test Battery (CogState Battery) Score at Week 12: Detection Task

| | |
|--|--|
| End point title | Change From Baseline in Cognitive Test Battery (CogState Battery) Score at Week 12: Detection Task |
| End point description: | |
| CogState battery:computerized test battery assessing cognitive domains through cognition tasks. Test battery presented on computer with external response buttons.In the study,Cogstate battery:2 tasks to measure psychomotor function (detection task);attention (paediatric identification task).Detection task:measure of simple reaction time and provided a valid assessment of psychomotor function in subjects.In this task, a playing card turning face up was presented in the center of the computer screen.As soon this happened, the subject was to press the 'Yes' response key.There was no minimum or maximum scores as it was a time-based assessment.Software measured the speed of accurate responses to each event.In the endpoint,speed of performance of subjects(calculated as mean of the logarithmic base 10 transformed reaction times) for correct responses was reported.Lower scores=better performance.Safety population.N=subjects evaluable for endpoint,n=subjects evaluable for specific | |
| End point type | Other pre-specified |
| End point timeframe: | |
| Baseline (pre-dose at Day 1), Week 12 | |

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|--------------------------------------|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 74 | 61 | 66 | |
| Units: log10 milliseconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n= 68, 56, 60) | 2.71 (± 0.21) | 2.72 (± 0.2) | 2.7 (± 0.18) | |
| Change At Week 12 (n= 61, 45, 53) | 0 (± 0.12) | -0.03 (± 0.12) | 0.01 (± 0.09) | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Cognitive Test Battery (CogState

Battery) Score at Week 12: Paediatric Identification (Go-No Go: attention) Tasks

| | |
|-----------------|---|
| End point title | Change From Baseline in Cognitive Test Battery (CogState Battery) Score at Week 12: Paediatric Identification (Go-No Go: attention) Tasks |
|-----------------|---|

End point description:

CogState battery: computerized test battery assessing cognitive domains through cognition tasks. Test battery was presented on computer with external response buttons. Paediatric identification task: a measure of choice reaction time and valid assessment of visual attention. In this, a playing card turning face up was presented in center of the computer screen. As soon this happened, participant had to decide whether color of card was black or not. If color was black, subject was to press "Yes" response key, otherwise "no". No minimum/maximum scores as it was a time-based assessment. Software measured speed of accurate responses (correct identification of color) to each event. In this endpoint, speed of performance of subjects to correctly identify the color (calculated as mean of the logarithmic base 10 transformed reaction times) for correct responses was reported. Lower scores = better performance. Safety population. N = subjects evaluable for endpoint, n = subjects evaluable for specific categories.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline (pre-dose at Day 1), Week 12

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|--------------------------------------|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 74 | 61 | 66 | |
| Units: log10 milliseconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 67, 56, 59) | 2.81 (± 0.15) | 2.8 (± 0.15) | 2.8 (± 0.14) | |
| Change At Week 12 (n = 60, 44, 51) | 0 (± 0.11) | 0 (± 0.12) | 0 (± 0.1) | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Clinically Significant Laboratory Abnormalities

| | |
|-----------------|---|
| End point title | Number of Subjects With Clinically Significant Laboratory Abnormalities |
|-----------------|---|

End point description:

Criteria for abnormality: hematology (hemoglobin, hematocrit, red blood cells count: <0.8*lower limit of normal [LLN], platelets: <0.5*LLN/greater than [>]1.75*upper limit of normal [ULN], leukocytes: <0.6*LLN or >1.5*ULN, lymphocytes, total neutrophils: <0.8*LLN or >1.2*ULN, basophils, eosinophil, monocytes: >1.2*ULN); Liver Function (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, Gamma glutamyl transferase: >0.3*ULN, total protein, albumin: <0.8*LLN or >1.2*ULN); bilirubin: >1.5*ULN; renal function (blood urea nitrogen, creatinine: >1.3*ULN); Electrolytes (sodium: <0.95*LLN or >1.05*ULN, potassium, chloride, calcium, bicarbonate: <0.9*LLN or >1.1*ULN); Lipids (cholesterol, triglycerides >1.3*ULN); creatine kinase: >2.0*ULN; glucose fasting: <0.6*LLN or >1.5*ULN, urine white blood corpuscles and RBC: >= 20/High Power Field [HPF]; urine casts: >1/Low Power Field (LPF); urine bacteria: >20/HPF. Hormones (tetraiodothyronine and thyroid stimulating hormone: <0.8*LLN or >1.2*ULN). Safety population.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline (from 8 weeks prior to Day 1 of treatment) up to Week 13

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|-----------------------------|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 102 | 95 | 93 | |
| Units: subjects | 61 | 63 | 61 | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Vital Signs Abnormalities

| | |
|---|---|
| End point title | Number of Subjects With Vital Signs Abnormalities |
| End point description: | |
| Criteria for abnormalities in vital signs included: sitting systolic blood pressure (SBP) values: maximum increase and decrease of ≥ 30 millimeter of mercury (mmHg) from baseline; sitting diastolic blood pressure (DBP) value: maximum increase and decrease of ≥ 20 mmHg from baseline. Safety population included all randomized subjects who took at least 1 dose of the study drug. Here, "N" signifies number of subjects who were evaluable for this endpoint. | |
| End point type | Other pre-specified |
| End point timeframe: | |
| Baseline (from 8 weeks prior to Day 1 of treatment) up to Week 13 | |

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|---|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 98 | 93 | 92 | |
| Units: subjects | | | | |
| Maximum Increase from Baseline in Sitting SBP | 2 | 1 | 1 | |
| Maximum Increase from Baseline in Sitting DBP | 6 | 8 | 11 | |
| Maximum Decrease from Baseline in Sitting SBP | 5 | 1 | 1 | |
| Maximum Decrease from Baseline in Sitting DBP | 15 | 6 | 10 | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Clinically Significant Change From Baseline in Neurological Examinations at Week 13

| | |
|---|---|
| End point title | Number of Subjects With Clinically Significant Change From Baseline in Neurological Examinations at Week 13 |
| End point description: Neurological examinations included: level of consciousness, mental status, cranial nerve assessment, muscle strength and tone, reflexes, pin prick and vibratory sensation (the latter using a 128-Hertz tuning fork), coordination and gait. Clinical significance was based on investigator's discretion. | |
| End point type | Other pre-specified |
| End point timeframe: Baseline (from 8 weeks prior to Day 1 of treatment) up to Week 13 | |

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|-----------------------------|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 | 97 | 94 | |
| Units: subjects | 0 | 1 | 0 | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Electrocardiogram (ECG) Abnormalities

| | |
|--|---|
| End point title | Number of Subjects With Electrocardiogram (ECG) Abnormalities |
| End point description: Criteria for abnormalities in:1) Time from ECG Q wave to the end of the S wave corresponding to ventricle depolarization (QRS complex): ≥ 140 milliseconds (msec);2) The interval between the start of the P wave and the start of the QRS complex,corresponding to the time between the onset of the atrial depolarization and onset of ventricular depolarization (PR interval): ≥ 200 msec;3)Time from ECG Q wave to the end of the T wave corresponding to electrical systole corrected for heart rate using Fridericia's formula (QTcf interval):absolute value 450 to < 480 msec, 480 to < 500 msec, ≥ 500 msec; 4) Maximum QT interval: ≥ 500 msec;5) Maximum QTcB interval (Bazett's correction):450 to < 480 msec,480 to < 500 msec, ≥ 500 msec.Only the categories of ECG abnormalities in which subjects were found abnormal, were reported in this endpoint.Safety population =all randomized subjects who took at least 1 dose of the study drug.Here,"N" signifies number of subjects who were evaluable for this endpoint. | |
| End point type | Other pre-specified |
| End point timeframe: Baseline (from 8 weeks prior to Day 1 of treatment) up to Week 13 | |

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|-----------------------------|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 102 | 97 | 94 | |
| Units: subjects | | | | |
| Maximum PR Interval | 1 | 0 | 1 | |

| | | | | |
|---|---|---|---|--|
| Maximum QT/QTc Interval (Bazett's Correction) | 2 | 0 | 2 | |
|---|---|---|---|--|

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Clinically Significant Change From Baseline in Physical Examinations at Week 13

| | |
|---|---|
| End point title | Number of Subjects With Clinically Significant Change From Baseline in Physical Examinations at Week 13 |
| End point description: Physical examinations evaluated the following body systems/organs: general appearance; dermatological; head and eyes; ears, nose, mouth, and throat; pulmonary; cardiovascular; abdominal; genitourinary (optional); lymphatic; musculoskeletal/extremities; and neurological. Clinical significance was determined by the investigator. Safety population included all randomized subjects who took at least 1 dose of the study drug. | |
| End point type | Other pre-specified |
| End point timeframe: Baseline (from 8 weeks prior to Day 1 of treatment) up to Week 13 | |

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|-----------------------------|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 | 97 | 94 | |
| Units: subjects | 5 | 5 | 2 | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects (6-16 Years of Age) With Positive Response to Columbia Suicide-Severity Rating Scale (C-SSRS) According to the Columbia Classification Algorithm of Suicide Assessment (C-CASA) Categories At Baseline

| | |
|--|---|
| End point title | Number of Subjects (6-16 Years of Age) With Positive Response to Columbia Suicide-Severity Rating Scale (C-SSRS) According to the Columbia Classification Algorithm of Suicide Assessment (C-CASA) Categories At Baseline |
| End point description: C-SSRS (mapped to C-CASA):subject-rated questionnaire assessing suicidal ideation and suicidal behavior.For suicidal ideation and behaviour,data from C-SSRS was mapped to C-CASA codes 1, 2, 3, 4 and 7.C-SSRS assessed whether subject experienced following:completed suicide (C-CASA code 1);suicide attempt (response of "Yes" on "actual attempt")(C-CASA code 2);preparatory acts toward imminent suicidal behavior (ISB)("Yes" on "preparatory acts or behavior")(C-CASA code 3);suicidal ideation("Yes" on "wish to be dead", "non-specific active suicidal thoughts", "active suicidal ideation with methods without intent to act or some intent to act,without specific plan or with specific plan and intent) | |

(C-CASA code 4);any self-injurious behavior with no suicidal intent (C-CASA code 7).In this endpoint, number of subjects with positive response (response of "yes") to C-SSRS (mapped to C-CASA categories 2, 3, 4 and 7) at baseline were reported.Safety population.N= subjects evaluable for endpoint.

| | |
|---|---------------------|
| End point type | Other pre-specified |
| End point timeframe: | |
| Baseline (4 week prior to Day 1 of treatment) | |

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|--|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 92 | 81 | 80 | |
| Units: subjects | | | | |
| Suicide attempt (C-CASA code 2) | 0 | 0 | 0 | |
| Preparatory acts towards ISB (C-CASA code 3) | 0 | 0 | 0 | |
| Suicidal ideation (C-CASA code 4) | 0 | 0 | 0 | |
| Self injurious behavior (C-CASA code 7) | 1 | 1 | 1 | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects (6-16 Years of Age) With Positive Response to Columbia Suicide-Severity Rating Scale (C-SSRS) According to the Columbia Classification Algorithm of Suicide Assessment (C-CASA) Categories During Post Baseline Time Period

| | |
|-----------------|--|
| End point title | Number of Subjects (6-16 Years of Age) With Positive Response to Columbia Suicide-Severity Rating Scale (C-SSRS) According to the Columbia Classification Algorithm of Suicide Assessment (C-CASA) Categories During Post Baseline Time Period |
|-----------------|--|

End point description:

C-SSRS (mapped to C-CASA):subject-rated questionnaire assessing suicidal ideation and suicidal behavior.For this,data from C-SSRS mapped to C-CASA codes 1, 2, 3, 4 and 7.C-SSRS assessed whether subject experienced following:completed suicide (C-CASA code 1); suicide attempt (response of "Yes" on "actual attempt") (C-CASA code 2);preparatory acts toward imminent suicidal behavior (ISB) ("Yes" on "preparatory acts or behavior")(C-CASA code 3);suicidal ideation("Yes" on "wish to be dead", "non-specific active suicidal thoughts", "active suicidal ideation with methods without intent to act or some intent to act, without specific plan or with specific plan and intent) (C-CASA code 4);any self-injurious behavior with no suicidal intent (C-CASA code 7). Number of subjects with positive response (response of "yes") to C-SSRS (mapped to C-CASA categories 1, 2, 3, 4 and 7) during post baseline time period (Day 1 up to Week 13) were reported. Safety population.N=subjects evaluable for endpoint.

| | |
|----------------------|---------------------|
| End point type | Other pre-specified |
| End point timeframe: | |
| Day 1 up to Week 13 | |

| End point values | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Pregabalin: 10 mg/kg/day or 14 mg/kg/day | Placebo | |
|--|--|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 91 | 83 | 80 | |
| Units: subjects | | | | |
| Completed suicide (C-CASA code 1) | 0 | 0 | 0 | |
| Suicide attempt (C-CASA code 2) | 0 | 0 | 0 | |
| Preparatory acts towards ISB (C-CASA code 3) | 0 | 0 | 0 | |
| Suicidal ideation (C-CASA code 4) | 1 | 0 | 1 | |
| Self injurious behavior (C-CASA code 7) | 1 | 2 | 2 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 1 week after last dose of study drug (Week 13)

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day |
|-----------------------|--|

Reporting group description:

Subjects aged 4 to 16 years and < 30 kg in weight, received pregabalin 3.5 mg/kg/day (up to a maximum of 150 mg/day) oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months). Subjects aged 4 to 16 years and ≥ 30 kg in weight, received pregabalin 2.5 mg/kg/day (up to a maximum of 150 mg/day) capsule or oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months).

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

Reporting group description:

Subjects aged 4 to 16 years received placebo matched to pregabalin, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months). Subjects <30 kg in weight received placebo in the form of oral solution while subjects ≥30 kg in weight received placebo in the form of oral solution or capsule.

| | |
|-----------------------|--|
| Reporting group title | Pregabalin: 10 mg/kg/day or 14 mg/kg/day |
|-----------------------|--|

Reporting group description:

Subjects aged 4 to 16 years and < 30 kg in weight, received pregabalin 14 mg/kg/day (up to a maximum of 600 mg/day) oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months). Subjects aged 4 to 16 years and ≥ 30 kg in weight, received pregabalin 10 mg/kg/day (up to a maximum of 600 mg/day) capsule or oral solution, orally twice daily in equally divided doses, for the double-blind treatment phase of 12 weeks (3 months).

| Serious adverse events | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Placebo | Pregabalin: 10 mg/kg/day or 14 mg/kg/day |
|---|--|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 104 (4.81%) | 7 / 94 (7.45%) | 10 / 97 (10.31%) |
| number of deaths (all causes) | 0 | 0 | 1 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Thermal burn | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (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 |
| Surgical and medical procedures | | | |
| Skin graft | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Drug withdrawal convulsions | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Partial seizures | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (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 |
| Seizure | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 3 / 94 (3.19%) | 3 / 97 (3.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Lymphadenitis | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|----------------|----------------|
| Respiratory, thoracic and mediastinal disorders | | | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Psychiatric disorders | | | |
| Hallucination | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (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 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 1 / 97 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (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 |
| Respiratory tract infection viral | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Pregabalin: 2.5 mg/kg/day or 3.5 mg/kg/day | Placebo | Pregabalin: 10 mg/kg/day or 14 mg/kg/day |
|---|--|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 66 / 104 (63.46%) | 55 / 94 (58.51%) | 64 / 97 (65.98%) |
| Vascular disorders | | | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 2 / 94 (2.13%) | 3 / 97 (3.09%) |
| occurrences (all) | 2 | 2 | 4 |
| Energy increased | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 6 / 104 (5.77%) | 3 / 94 (3.19%) | 4 / 97 (4.12%) |
| occurrences (all) | 6 | 3 | 4 |
| Feeling abnormal | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Feeling hot | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Malaise | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 1 | 1 |
| Pyrexia | | | |
| subjects affected / exposed | 9 / 104 (8.65%) | 7 / 94 (7.45%) | 9 / 97 (9.28%) |
| occurrences (all) | 10 | 8 | 10 |
| Sluggishness | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 2 / 97 (2.06%) |
| occurrences (all) | 0 | 0 | 9 |
| Reproductive system and breast disorders | | | |
| Breast swelling | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pruritus genital | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Bronchial obstruction | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 2 / 94 (2.13%) | 2 / 97 (2.06%) |
| occurrences (all) | 0 | 3 | 2 |
| Cough | | | |
| subjects affected / exposed | 9 / 104 (8.65%) | 3 / 94 (3.19%) | 2 / 97 (2.06%) |
| occurrences (all) | 9 | 3 | 2 |
| Hypopnoea | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Interstitial lung disease | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 2 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 2 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 2 / 104 (1.92%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 2 / 97 (2.06%) |
| occurrences (all) | 1 | 0 | 3 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Psychiatric disorders | | | |
| Abnormal behaviour | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Aggression | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| Agitation | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 1 | 0 | 1 |
| Disinhibition | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Initial insomnia | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 1 | 1 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 1 | 0 | 1 |
| Irritability | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 1 / 94 (1.06%) | 3 / 97 (3.09%) |
| occurrences (all) | 1 | 1 | 3 |
| Middle insomnia | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Mood altered | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Mutism | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Mood swings | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nervousness | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Tic | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|--|-----------------|----------------|------------------|
| Investigations | | | |
| Body temperature increased | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gamma-glutamyl transferase increased | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Heart rate decreased | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Weight increased | | | |
| subjects affected / exposed | 4 / 104 (3.85%) | 4 / 94 (4.26%) | 13 / 97 (13.40%) |
| occurrences (all) | 4 | 4 | 13 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injury, poisoning and procedural complications | | | |
| Clavicle fracture | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Animal bite | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 1 | 0 | 1 |
| Contusion | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 1 / 94 (1.06%) | 2 / 97 (2.06%) |
| occurrences (all) | 1 | 1 | 4 |
| Ear abrasion | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye contusion | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 2 / 97 (2.06%) |
| occurrences (all) | 0 | 0 | 2 |
| Fall | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 104 (0.96%) | 2 / 94 (2.13%) | 2 / 97 (2.06%) |
| occurrences (all) | 1 | 2 | 5 |
| Head injury | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Laceration | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 2 / 104 (1.92%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lip injury | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Periorbital haematoma | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 1 | 1 |
| Scar | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Scratch | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Skin abrasion | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 3 / 94 (3.19%) | 2 / 97 (2.06%) |
| occurrences (all) | 2 | 3 | 2 |
| Soft tissue injury | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Thermal burn | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Wound | | | |

| | | | |
|---|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 104 (0.96%) 1 | 0 / 94 (0.00%) 0 | 1 / 97 (1.03%) 1 |
| Cardiac disorders | | | |
| Atrioventricular block first degree subjects affected / exposed occurrences (all) | 0 / 104 (0.00%) 0 | 1 / 94 (1.06%) 1 | 0 / 97 (0.00%) 0 |
| Nervous system disorders | | | |
| Aphasia subjects affected / exposed occurrences (all) | 1 / 104 (0.96%) 1 | 0 / 94 (0.00%) 0 | 0 / 97 (0.00%) 0 |
| Balance disorder subjects affected / exposed occurrences (all) | 1 / 104 (0.96%) 1 | 0 / 94 (0.00%) 0 | 0 / 97 (0.00%) 0 |
| Clonus subjects affected / exposed occurrences (all) | 0 / 104 (0.00%) 0 | 1 / 94 (1.06%) 1 | 0 / 97 (0.00%) 0 |
| Disturbance in attention subjects affected / exposed occurrences (all) | 1 / 104 (0.96%) 1 | 0 / 94 (0.00%) 0 | 1 / 97 (1.03%) 1 |
| Dizziness subjects affected / exposed occurrences (all) | 4 / 104 (3.85%) 5 | 1 / 94 (1.06%) 1 | 3 / 97 (3.09%) 3 |
| Headache subjects affected / exposed occurrences (all) | 4 / 104 (3.85%) 4 | 6 / 94 (6.38%) 17 | 7 / 97 (7.22%) 12 |
| Hypersomnia subjects affected / exposed occurrences (all) | 2 / 104 (1.92%) 2 | 2 / 94 (2.13%) 2 | 1 / 97 (1.03%) 1 |
| Lethargy subjects affected / exposed occurrences (all) | 2 / 104 (1.92%) 2 | 0 / 94 (0.00%) 0 | 2 / 97 (2.06%) 2 |
| Migraine subjects affected / exposed occurrences (all) | 1 / 104 (0.96%) 1 | 0 / 94 (0.00%) 0 | 0 / 97 (0.00%) 0 |
| Nystagmus | | | |

| | | | |
|---|-------------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 1 / 104 (0.96%) 1 | 0 / 94 (0.00%) 0 | 0 / 97 (0.00%) 0 |
| Partial seizures with secondary generalisation subjects affected / exposed occurrences (all) | 1 / 104 (0.96%) 2 | 1 / 94 (1.06%) 1 | 1 / 97 (1.03%) 1 |
| Poor quality sleep subjects affected / exposed occurrences (all) | 0 / 104 (0.00%) 0 | 0 / 94 (0.00%) 0 | 1 / 97 (1.03%) 1 |
| Psychomotor hyperactivity subjects affected / exposed occurrences (all) | 1 / 104 (0.96%) 1 | 1 / 94 (1.06%) 1 | 0 / 97 (0.00%) 0 |
| Seizure subjects affected / exposed occurrences (all) | 6 / 104 (5.77%) 11 | 4 / 94 (4.26%) 5 | 1 / 97 (1.03%) 1 |
| Somnolence subjects affected / exposed occurrences (all) | 18 / 104 (17.31%) 23 | 13 / 94 (13.83%) 16 | 25 / 97 (25.77%) 50 |
| Tunnel vision subjects affected / exposed occurrences (all) | 1 / 104 (0.96%) 1 | 0 / 94 (0.00%) 0 | 0 / 97 (0.00%) 0 |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 1 / 104 (0.96%) 1 | 0 / 94 (0.00%) 0 | 0 / 97 (0.00%) 0 |
| Lymphadenitis subjects affected / exposed occurrences (all) | 0 / 104 (0.00%) 0 | 1 / 94 (1.06%) 1 | 0 / 97 (0.00%) 0 |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 2 / 104 (1.92%) 2 | 0 / 94 (0.00%) 0 | 3 / 97 (3.09%) 5 |
| Eye disorders Asthenopia subjects affected / exposed occurrences (all) | 0 / 104 (0.00%) 0 | 0 / 94 (0.00%) 0 | 1 / 97 (1.03%) 1 |
| Blepharospasm | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Diplopia | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 10 |
| Eye swelling | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypermetropia | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Myopia | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Visual brightness | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Visual impairment | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 104 (2.88%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 4 | 1 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 3 / 94 (3.19%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 1 / 94 (1.06%) | 3 / 97 (3.09%) |
| occurrences (all) | 1 | 1 | 3 |
| Dental caries | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 4 / 94 (4.26%) | 5 / 97 (5.15%) |
| occurrences (all) | 0 | 4 | 6 |
| Enterocolitis | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lip dry | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nausea | | | |
| subjects affected / exposed | 3 / 104 (2.88%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 4 | 2 | 0 |
| Oral pain | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Retching | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Salivary hypersecretion | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 4 / 97 (4.12%) |
| occurrences (all) | 1 | 0 | 19 |
| Tongue disorder | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tooth disorder | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tooth erosion | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|----------------------|---------------------|---------------------|
| Toothache subjects affected / exposed occurrences (all) | 1 / 104 (0.96%) 1 | 2 / 94 (2.13%) 2 | 0 / 97 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 5 / 104 (4.81%) 6 | 4 / 94 (4.26%) 4 | 4 / 97 (4.12%) 5 |
| Skin and subcutaneous tissue disorders | | | |
| Eczema subjects affected / exposed occurrences (all) | 0 / 104 (0.00%) 0 | 0 / 94 (0.00%) 0 | 2 / 97 (2.06%) 3 |
| Erythema subjects affected / exposed occurrences (all) | 0 / 104 (0.00%) 0 | 0 / 94 (0.00%) 0 | 1 / 97 (1.03%) 1 |
| Rash subjects affected / exposed occurrences (all) | 0 / 104 (0.00%) 0 | 0 / 94 (0.00%) 0 | 1 / 97 (1.03%) 1 |
| Rash erythematous subjects affected / exposed occurrences (all) | 0 / 104 (0.00%) 0 | 0 / 94 (0.00%) 0 | 1 / 97 (1.03%) 1 |
| Rash maculo-papular subjects affected / exposed occurrences (all) | 0 / 104 (0.00%) 0 | 1 / 94 (1.06%) 2 | 0 / 97 (0.00%) 0 |
| Skin erosion subjects affected / exposed occurrences (all) | 0 / 104 (0.00%) 0 | 0 / 94 (0.00%) 0 | 1 / 97 (1.03%) 1 |
| Renal and urinary disorders | | | |
| Urinary retention subjects affected / exposed occurrences (all) | 0 / 104 (0.00%) 0 | 1 / 94 (1.06%) 1 | 0 / 97 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 1 / 104 (0.96%) 1 | 1 / 94 (1.06%) 1 | 0 / 97 (0.00%) 0 |
| Myalgia subjects affected / exposed occurrences (all) | 0 / 104 (0.00%) 0 | 1 / 94 (1.06%) 1 | 0 / 97 (0.00%) 0 |

| | | | |
|----------------------------------|-----------------|----------------|----------------|
| Infections and infestations | | | |
| Ascariasis | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 3 / 94 (3.19%) | 2 / 97 (2.06%) |
| occurrences (all) | 1 | 3 | 2 |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 1 | 0 | 1 |
| Conjunctivitis viral | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermatitis infected | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 2 / 94 (2.13%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 3 / 94 (3.19%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal candidiasis | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Nasopharyngitis | | | |

| | | | |
|-----------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 9 / 104 (8.65%) | 6 / 94 (6.38%) | 7 / 97 (7.22%) |
| occurrences (all) | 9 | 8 | 8 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Parasitic gastroenteritis | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 2 / 104 (1.92%) | 2 / 94 (2.13%) | 3 / 97 (3.09%) |
| occurrences (all) | 2 | 3 | 3 |
| Pharyngotonsillitis | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 1 | 0 | 1 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash pustular | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 2 / 94 (2.13%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 1 | 1 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Tonsillitis | | | |

| | | | |
|---|------------------|----------------|------------------|
| subjects affected / exposed | 1 / 104 (0.96%) | 2 / 94 (2.13%) | 1 / 97 (1.03%) |
| occurrences (all) | 1 | 2 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 10 / 104 (9.62%) | 9 / 94 (9.57%) | 8 / 97 (8.25%) |
| occurrences (all) | 11 | 12 | 10 |
| Varicella | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 1 / 94 (1.06%) | 1 / 97 (1.03%) |
| occurrences (all) | 1 | 1 | 1 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 1 | 1 |
| Viral infection | | | |
| subjects affected / exposed | 2 / 104 (1.92%) | 0 / 94 (0.00%) | 3 / 97 (3.09%) |
| occurrences (all) | 2 | 0 | 3 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 1 | 1 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 0 / 94 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperphagia | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | 1 / 94 (1.06%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Increased appetite | | | |
| subjects affected / exposed | 7 / 104 (6.73%) | 4 / 94 (4.26%) | 10 / 97 (10.31%) |
| occurrences (all) | 7 | 4 | 10 |
| Overweight | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | 0 / 94 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 18 November 2011 | 1- Clarified that mentally or physically handicapped subjects do not have to complete CogState if they are unable.2- Clarified procedure if dose escalation phase not tolerated.3- Clarified that Greek and Cebuano speaking subjects/parents will be excluded. Greek and Cebuano subjects age 6 years and older can be included.4- Added "allergy to pregabalin or excipients..." in exclusion criteria 18.5- On SOA, footnote "d", added information on need for additional pregnancy tests based upon local regulations. |
| 16 March 2015 | 1-Section 3.1 Screening and Baseline: AED changed to anti-epileptic treatments which include VNS; further detail added to diagnostic and risk assessment procedures.2- Section 4.3.1 Contraceptive Guidelines: updated with current standard wording.3- Section 7.2.1 Assessment of Suicidal Ideation: clarifications added.4- Section 9.4 Interim Safety Analysis: added clarifying text regarding E-DMC.5- Protocol Summary: updated, Lyrica approved in 130 countries, considered a PASS study, external DMC added. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported