Clinical trial results:
A 12-Month Open-Label Study To Evaluate The Safety And Tolerability Of Pregabalin As Adjunctive Therapy In Pediatric Subjects 1 Month To 16 Years Of Age With Partial Onset Seizures And Pediatric And Adult Subjects 5 To 65 Years Of Age With Primary Generalized Tonic-Clonic Seizures

Summary

EudraCT number	2011-001412-65
Trial protocol	HU CZ PL EE SE BE FR IT BG GR NL LT FI AT SK ES GB DE HR PT DK
Global end of trial date	22 August 2019

Results information

Result version number	v1 (current)
This version publication date	16 February 2020
First version publication date	16 February 2020

Trial information

Trial identification

Sponsor protocol code	A0081106

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01463306
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 September 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	22 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of pregabalin in pediatric subjects 1 month through 16 years of age with partial onset seizures and pediatric and adult subjects 5 to 65 years of age with primary generalized tonic-clonic (PGTC) seizures.

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 Conference for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 February 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Taiwan: 4
Country: Number of subjects enrolled	Thailand: 2
Country: Number of subjects enrolled	Turkey: 12
Country: Number of subjects enrolled	Ukraine: 162
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 35
Country: Number of subjects enrolled	Belarus: 5
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Bosnia and Herzegovina: 4
Country: Number of subjects enrolled	Bulgaria: 31
Country: Number of subjects enrolled	China: 6
Country: Number of subjects enrolled	Czech Republic: 4
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Greece: 2
Country: Number of subjects enrolled	Hungary: 77
Country: Number of subjects enrolled	India: 8
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Korea, Republic of: 7

Country: Number of subjects enrolled	Lebanon: 6
Country: Number of subjects enrolled	Malaysia: 6
Country: Number of subjects enrolled	Montenegro: 1
Country: Number of subjects enrolled	Philippines: 89
Country: Number of subjects enrolled	Poland: 21
Country: Number of subjects enrolled	Romania: 28
Country: Number of subjects enrolled	Russian Federation: 43
Country: Number of subjects enrolled	Serbia: 21
Country: Number of subjects enrolled	Singapore: 8
Worldwide total number of subjects	605
EEA total number of subjects	184

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)	60
Children (2-11 years)	291
Adolescents (12-17 years)	140
Adults (18-64 years)	114
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Reporting arms are on basis of pediatric and adult subjects who consented to continue from previous studies receiving either pregabalin or placebo and pediatric subjects who directly enrolled in this study. Previous studies- A0081041 (NCT01389596), A0081042 (NCT02072824), A0081105 (NCT01747915).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Pregabalin: Previous and Current

Arm description:

Pediatric and adult subjects with POS and PGTC seizures included in this arm are those who received pregabalin in previous studies. Pregabalin was administered in 3 equally divided doses per day (TID) when age less than (<) 4 years and in 2 equally divided doses per day (BID) when age greater than or equal to (>=) 4 years. Pediatric subjects with body weight >=30 kilogram (kg) received pregabalin 2.5 milligram per kilogram per day (mg/kg/day) as liquid oral solution/capsule up to maximum of 10.0 mg/kg/day and with body weight <30 kg received pregabalin 3.5 mg/kg/day as liquid oral solution up to maximum of 14.0 mg/kg/day. Adult subjects received pregabalin 150 milligram per day (mg/day) as liquid oral solution/oral capsule up to maximum of 600 mg/day. Maximum duration for treatment was 12 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:

Pediatric subjects with body weight >=30 kg received pregabalin 2.5 mg/kg/day as liquid oral solution/capsule up to maximum of 10.0 mg/kg/day and with body weight <30 kg received pregabalin 3.5 mg/kg/day as liquid oral solution up to maximum of 14.0 mg/kg/day. Adult subjects received pregabalin 150 mg/day as liquid oral solution/capsule up to maximum of 600 mg/day.

Arm title	Placebo-Previous to Pregabalin-Current

Arm description:

Pediatric and adult subjects with POS and PGTC seizures included in this arm are those who received placebo in previous studies. Pregabalin was administered TID when age <4 years and BID when age >= 4 years. Pediatric subjects with body weight >=30 kg received pregabalin 2.5 mg/kg/day as liquid oral solution/capsule up to maximum of 10.0 mg/kg/day and with body weight <30 kg received pregabalin 3.5 mg/kg/day as liquid oral solution up to maximum of 14.0 mg/kg/day. Adult subjects received pregabalin 150 mg/day as liquid oral solution/capsule up to maximum of 600 mg/day. Maximum duration for treatment was 12 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:

Pediatric subjects with body weight >=30 kg received pregabalin 2.5 mg/kg/day as liquid oral solution/capsule up to maximum of 10.0 mg/kg/day and with body weight <30 kg received pregabalin 3.5 mg/kg/day as liquid oral solution up to maximum of 14.0 mg/kg/day. Adult subjects received pregabalin 150 mg/day as liquid oral solution/oral capsule up to maximum of 600 mg/day. Maximum duration for treatment was 12 months.

Arm title	Direct Pregabalin

Arm description:

Only pediatric subjects with POS were enrolled in this arm who did not participate in any study previously. Pregabalin was administered TID when age <4 years and BID when age >= 4 years. Pediatric subjects with body weight >=30 kg received pregabalin 2.5 mg/kg/day as liquid oral solution/capsule up to maximum of 10.0 mg/kg/day and with body weight <30 kg received pregabalin 3.5 mg/kg/day as liquid oral solution up to maximum of 14.0 mg/kg/day. Maximum duration for treatment was 12 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:

Pediatric subjects with body weight >=30 kg received pregabalin 2.5 mg/kg/day as liquid oral solution/capsule up to maximum of 10.0 mg/kg/day and with body weight <30 kg received pregabalin 3.5 mg/kg/day as liquid oral solution up to maximum of 14.0 mg/kg/day.

Number of subjects in period 1	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin
Started	384	210	11
Completed	298	158	6
Not completed	86	52	5
Protocol deviation	4	-	-
Death	3	3	-
Lack of efficacy	22	16	1
Approval expiry at site	1	-	-
Unspecified	26	13	-
Consent withdrawn by subject	19	9	1
Adverse Events	6	9	3
Lost to follow-up	5	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Pregabalin: Previous and Current

Reporting group description:

Pediatric and adult subjects with POS and PGTC seizures included in this arm are those who received pregabalin in previous studies. Pregabalin was administered in 3 equally divided doses per day (TID) when age less than (<) 4 years and in 2 equally divided doses per day (BID) when age greater than or equal to (>=) 4 years. Pediatric subjects with body weight >=30 kilogram (kg) received pregabalin 2.5 milligram per kilogram per day (mg/kg/day) as liquid oral solution/capsule up to maximum of 10.0 mg/kg/day and with body weight <30 kg received pregabalin 3.5 mg/kg/day as liquid oral solution up to maximum of 14.0 mg/kg/day. Adult subjects received pregabalin 150 milligram per day (mg/day) as liquid oral solution/oral capsule up to maximum of 600 mg/day. Maximum duration for treatment was 12 months.

Reporting group title	Placebo-Previous to Pregabalin-Current

Reporting group description:

Pediatric and adult subjects with POS and PGTC seizures included in this arm are those who received placebo in previous studies. Pregabalin was administered TID when age <4 years and BID when age >= 4 years. Pediatric subjects with body weight >=30 kg received pregabalin 2.5 mg/kg/day as liquid oral solution/capsule up to maximum of 10.0 mg/kg/day and with body weight <30 kg received pregabalin 3.5 mg/kg/day as liquid oral solution up to maximum of 14.0 mg/kg/day. Adult subjects received pregabalin 150 mg/day as liquid oral solution/capsule up to maximum of 600 mg/day. Maximum duration for treatment was 12 months.

Reporting group title	Direct Pregabalin

Reporting group description:

Only pediatric subjects with POS were enrolled in this arm who did not participate in any study previously. Pregabalin was administered TID when age <4 years and BID when age >= 4 years. Pediatric subjects with body weight >=30 kg received pregabalin 2.5 mg/kg/day as liquid oral solution/capsule up to maximum of 10.0 mg/kg/day and with body weight <30 kg received pregabalin 3.5 mg/kg/day as liquid oral solution up to maximum of 14.0 mg/kg/day. Maximum duration for treatment was 12 months.

Reporting group values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin
Number of subjects	384	210	11
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)	37	23	0
Children (2-11 years)	189	97	5
Adolescents (12-17 years)	89	45	6
Adults (18-64 years)	69	45	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	12.56	13.03	11.80
standard deviation	± 11.43	± 12.39	± 3.87
Sex: Female, Male Units: Subjects			
Female	176	103	7

Male	208	107	4

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	85	47	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	1	0
White	294	160	9
More than one race	0	0	0
Unknown or Not Reported	2	2	1

Reporting group values	Total		
Number of subjects	605		
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)	60		
Children (2-11 years)	291		
Adolescents (12-17 years)	140		
Adults (18-64 years)	114		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	286		
Male	319		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	133		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	4		
White	463		
More than one race	0		
Unknown or Not Reported	5		

End points

End points reporting groups

Reporting group title	Pregabalin: Previous and Current

Reporting group description:

Pediatric and adult subjects with POS and PGTC seizures included in this arm are those who received pregabalin in previous studies. Pregabalin was administered in 3 equally divided doses per day (TID) when age less than (<) 4 years and in 2 equally divided doses per day (BID) when age greater than or equal to (>=) 4 years. Pediatric subjects with body weight >=30 kilogram (kg) received pregabalin 2.5 milligram per kilogram per day (mg/kg/day) as liquid oral solution/capsule up to maximum of 10.0 mg/kg/day and with body weight <30 kg received pregabalin 3.5 mg/kg/day as liquid oral solution up to maximum of 14.0 mg/kg/day. Adult subjects received pregabalin 150 milligram per day (mg/day) as liquid oral solution/oral capsule up to maximum of 600 mg/day. Maximum duration for treatment was 12 months.

Reporting group title	Placebo-Previous to Pregabalin-Current

Reporting group description:

Pediatric and adult subjects with POS and PGTC seizures included in this arm are those who received placebo in previous studies. Pregabalin was administered TID when age <4 years and BID when age >= 4 years. Pediatric subjects with body weight >=30 kg received pregabalin 2.5 mg/kg/day as liquid oral solution/capsule up to maximum of 10.0 mg/kg/day and with body weight <30 kg received pregabalin 3.5 mg/kg/day as liquid oral solution up to maximum of 14.0 mg/kg/day. Adult subjects received pregabalin 150 mg/day as liquid oral solution/capsule up to maximum of 600 mg/day. Maximum duration for treatment was 12 months.

Reporting group title	Direct Pregabalin

Reporting group description:

Only pediatric subjects with POS were enrolled in this arm who did not participate in any study previously. Pregabalin was administered TID when age <4 years and BID when age >= 4 years. Pediatric subjects with body weight >=30 kg received pregabalin 2.5 mg/kg/day as liquid oral solution/capsule up to maximum of 10.0 mg/kg/day and with body weight <30 kg received pregabalin 3.5 mg/kg/day as liquid oral solution up to maximum of 14.0 mg/kg/day. Maximum duration for treatment was 12 months.

Primary: Number of Subjects With Treatment Emergent Adverse Events (AEs), Treatment Emergent Serious Adverse Events (SAEs), Treatment Related AEs and Treatment Related SAEs

End point title	Number of Subjects With Treatment Emergent Adverse Events (AEs), Treatment Emergent Serious Adverse Events (SAEs), Treatment Related AEs and Treatment Related SAEs[1]

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 are events between first dose of study drug and up to 28 days after last dose of study drug (up to 13 months) that were absent before treatment or that worsened relative to pretreatment state. AEs included both serious and non-serious AEs. Treatment-related AE was any untoward medical occurrence attributed to study drug in a subject who received study drug. Relatedness to study drug was assessed by the investigator. Safety population included subjects who took at least 1 dose of the study medication in the study.

End point type	Primary

End point timeframe:

Baseline up to 13 Months

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: No statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	384	210	11	
Units: Subjects				
Subjects With AEs	252	140	10	
Subjects With SAEs	53	23	1	
Subjects With Treatment Related AEs	104	65	9	
Subjects With Treatment Related SAEs	0	1	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Change From Baseline in Physical and Neurological Examination Findings up to 12 Months

End point title	Number of Subjects With Clinically Significant Change From Baseline in Physical and Neurological Examination Findings up to 12 Months[2]

End point description:

Physical examination assessed: general appearance, dermatological, head and eyes, ears, nose, mouth, and throat, pulmonary, cardiovascular, abdominal, genitourinary (optional), lymphatic, musculoskeletal/extremities. Neurological examination assessed: level of consciousness, mental status, cranial nerve assessment, muscle strength and tone, reflexes, pin prick and vibratory sensation, coordination and gait. Investigator judged clinically significant change from baseline in physical and neurological examination findings. Safety population included subjects who took at least 1 dose of the study medication in the study. Here, "n" signifies number of subjects evaluable for the specified categories.

End point type	Primary

End point timeframe:

Baseline up to 12 Months

Notes:

[2] - 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: No statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	384	210	11	
Units: Subjects				
Physical Examination (n =369, 199, 9)	8	6	0	
Neurological Examination (n =368, 199, 9)	10	4	2	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Meeting Pre-defined Criteria for Vital Signs Abnormalities

End point title	Number of Subjects Meeting Pre-defined Criteria for Vital Signs Abnormalities[3]

End point description:

Pre-defined criteria of vital signs abnormalities: maximum (max.) increase or decrease from baseline in sitting/supine systolic blood pressure (SBP) >=30 millimeter of mercury (mmHg); maximum increase or decrease from baseline in sitting/supine diastolic blood pressure (DBP) >=20 mmHg. Safety population included subjects who took at least 1 dose of the study medication in the study.

End point type	Primary

End point timeframe:

Baseline up to 12 months

Notes:

[3] - 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: No statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	384	210	11	
Units: Subjects				
Max. increase from baseline in SBP>=30 mmHg|	9	1	0	
Max. decrease from baseline in SBP>=30 mmHg|	8	5	0	
Max. increase from baseline in DBP>=20 mmHg|	34	16	1	
Max. decrease from baseline in DBP>=20 mmHg|	22	6	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Tanner Staging Evaluation at Baseline

End point title	Number of Subjects With Tanner Staging Evaluation at

End point description:

Tanner stage defines physical measurements of development based on external primary and secondary sex characteristics. Subjects are evaluated for breast development, pubic hair distribution and genital development, with values ranging from stage 1 (pre-pubertal characteristics) to stage 5 (adult or mature characteristics). Analysis population included subjects who took at least 1 dose of the study medication in the study and with age 4 years to less than 17 years. Here "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint. "n" signifies number of subjects evaluable for the specified categories.

End point type	Primary

End point timeframe:

Baseline

Notes:

[4] - 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: No statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	213	98	9	
Units: Subjects				
Pubic Hair: Stage 1 (n =212, 98, 9)	95	44	4	
Pubic Hair: Stage 2 (n =212, 98, 9)	34	17	1	
Pubic Hair: Stage 3 (n =212, 98, 9)	33	16	0	
Pubic Hair: Stage 4 (n =212, 98, 9)	34	15	0	
Pubic Hair: Stage 5 (n =212, 98, 9)	16	6	2	
Pubic Hair: Not Done (n =212, 98, 9)	0	0	2	
Pubic Hair: Missing (n =212, 98, 9)	0	0	0	
Breast: Stage 1 (n =122, 52, 6)	37	18	2	
Breast: Stage 2 (n =122, 52, 6)	17	7	1	
Breast: Stage 3 (n =122, 52, 6)	15	7	0	
Breast: Stage 4 (n =122, 52, 6)	19	7	0	
Breast: Stage 5 (n =122, 52, 6)	9	3	2	
Breast: Not Done (n =122, 52, 6)	1	0	1	
Breast: Missing (n =122, 52, 6)	24	9	0	
Genitalia: Stage 1 (n =133, 64, 3)	50	23	2	
Genitalia: Stage 2 (n =133, 64, 3)	24	11	0	
Genitalia: Stage 3 (n =133, 64, 3)	20	10	0	
Genitalia: Stage 4 (n =133, 64, 3)	13	7	0	
Genitalia: Stage 5 (n =133, 64, 3)	7	3	0	
Genitalia: Not Done (n =133, 64, 3)	0	1	1	
Genitalia: Missing (n =133, 64, 3)	19	9	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Tanner Staging Evaluation at Month 12

End point title	Number of Subjects With Tanner Staging Evaluation at Month 12[5]

End point description:

Tanner stage defines physical measurements of development based on external primary and secondary sex characteristics. Subjects are evaluated for breast development, pubic hair distribution and genital development, with values ranging from stage 1 (pre-pubertal characteristics) to stage 5 (adult or mature characteristics). Analysis population included subjects who took at least 1 dose of the study medication in the study and with age 4 years to less than 17 years. Here "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint. "n" signifies number of subjects evaluable for the specified categories.

End point type	Primary

End point timeframe:

Month 12

Notes:

[5] - 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: No statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	186	89	5	
Units: Subjects				
Pubic Hair: Stage 1 (n =186, 89, 5)	68	38	2	
Pubic Hair: Stage 2 (n =186, 89, 5)	35	17	1	
Pubic Hair: Stage 3 (n =186, 89, 5)	38	12	0	
Pubic Hair: Stage 4 (n =186, 89, 5)	21	11	0	
Pubic Hair: Stage 5 (n =186, 89, 5)	23	10	1	
Pubic Hair: Not Done (n =186, 89, 5)	1	1	1	
Pubic Hair: Missing (n =186, 89, 5)	0	0	0	
Breast: Stage 1 (n =82, 37, 4)	27	15	2	
Breast: Stage 2 (n =82, 37, 4)	17	8	1	
Breast: Stage 3 (n =82, 37, 4)	19	5	0	
Breast: Stage 4 (n =82, 37, 4)	7	3	0	
Breast: Stage 5 (n =82, 37, 4)	12	5	1	
Breast: Not Done (n =82, 37, 4)	0	1	0	
Breast: Missing (n =82, 37, 4)	0	0	0	
Genitalia: Stage 1 (n =104, 52, 1)	40	19	1	
Genitalia: Stage 2 (n =104, 52, 1)	22	12	0	
Genitalia: Stage 3 (n =104, 52, 1)	20	10	0	
Genitalia: Stage 4 (n =104, 52, 1)	9	5	0	
Genitalia: Stage 5 (n =104, 52, 1)	13	6	0	
Genitalia: Not Done (n =104, 52,1)	82	37	4	
Genitalia: Missing (n =104, 52, 1)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With >=7 Percent (%) Change From Baseline in Body Weight up to 12 Months

End point title	Number of Subjects With >=7 Percent (%) Change From Baseline in Body Weight up to 12 Months[6]

End point description:

In this endpoint number of subjects with increase and decrease of >=7% in body weight, from baseline up to 12 months are reported. Safety population included subjects who took at least 1 dose of the study medication in the study. Here "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline up to 12 Months

Notes:

[6] - 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: No statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	377	203	9	
Units: Subjects				
Weight increase from baseline >=7%	290	147	8	
Weight decrease from baseline >=7%	2	4	0	

Statistical analyses

No statistical analyses for this end point

Primary: Absolute Values for Body Height at Baseline

End point title	Absolute Values for Body Height at Baseline[7]

End point description:

Safety population included subjects who took at least 1 dose of the study medication in the study. Here, "n" signifies number of subjects evaluable for the specified categories. "99999" signifies arithmetic mean and standard deviation was not evaluated as no subject was analyzed.

End point type	Primary

End point timeframe:

Baseline

Notes:

[7] - 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: No statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	384	210	11	
Units: Centimeters				
arithmetic mean (standard deviation)				
Age: 1 Month to <2 Years (n =37, 23, 0)	74.7 (± 7.91)	74.8 (± 8.24)	99999 (± 99999)	
Age: 2 Years to <4 Years (n =60, 42, 0)	92.2 (± 7.13)	91.0 (± 8.21)	99999 (± 99999)	
Age: 4 Years to <10 Years (n =92, 43, 4)	119.3 (± 15.16)	118.5 (± 11.36)	126.0 (± 12.60)	
Age: 10 Years to 16 Years (n =126, 57, 7)	153.5 (± 14.50)	154.7 (± 11.88)	153.4 (± 7.06)	
Age Cohort: >=17 Years (n =69, 45, 0)	170.4 (± 9.18)	170.7 (± 9.99)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Primary: Absolute Values for Body Height at Month 12

End point title	Absolute Values for Body Height at Month 12[8]

End point description:

Safety population included subjects who took at least 1 dose of the study medication in the study. Here, "n" signifies number of subjects evaluable for the specified categories. "99999" signifies arithmetic mean and standard deviation was not evaluated as no subject was analyzed.

End point type	Primary

End point timeframe:

Month 12

Notes:

[8] - 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: No statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	377	202	9	
Units: Centimeters				
arithmetic mean (standard deviation)				
Age: 1 Month to <2 Years (n =36, 22 ,0)	84.4 (± 7.27)	85.3 (± 9.01)	99999 (± 99999)	
Age: 2 Years to <4 Years (n =58, 39, 0)	99.3 (± 7.90)	98.1 (± 8.94)	99999 (± 99999)	
Age: 4 Years to <10 Years (n =91, 43, 3)	128.2 (± 15.94)	126.6 (± 10.80)	128.2 (± 13.08)	
Age: 10 Years to 16 Years (n =125, 55, 6)	158.1 (± 13.64)	160.5 (± 11.87)	153.7 (± 6.58)	
Age: >=17 Years (n =67, 43, 0)	170.8 (± 9.54)	170.6 (± 10.14)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Incidence of Laboratory Abnormalities

End point title	Number of Subjects With Incidence of Laboratory

End point description:

Hemoglobin, hematocrit, RBC count: <0.8*lower limit of normal(LLN), platelet: <0.5*LLN/greater than

(>)1.75*upper limit of normal (ULN), WBC: <0.6*LLN/>1.5*ULN, lymphocyte, neutrophil-absolute/%:<0.8*LLN/>1.2*ULN, basophil, eosinophil, monocyte- absolute/%:>1.2*ULN; total/direct/indirect bilirubin >1.5*ULN, aspartate aminotransferase (AT), alanine AT, gammaglutamyl transferase, alkaline phosphatase:> 3.0*ULN, total protein, albumin: <0.8*LLN/>1.2*ULN; thyroxine, thyroid stimulating hormone <0.8*LLN/>1.2*ULN; cholesterol, triglycerides:> >1.3*ULN; blood urea nitrogen, creatinine:>1.3*ULN; sodium <0.95*LLN/>1.05*ULN, potassium, chloride, calcium: <0.9*LLN or >1.1*ULN; glucose <0.6*LLN/>1.5*ULN, creatine kinase>2.0*ULN; urine (specific gravity <1.003/>1.030, pH <4.5/>8, glucose, ketones, protein: >=1, WBC, RBC:>=20, bacteria >20, hyaline casts/casts >1); prothrombin (PT), PT international ratio>1.1*ULN. Safety set. "Number of Subjects Analyzed"=subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline up to 12 Months

Notes:

[9] - 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: No statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	374	204	9	
Units: Subjects	297	164	8	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Maximum Change from Baseline up to 12 Months in 12-Lead Electrocardiogram (ECG) Parameters

End point title	Number of Subjects With Maximum Change from Baseline up to 12 Months in 12-Lead Electrocardiogram (ECG) Parameters[10]

End point description:

Categories for which data is reported are: 1) maximum (max) PR interval increase from baseline (IFB) (millisecond [msec]) percent change (PctChg) >=25/50%; 2) maximum QRS complex increase from baseline (msec) PctChg>=50%; 3) maximum QTCB interval (Bazett's correction) increase from baseline (msec): change >=30 to <60; change >=60; 4) maximum QTCF interval (Fridericia's correction) increase from baseline (msec): change >=30 to <60; change >=60. 'PctChg>=25/50%': >= 25% increase from baseline when baseline ECG is > 200, and is >= 50% increase from baseline when baseline ECG is non-missing and <=200. Safety population included subjects who took at least 1 dose of the study medication in the study. Here "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline up to 12 Months

Notes:

[10] - 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: bbbbNo statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	357	194	9	
Units: Subjects				
Max PR interval IFB PctChg >=25/50%	1	0	0	
Max QRS complex IFB PctChg >=50%	0	0	0	
Max QTcB interval IFB change >=30 - <60	29	11	0	
Max QTcB interval IFB change >=60	0	0	0	
Max QTcF interval IFB change >=30 - <60	18	9	1	
Max QTcF interval IFB change >=60	1	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: 28-Days Seizure Rate at Week 1

End point title	28-Days Seizure Rate at Week 1[11]

End point description:

28-days seizure rate was defined as number of seizures per 28-day period. 28-days seizure rate have been reported separately for partial onset seizure and primary generalized tonic clonic seizure. Partial onset seizure: a seizure that starts in one area of the brain. This kind of seizure is brief, lasting seconds to less than 2 minutes. Primary generalized tonic clonic seizure: a seizure that starts in one area of the brain, then spreads to both sides of the brain as a tonic-clonic seizure and usually last 1 to 3 minutes. Safety population included subjects who took at least 1 dose of the study medication in the study. Here, "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint and "n" signifies number of subjects evaluable for the specified categories. "99999" signifies arithmetic mean and standard deviation was not evaluated as no participants were analyzed.

End point type	Primary

End point timeframe:

Week 1

Notes:

[11] - 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: No statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	380	209	11	
Units: Seizures Per 28-Days				
arithmetic mean (standard deviation)				
POS (n =270, 147, 11)	102.89 (± 235.73)	190.45 (± 1143.83)	17.83 (± 32.18)	
PGTC (n =110, 62, 0)	2.07 (± 2.98)	2.39 (± 4.53)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Primary: 28-Days Seizure Rate at Month 1

End point title	28-Days Seizure Rate at Month 1[12]

End point description:

28-days seizure rate was defined as number of seizures per 28-day period. 28-days seizure rate have been reported separately for partial onset seizure and primary generalized tonic clonic seizure. Partial onset seizure: a seizure that starts in one area of the brain. This kind of seizure is brief, lasting seconds to less than 2 minutes. Primary generalized tonic clonic seizure: a seizure that starts in one area of the brain, then spreads to both sides of the brain as a tonic-clonic seizure and usually last 1 to 3 minutes. Safety population included subjects who took at least 1 dose of the study medication in the study. Here, "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint and "n" signifies number of subjects evaluable for the specified categories. "99999" signifies arithmetic mean and standard deviation was not evaluated as no participants were analyzed.

End point type	Primary

End point timeframe:

Month 1

Notes:

[12] - 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: No statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	378	203	10	
Units: Seizures Per 28-Days				
arithmetic mean (standard deviation)				
POS (n =269, 142, 10)	96.39 (± 258.09)	178.53 (± 1114.79)	33.42 (± 54.21)	
PGTC (n =109, 61, 0)	1.43 (± 2.16)	1.66 (± 2.86)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Primary: 28-Days Seizure Rate at Month 2

End point title	28-Days Seizure Rate at Month 2[13]

End point description:

28-days seizure rate was defined as number of seizures per 28-day period. 28-days seizure rate have been reported separately for partial onset seizure and primary generalized tonic clonic seizure. Partial onset seizure: a seizure that starts in one area of the brain. This kind of seizure is brief, lasting seconds

to less than 2 minutes. Primary generalized tonic clonic seizure: a seizure that starts in one area of the brain, then spreads to both sides of the brain as a tonic-clonic seizure and usually last 1 to 3 minutes. Safety population included subjects who took at least 1 dose of the study medication in the study. Here, "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint and "n" signifies number of subjects evaluable for the specified categories. "99999" signifies arithmetic mean and standard deviation was not evaluated as no participants were analyzed.

End point type	Primary

End point timeframe:

Month 2

Notes:

[13] - 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: No statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	373	193	8	
Units: Seizures Per 28-Days				
arithmetic mean (standard deviation)				
POS (n =263, 135, 8)	79.33 (± 196.31)	89.09 (± 579.42)	22.16 (± 46.70)	
PGTC (n =110, 58, 0)	1.27 (± 1.80)	1.36 (± 2.63)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Primary: 28-Days Seizure Rate at Month 4

End point title	28-Days Seizure Rate at Month 4[14]

End point description:

28-days seizure rate was defined as number of seizures per 28-day period. 28-days seizure rate have been reported separately for partial onset seizure and primary generalized tonic clonic seizure. Partial onset seizure: a seizure that starts in one area of the brain. This kind of seizure is brief, lasting seconds to less than 2 minutes. Primary generalized tonic clonic seizure: a seizure that starts in one area of the brain, then spreads to both sides of the brain as a tonic-clonic seizure and usually last 1 to 3 minutes. Safety population included subjects who took at least 1 dose of the study medication in the study. Here, "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint and "n" signifies number of subjects evaluable for the specified categories. "99999" signifies arithmetic mean and standard deviation was not evaluated as no participants were analyzed.

End point type	Primary

End point timeframe:

Month 4

Notes:

[14] - 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: No statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	352	185	6	
Units: Seizures Per 28-Days				
arithmetic mean (standard deviation)				
POS (n =247, 131, 6)	67.32 (± 190.44)	58.33 (± 320.32)	15.45 (± 25.23)	
PGTC (n =105, 54, 0)	1.09 (± 1.88)	0.72 (± 0.91)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Primary: 28-Days Seizure Rate at Month 6

End point title	28-Days Seizure Rate at Month 6[15]

End point description:

28-days seizure rate was defined as number of seizures per 28-day period. 28-days seizure rate have been reported separately for partial onset seizure and primary generalized tonic clonic seizure. Partial onset seizure: a seizure that starts in one area of the brain. This kind of seizure is brief, lasting seconds to less than 2 minutes. Primary generalized tonic clonic seizure: a seizure that starts in one area of the brain, then spreads to both sides of the brain as a tonic-clonic seizure and usually last 1 to 3 minutes. Safety population included subjects who took at least 1 dose of the study medication in the study. Here, "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint and "n" signifies number of subjects evaluable for the specified categories. "99999" signifies arithmetic mean and standard deviation was not evaluated as no participants were analyzed.

End point type	Primary

End point timeframe:

Month 6

Notes:

[15] - 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: No statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	330	175	6	
Units: Seizures Per 28-Days				
arithmetic mean (standard deviation)				
POS (n =237, 124, 6)	50.18 (± 125.26)	51.10 (± 212.59)	4.25 (± 6.06)	
PGTC (n =93, 51, 0)	1.02 (± 1.61)	0.79 (± 1.21)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Primary: 28-Days Seizure Rate at Month 9

End point title	28-Days Seizure Rate at Month 9[16]

End point description:

28-days seizure rate was defined as number of seizures per 28-day period. 28-days seizure rate have been reported separately for partial onset seizure and primary generalized tonic clonic seizure. Partial onset seizure: a seizure that starts in one area of the brain. This kind of seizure is brief, lasting seconds to less than 2 minutes. Primary generalized tonic clonic seizure: a seizure that starts in one area of the brain, then spreads to both sides of the brain as a tonic-clonic seizure and usually last 1 to 3 minutes. Safety population included subjects who took at least 1 dose of the study medication in the study. Here, "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint and "n" signifies number of subjects evaluable for the specified categories. "99999" signifies arithmetic mean and standard deviation was not evaluated as no participants were analyzed.

End point type	Primary

End point timeframe:

Month 9

Notes:

[16] - 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: No statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	310	164	6	
Units: Seizures Per 28-Days				
arithmetic mean (standard deviation)				
POS (n =225, 121, 6)	38.17 (± 87.75)	43.13 (± 141.96)	3.00 (± 3.93)	
PGTC (n =85, 43, 0)	0.96 (± 1.69)	0.62 (± 0.99)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Primary: 28-Days Seizure Rate at Month 12/Early Termination

End point title	28-Days Seizure Rate at Month 12/Early Termination[17]

End point description:

28-days seizure rate was defined as number of seizures per 28-day period. 28-days seizure rate have been reported separately for partial onset seizure and primary generalized tonic clonic seizure. Partial onset seizure: a seizure that starts in one area of the brain. This kind of seizure is brief, lasting seconds to less than 2 minutes. Primary generalized tonic clonic seizure: a seizure that starts in one area of the brain, then spreads to both sides of the brain as a tonic-clonic seizure and usually last 1 to 3 minutes. Safety population included subjects who took at least 1 dose of the study medication in the study. Here, "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint and "n" signifies number of subjects evaluable for the specified categories. "99999" signifies arithmetic mean and standard deviation was not evaluated as no participants were analyzed.

End point type	Primary

End point timeframe:

Month 12/Early Termination

Notes:

[17] - 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: No statistical analysis was performed for this endpoint

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	374	206	8	
Units: Seizures Per 28-Days				
arithmetic mean (standard deviation)				
POS (n =266, 146, 8)	56.04 (± 147.20)	117.88 (± 896.40)	11.08 (± 16.55)	
PGTC (n =108, 60, 0)	1.02 (± 1.71)	1.33 (± 3.20)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Suicidal Ideation as per Columbia Suicide Severity Rating Scale (C-SSRS) Mapped to Columbia Classification Algorithm of Suicide Assessment (C-CASA)

End point title	Number of Subjects With Suicidal Ideation as per Columbia Suicide Severity Rating Scale (C-SSRS) Mapped to Columbia Classification Algorithm of Suicide Assessment (C-CASA)

End point description:

Number of subjects with C-CASA code 4 are reported. C-SSRS responses mapping to C-CASA suicidal ideation code 4 are as follows: "Yes" on "wish to be dead", "non-specific active suicidal thoughts", “active suicidal ideation with any methods (not plan) without intent to act”, “active suicidal ideation with some intent to act, without specific plan”, “active suicidal ideation with some intent to act, without specific plan". Safety analysis set. "Number of Subjects Analyzed”=subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Post-baseline on Day 1 up to 12 Months

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	258	134	10	
Units: Subjects				
Baseline (n =254, 132, 10)	3	2	1	
Post-baseline up to 12 Months (n =257, 134, 10)	3	2	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Suicidal Behavior as per Columbia Suicide Severity Rating Scale (C-SSRS) Mapped to Columbia Classification Algorithm of Suicide Assessment (C-CASA)

End point title	Number of Subjects With Suicidal Behavior as per Columbia Suicide Severity Rating Scale (C-SSRS) Mapped to Columbia Classification Algorithm of Suicide Assessment (C-CASA)

End point description:

Number of subjects with C-CASA code 1 or 2 or 3 are reported. C-SSRS responses mapping to C-CASA suicidal behavior codes 1, 2, or 3 are as follows: (1) completed suicide; (2) suicide attempt (response of "Yes" on "actual attempt"); (3) preparatory acts toward imminent suicidal behavior ("Yes" on "aborted attempt", "interrupted attempt", "preparatory acts or behavior"). Safety analysis set. "Number of Subjects Analyzed"=subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Post-baseline on Day 1 up to 12 Months

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	258	134	10	
Units: Subjects				
Screening (n =254, 132, 10)	1	1	0	
Post-baseline up to 12 Months (n =257, 134, 10)	2	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects as per Reliable Change Index (RCI) Category for Cogstate Detection Task

End point title	Number of Subjects as per Reliable Change Index (RCI) Category for Cogstate Detection Task

End point description:

CogState brief battery consisted of 2 tasks-detection and pediatric identification task using a laptop computer with external response buttons.Prior tasks, subjects were briefed rules,given an interactive demonstration and a sufficient number of practice trials.For each task, subject responded "yes" using a response button with dominant hand. Subjects had to "respond as fast and as accurately as possible."Detection task:measured simple reaction time to assess psychomotor function.Subject pressed

response key as soon as they detected an event (ie, a card turning face up presented in the center of the computer screen).A subject's RCI was calculated by dividing the change from individual baseline score by ([square root 2] times WSD),where WSD is within-subject standard deviation from Cogstate detection task normative data.Improvement in cognition when RCI <=-1.65, decline in cognition when RCI >=1.65.Safety set."Number of Subjects Analyzed”=subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Month 12

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	97	51	7	
Units: Subjects				
Improvement (RCI <= -1.65)	21	8	2	
Decline (RCI >=1.65)	13	6	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects as per Reliable Change Index Category for Cogstate Pediatric Identification Task

End point title	Number of Subjects as per Reliable Change Index Category for Cogstate Pediatric Identification Task

End point description:

CogState brief battery consisted of 2 tasks-detection and pediatric identification task using a laptop computer with external response buttons.Prior tasks,subjects were briefed rules,given an interactive demonstration and a sufficient number of practice trials.For each task,subject responded “yes” using a response button with dominant hand. Subjects had to “respond as fast and as accurately as possible.”Detection task: measured simple reaction time to assess psychomotor function.Subject pressed a “YES” response key as soon as they detected an event (ie, a card turning face up presented in the center of the computer screen).A subject's RCI was calculated by dividing the change from individual baseline score by ([square root 2] times WSD),where WSD is within-subject standard deviation from Cogstate detection task normative data.Improvement in cognition when RCI <=-1.65, decline in cognition when RCI >=1.65.Safety set."Number of Subjects Analyzed”=subjects evaluable for this

End point type	Secondary

End point timeframe:

Month 12

End point values	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96	50	7	
Units: Subjects				

Improvement (RCI <=-1.65)	17	9	2	
Decline (RCI >=1.65)	16	6	2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 13 Months

Adverse event reporting additional description:

Same event may appear as adverse event (AE) and serious AE, what is presented are distinct events. Event may be categorized as serious in 1 subject and as nonserious in another subject or 1 subject may have experienced both serious and nonserious event during study. Safety population was evaluated.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Pregabalin: Previous and Current

Reporting group description:

Pediatric and adult subjects included in this arm are those who received pregabalin in previous studies. Pregabalin was administered TID when age <4 years and BID when age >=4 years. Pediatric subjects with body weight >=30 kg received pregabalin 2.5 mg/kg/day as liquid oral solution/capsule up to maximum of 10.0 mg/kg/day and with body weight <30 kg received pregabalin 3.5 mg/kg/day as liquid oral solution up to maximum of 14.0 mg/kg/day. Adult subjects received pregabalin 150 mg/day as liquid oral solution/capsule up to maximum of 600 mg/day. Maximum duration for treatment was 12 months.

Reporting group title	Placebo-Previous to Pregabalin-Current

Reporting group description:

Pediatric and adult subjects included in this arm are those who received placebo in previous studies. Pregabalin was administered TID when age <4 years and BID when age >=4 years. Pediatric subjects with body weight >=30 kg received pregabalin 2.5 mg/kg/day as liquid oral solution/capsule up to maximum of 10.0 mg/kg/day and with body weight <30 kg received pregabalin 3.5 mg/kg/day as liquid oral solution up to maximum of 14.0 mg/kg/day. Adult subjects received pregabalin 150 mg/day as liquid oral solution/capsule up to maximum of 600 mg/day. Maximum duration for treatment was 12 months.

Reporting group title	Direct Pregabalin

Reporting group description:

Only pediatric subjects were enrolled in this arm who did not participate in any study previously. Pregabalin was administered TID when age <4 years and BID when age >= 4 years. Pediatric subjects with body weight >=30 kg received pregabalin 2.5 mg/kg/day as liquid oral solution/capsule up to maximum of 10.0 mg/kg/day and with body weight <30 kg received pregabalin 3.5 mg/kg/day as liquid oral solution up to maximum of 14.0 mg/kg/day. Maximum duration for treatment was 12 months.

Serious adverse events	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin
Total subjects affected by serious adverse events			
subjects affected / exposed	53 / 384 (13.80%)	23 / 210 (10.95%)	1 / 11 (9.09%)
number of deaths (all causes)	3	4	0
number of deaths resulting from adverse events			
Social circumstances			
Physical abuse			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (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
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (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
Emotional disorder			
subjects affected / exposed	0 / 384 (0.00%)	0 / 210 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	2 / 384 (0.52%)	0 / 210 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Brain herniation			
subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Concussion			
subjects affected / exposed	2 / 384 (0.52%)	0 / 210 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiphyseal injury			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Humerus fracture			

subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Unintentional medical device removal			
subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (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
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Cardiopulmonary failure			
subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cyanosis			
subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (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
Blood and lymphatic system disorders			
Deficiency anaemia			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (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
Asthma			
subjects affected / exposed	1 / 384 (0.26%)	1 / 210 (0.48%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchial obstruction			
subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (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
Dyspnoea			
subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (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
Pneumonia aspiration			
subjects affected / exposed	2 / 384 (0.52%)	0 / 210 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (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
Nervous system disorders			
Brain oedema			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (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	1 / 384 (0.26%)	2 / 210 (0.95%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Partial seizures			

subjects affected / exposed	3 / 384 (0.78%)	0 / 210 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postictal state			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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	8 / 384 (2.08%)	6 / 210 (2.86%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 8	1 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Status epilepticus			
subjects affected / exposed	2 / 384 (0.52%)	0 / 210 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (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
Constipation			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Gingival hypertrophy			
subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (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
Saliva discolouration			
subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (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
Product issues			
Device dislocation			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Device occlusion			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Skin and subcutaneous tissue disorders			
Henoch-Schonlein purpura			
subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (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
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Periostitis			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 384 (0.52%)	1 / 210 (0.48%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Electrolyte imbalance			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Hyponatraemia			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Bronchitis			
subjects affected / exposed	3 / 384 (0.78%)	1 / 210 (0.48%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Dengue fever			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Ear infection			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Gastroenteritis			
subjects affected / exposed	0 / 384 (0.00%)	3 / 210 (1.43%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Giardiasis			

subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (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
Peritonitis			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Pharyngotonsillitis			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Pneumonia			
subjects affected / exposed	17 / 384 (4.43%)	6 / 210 (2.86%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 23	0 / 10	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 0
Respiratory tract chlamydial infection			
subjects affected / exposed	0 / 384 (0.00%)	1 / 210 (0.48%)	0 / 11 (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
Respiratory tract infection			
subjects affected / exposed	1 / 384 (0.26%)	1 / 210 (0.48%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic viral infection			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Upper respiratory tract infection			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	0 / 11 (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
Urinary tract infection			
subjects affected / exposed	2 / 384 (0.52%)	0 / 210 (0.00%)	0 / 11 (0.00%)

occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	2 / 384 (0.52%)	0 / 210 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Pregabalin: Previous and Current	Placebo-Previous to Pregabalin-Current	Direct Pregabalin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	186 / 384 (48.44%)	103 / 210 (49.05%)	10 / 11 (90.91%)
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	6 / 384 (1.56%)	0 / 210 (0.00%)	1 / 11 (9.09%)
occurrences (all)	7	0	1
Concussion			
subjects affected / exposed	1 / 384 (0.26%)	1 / 210 (0.48%)	1 / 11 (9.09%)
occurrences (all)	1	1	1
Foot fracture			
subjects affected / exposed	0 / 384 (0.00%)	0 / 210 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Investigations			
Blood triglycerides increased			
subjects affected / exposed	1 / 384 (0.26%)	3 / 210 (1.43%)	1 / 11 (9.09%)
occurrences (all)	1	3	1
Platelet count abnormal			
subjects affected / exposed	0 / 384 (0.00%)	0 / 210 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Red blood cell count abnormal			
subjects affected / exposed	0 / 384 (0.00%)	0 / 210 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	28 / 384 (7.29%)	12 / 210 (5.71%)	2 / 11 (18.18%)
occurrences (all)	29	13	2

White blood cell count abnormal			
subjects affected / exposed	0 / 384 (0.00%)	0 / 210 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	23 / 384 (5.99%)	14 / 210 (6.67%)	0 / 11 (0.00%)
occurrences (all)	35	21	0
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	3 / 384 (0.78%)	2 / 210 (0.95%)	1 / 11 (9.09%)
occurrences (all)	3	2	1
Dizziness			
subjects affected / exposed	19 / 384 (4.95%)	10 / 210 (4.76%)	1 / 11 (9.09%)
occurrences (all)	25	11	1
Dysdiadochokinesis			
subjects affected / exposed	0 / 384 (0.00%)	0 / 210 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	24 / 384 (6.25%)	8 / 210 (3.81%)	4 / 11 (36.36%)
occurrences (all)	108	39	4
Lethargy			
subjects affected / exposed	1 / 384 (0.26%)	1 / 210 (0.48%)	1 / 11 (9.09%)
occurrences (all)	1	1	1
Psychomotor hyperactivity			
subjects affected / exposed	4 / 384 (1.04%)	2 / 210 (0.95%)	1 / 11 (9.09%)
occurrences (all)	4	3	1
Resting tremor			
subjects affected / exposed	0 / 384 (0.00%)	0 / 210 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Seizure			
subjects affected / exposed	22 / 384 (5.73%)	12 / 210 (5.71%)	1 / 11 (9.09%)
occurrences (all)	41	13	1
Somnolence			
subjects affected / exposed	26 / 384 (6.77%)	27 / 210 (12.86%)	1 / 11 (9.09%)
occurrences (all)	30	33	1
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	8 / 384 (2.08%)	2 / 210 (0.95%)	1 / 11 (9.09%)
occurrences (all)	12	2	1
Pyrexia			
subjects affected / exposed	54 / 384 (14.06%)	22 / 210 (10.48%)	1 / 11 (9.09%)
occurrences (all)	113	35	1
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Aggression			
subjects affected / exposed	5 / 384 (1.30%)	2 / 210 (0.95%)	1 / 11 (9.09%)
occurrences (all)	6	2	1
Behaviour disorder			
subjects affected / exposed	2 / 384 (0.52%)	2 / 210 (0.95%)	1 / 11 (9.09%)
occurrences (all)	2	2	1
Mood altered			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Mood swings			
subjects affected / exposed	0 / 384 (0.00%)	0 / 210 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Staring			
subjects affected / exposed	1 / 384 (0.26%)	0 / 210 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	4 / 384 (1.04%)	1 / 210 (0.48%)	2 / 11 (18.18%)
occurrences (all)	8	1	2
Constipation			
subjects affected / exposed	10 / 384 (2.60%)	4 / 210 (1.90%)	1 / 11 (9.09%)
occurrences (all)	14	6	1
Diarrhoea			
subjects affected / exposed	20 / 384 (5.21%)	9 / 210 (4.29%)	1 / 11 (9.09%)
occurrences (all)	26	14	1
Vomiting			
subjects affected / exposed	15 / 384 (3.91%)	11 / 210 (5.24%)	2 / 11 (18.18%)

occurrences (all)	18	11	2

Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	9 / 384 (2.34%)	3 / 210 (1.43%)	1 / 11 (9.09%)
occurrences (all)	12	3	1
Rash macular			
subjects affected / exposed	0 / 384 (0.00%)	0 / 210 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthropathy			
subjects affected / exposed	0 / 384 (0.00%)	0 / 210 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Increased appetite			
subjects affected / exposed	10 / 384 (2.60%)	9 / 210 (4.29%)	2 / 11 (18.18%)
occurrences (all)	11	9	2
Infections and infestations			
Lyme disease			
subjects affected / exposed	0 / 384 (0.00%)	0 / 210 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	26 / 384 (6.77%)	12 / 210 (5.71%)	0 / 11 (0.00%)
occurrences (all)	38	17	0
Pneumonia			
subjects affected / exposed	13 / 384 (3.39%)	12 / 210 (5.71%)	0 / 11 (0.00%)
occurrences (all)	32	21	0
Sinusitis			
subjects affected / exposed	2 / 384 (0.52%)	2 / 210 (0.95%)	1 / 11 (9.09%)
occurrences (all)	2	2	2
Upper respiratory tract infection			
subjects affected / exposed	60 / 384 (15.63%)	30 / 210 (14.29%)	0 / 11 (0.00%)
occurrences (all)	113	62	0
Viral infection			
subjects affected / exposed	15 / 384 (3.91%)	11 / 210 (5.24%)	0 / 11 (0.00%)
occurrences (all)	20	16	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 July 2012	Safety reporting section updated due to protocol template updates.
07 May 2014	Updated to TID regimen for subjects <4 years old.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

1 death occurred in reporting arm "Placebo-Previous to Pregabalin-Current" after subject completed the study and is captured in All-cause mortality section.

Notes: