Clinical trial results:
A RANDOMIZED, DOUBLE-BLIND, PARALLEL-GROUP, MULTI-CENTER, COMPARATIVE, FLEXIBLE DOSE TRIAL OF PREGABALIN VERSUS GABAPENTIN AS ADJUNCTIVE THERAPY IN SUBJECTS WITH PARTIAL SEIZURES

Summary

EudraCT number	2007-003161-40
Trial protocol	PT ES BG SK
Global end of trial date	24 July 2013

Results information

Result version number	v1 (current)
This version publication date	30 May 2016
First version publication date	30 July 2015

Trial information

Trial identification

Sponsor protocol code	A0081143

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00537940
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., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 800-718-1021, 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	22 September 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 July 2013
Global end of trial reached?	Yes
Global end of trial date	24 July 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of pregabalin (300-600 milligram (mg)/day flexible dose) and gabapentin (1200-1800 mg/day flexible dose), both administered three times daily (TID), as adjunctive therapy in subjects with refractory partial seizures.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed; in particular, those affording greater protection to the safety of study subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 February 2008
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	Portugal: 1
Country: Number of subjects enrolled	Romania: 32
Country: Number of subjects enrolled	Slovakia: 26
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Bulgaria: 86
Country: Number of subjects enrolled	Croatia: 15
Country: Number of subjects enrolled	Costa Rica: 32
Country: Number of subjects enrolled	China: 54
Country: Number of subjects enrolled	El Salvador: 24
Country: Number of subjects enrolled	Guatemala: 23
Country: Number of subjects enrolled	India: 84
Country: Number of subjects enrolled	Pakistan: 51
Country: Number of subjects enrolled	Peru: 19
Country: Number of subjects enrolled	Serbia: 31
Worldwide total number of subjects	482
EEA total number of subjects	164

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	474
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

561 subjects were screened and 484 were randomized. Of these 1 in each arm were not treated. 482 total (241 per arm) were treated. 187 (pregabalin) and 172 (gabapentin) subjects completed the maintenance phase and 58 (pregabalin) and 62 (gabapentin) subjects completed the optional blinded continuation phase. Subjects were randomized at 56 centers.

Pre-assignment

Screening details:

One subject from the pregabalin group and one subject from the gabapentin group were randomized but not treated.

Period 1

Period 1 title	Overall Period (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

Arm description:

Pregabalin was initiated at 150mg/day[50 mg capsules orally three times a day(TID)] for 1 Week followed by pregabalin 300mg/day(100 mg TID) orally TID up to Week 5 in Titration Phase(TP). Subjects who had adequate seizure control (adequate:>=50 % reduction in seizures) with acceptable tolerability with pregabalin 300mg/day in TP,continued same dose until the end of TP(Week 9) and then entered maintenance phase(MP) on this dose. If seizure control was inadequate, pregabalin dose was escalated to 450mg/day orally(150mg TID) from Weeks 5 through 9. If subjects had adequate seizure control with acceptable tolerability on this dose,then they entered the MP on this dose. If there was inadequate seizure control at end of Week 9,dose was escalated a final time to 600mg/day(200mg TID) at which time they entered the MP. With reference to subject disposition table, Pregabalin reporting arm: 2 subjects had both treatment related and non-treatment related Adverse Event leading to discontinuation.

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

Dosage and administration details:

Pregabalin was initiated at 150 mg/day [50 mg capsules orally three times a day (TID)] for 1 Week followed by pregabalin 300 mg/day (100 mg TID) orally TID up to Week 5 in the Titration Phase (TP). Subjects who had adequate seizure control (adequate: >=50% reduction in seizures) with acceptable tolerability with pregabalin 300 mg/day in TP, continued same dose until the end of TP (Week 9) and then entered the maintenance phase (MP) on this dose. If seizure control was inadequate, the pregabalin dose was escalated to 450 mg/day orally (150 mg TID) from Weeks 5 through 9. If the subjects had adequate seizure control with acceptable tolerability on this dose, then they entered the MP on this dose. If there was inadequate seizure control at the end of Week 9, the dose was escalated a final time to 600 mg/day (200 mg TID) at which time they entered the MP.

Arm title	Gabapentin

Arm description:

Gabapentin was initiated at 300mg/day [100 mg capsules orally three times a day (TID)] followed by gabapentin 600mg/day (200mg TID) on Day 3. At the end of Week 1 (Day 7), the dose was increased to 1200mg/day (400 mg TID) and remained on this dose for the next 4 weeks). Subjects who had adequate seizure control (>=50% reduction in seizure frequency) with acceptable tolerability during this initial 5-week period, remained on this dose until the end of theTP (Week 9), then entered the MP on

this dose. If seizure control was inadequate, the gabapentin dose was escalated to 1500mg/day (500mg TID) during Weeks 5 through 9. If they had adequate seizure control with acceptable tolerability on this dose, they entered the MP on this dose. If there was inadequate seizure control at the end of Week 9, the dose was escalated a final time to 1800mg/day (600mg TID), at which time they entered the MP.

Arm type	Active comparator
Investigational medicinal product name	Gabapentin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Gabapentin was initiated at 300 mg/day [100 mg capsules orally three times a day (TID)] followed by gabapentin 600 mg/day (200 mg TID) on Day 3. At the end of Week 1 (Day 7), the dose was increased to 1200 mg/day (400 mg TID) and remained on this dose for the next 4 weeks). Subjects who had adequate seizure control (>=50% reduction in seizure frequency) with acceptable tolerability during this initial 5-week period, remained on this dose until the end of theTP (Week 9), then entered the MP on this dose. If seizure control was inadequate, the gabapentin dose was escalated to 1500 mg/day (500 mg TID) during Weeks 5 through 9. If they had adequate seizure control with acceptable tolerability on this dose, they entered the MP on this dose. If there was inadequate seizure control at the end of Week 9, the dose was escalated a final time to 1800 mg/day (600 mg TID), at which time they entered the MP.

Number of subjects in period 1	Pregabalin	Gabapentin
Started	241	241
Completed Titration Phase	213	210
Completed Maintenance Phase	187	172
Entered Opt Blinded Continuation Phase	140	139
Completed	58	62
Not completed	183	179
'Protocol Violation '	6	4
' Unspecified'	10	12
Consent withdrawn by subject	113	95
'Adverse Event '	20	19
Pregnancy	1	1
Study terminated by sponsor	2	3
Lost to follow-up	23	29
Lack of efficacy	8	16

Baseline characteristics

Reporting groups	
Reporting group title	Pregabalin

Reporting group description:

Pregabalin was initiated at 150mg/day[50 mg capsules orally three times a day(TID)] for 1 Week followed by pregabalin 300mg/day(100 mg TID) orally TID up to Week 5 in Titration Phase(TP). Subjects who had adequate seizure control (adequate:>=50 % reduction in seizures) with acceptable tolerability with pregabalin 300mg/day in TP,continued same dose until the end of TP(Week 9) and then entered maintenance phase(MP) on this dose. If seizure control was inadequate, pregabalin dose was escalated to 450mg/day orally(150mg TID) from Weeks 5 through 9. If subjects had adequate seizure control with acceptable tolerability on this dose,then they entered the MP on this dose. If there was inadequate seizure control at end of Week 9,dose was escalated a final time to 600mg/day(200mg TID) at which time they entered the MP. With reference to subject disposition table, Pregabalin reporting arm: 2 subjects had both treatment related and non-treatment related Adverse Event leading to discontinuation.

Reporting group title	Gabapentin

Reporting group description:

Gabapentin was initiated at 300mg/day [100 mg capsules orally three times a day (TID)] followed by gabapentin 600mg/day (200mg TID) on Day 3. At the end of Week 1 (Day 7), the dose was increased to 1200mg/day (400 mg TID) and remained on this dose for the next 4 weeks). Subjects who had adequate seizure control (>=50% reduction in seizure frequency) with acceptable tolerability during this initial 5-week period, remained on this dose until the end of theTP (Week 9), then entered the MP on this dose. If seizure control was inadequate, the gabapentin dose was escalated to 1500mg/day (500mg TID) during Weeks 5 through 9. If they had adequate seizure control with acceptable tolerability on this dose, they entered the MP on this dose. If there was inadequate seizure control at the end of Week 9, the dose was escalated a final time to 1800mg/day (600mg TID), at which time they entered the MP.

Reporting group values	Pregabalin	Gabapentin	Total
Number of subjects	241	241	482
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 34.9 ± 13	 35.3 ± 12.9	 -
Gender categorical Units: Subjects			
Female Male	114 127	111 130	225 257

End points

End points reporting groups

Reporting group title	Pregabalin

Reporting group description:

Pregabalin was initiated at 150mg/day[50 mg capsules orally three times a day(TID)] for 1 Week followed by pregabalin 300mg/day(100 mg TID) orally TID up to Week 5 in Titration Phase(TP). Subjects who had adequate seizure control (adequate:>=50 % reduction in seizures) with acceptable tolerability with pregabalin 300mg/day in TP,continued same dose until the end of TP(Week 9) and then entered maintenance phase(MP) on this dose. If seizure control was inadequate, pregabalin dose was escalated to 450mg/day orally(150mg TID) from Weeks 5 through 9. If subjects had adequate seizure control with acceptable tolerability on this dose,then they entered the MP on this dose. If there was inadequate seizure control at end of Week 9,dose was escalated a final time to 600mg/day(200mg TID) at which time they entered the MP. With reference to subject disposition table, Pregabalin reporting arm: 2 subjects had both treatment related and non-treatment related Adverse Event leading to discontinuation.

Reporting group title	Gabapentin

Reporting group description:

Gabapentin was initiated at 300mg/day [100 mg capsules orally three times a day (TID)] followed by gabapentin 600mg/day (200mg TID) on Day 3. At the end of Week 1 (Day 7), the dose was increased to 1200mg/day (400 mg TID) and remained on this dose for the next 4 weeks). Subjects who had adequate seizure control (>=50% reduction in seizure frequency) with acceptable tolerability during this initial 5-week period, remained on this dose until the end of theTP (Week 9), then entered the MP on this dose. If seizure control was inadequate, the gabapentin dose was escalated to 1500mg/day (500mg TID) during Weeks 5 through 9. If they had adequate seizure control with acceptable tolerability on this dose, they entered the MP on this dose. If there was inadequate seizure control at the end of Week 9, the dose was escalated a final time to 1800mg/day (600mg TID), at which time they entered the MP.

Primary: Percent Change From Baseline in 28-day Seizure Frequency at Week 21

End point title	Percent Change From Baseline in 28-day Seizure Frequency at Week 21

End point description:

The seizures were recorded by the subjects, by a family member, by a caregiver, or by a legal guardian and documented in a daily seizure diary. Subject’s 28-day seizure frequency of all partial seizure was assessed during double blind (TP + MP) phase compared with baseline. Total partial seizure is defined as the total number of (simple partial seizure + complex partial seizure + secondary generalized tonic clonic seizure [SGTC]). Full analysis set (FAS) included all randomized subjects who had received at least 1 blinded dose of study drug and had at least 1 baseline and post baseline primary efficacy evaluation.

End point type	Primary

End point timeframe:

6 weeks Baseline, 21 weeks through End of MP for 27 weeks

End point values	Pregabalin	Gabapentin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	240		
Units: percent change				
median (full range (min-max))	-58.65 (-100 to 180)	-57.43 (-100 to 392.4)		

Statistical analyses

Statistical analysis title	Seizure Frequency at Week 21

Statistical analysis description:

Rank analysis of covariance (ANCOVA) model was used to derive p-value with treatment as main effect and cluster as cofactor, percent change in 28-day seizure counts between Baseline and treatment periods as dependent variable. Median differences and 95% confidence interval (CI) were based on Hodges-Lehmann estimation.

Comparison groups	Gabapentin v Pregabalin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8708
Method	Ranked ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	7

Secondary: Percentage of Subjects With 50% Reduction From Baseline in 28-day Seizure Rate at Week 21

End point title	Percentage of Subjects With 50% Reduction From Baseline in 28-day Seizure Rate at Week 21

End point description:

Subjects who had at least 50% reduction in seizure frequency from Baseline to double-blind treatment (TP + MP) were considered as 50% responders. If percent change from baseline <= -50 then responder rate = 1 (yes) otherwise responder rate = 0 (no). FAS included all randomized subjects who had received at least 1 blinded dose of study drug and had at least 1 Baseline and post Baseline primary efficacy evaluation. n= is the number of subjects that can be analyzed for each treatment group.

End point type	Secondary

End point timeframe:

6 weeks Baseline, 21 weeks through End of MP for 27 weeks

End point values	Pregabalin	Gabapentin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	240		
Units: percentage of subjects				
number (confidence interval 95%)				
All Partial Seizure (n= 238,240)	56.3 (50 to 62.6)	58.3 (52.1 to 64.6)		
Simple Partial (n= 87,88)	55.2 (44.7 to 65.6)	53.4 (43 to 63.8)		
Complex Partial (n= 161, 158)	56.5 (48.9 to 64.2)	55.1 (47.3 to 62.8)		
SGTC (n= 112,114)	50.9 (41.6 to 60.2)	60.5 (51.6 to 69.5)		

Statistical analyses

Statistical analysis title	50% Reduction in 28-day Seizure Rate at Week 21

Statistical analysis description:

The odds ratio and its 95% CI are calculated by exponentiating the log odds ratio and 95% CI that correspond to the treatment contrast in the logistic regression model with treatment as fixed effect and Baseline term and country as covariate. All statistical tests for secondary efficacy parameters were two sided and performed at significance level of α = 0.05. The above statistical analysis applies to All Partial Seizures - FAS Population.

Comparison groups	Gabapentin v Pregabalin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.662
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.635
upper limit	1.335

Secondary: Percentage of Subjects With 75% Reduction From Baseline in 28-day Seizure Rate at Week 21

End point title	Percentage of Subjects With 75% Reduction From Baseline in 28-day Seizure Rate at Week 21

End point description:

Subjects who had at least 75% reduction in seizure frequency from Baseline to double-blind treatment (TP + MP) were considered as 75% responders. If percent change from baseline <= -75 then 75% responder rate = 1 (yes) otherwise responder rate = 0 (no). Total partial seizure is defined as the total number of (simple partial seizure + complex partial seizure + SGTC). FAS included all randomized subjects who had received at least 1 blinded dose of study drug and had at least 1 Baseline and post Baseline primary efficacy evaluation. n= is the number of subjects that can be analyzed for each treatment group.

End point type	Secondary

End point timeframe:

6 weeks Baseline, 21 weeks through End of MP for 27 weeks

End point values	Pregabalin	Gabapentin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	240		
Units: percentage of subjects				
number (confidence interval 95%)				
All Partial Seizure (n= 238,240)	33.6 (27.6 to 39.6)	34.2 (28.2 to 40.2)		
Simple Partial (n= 87,88)	36.8 (26.7 to 46.9)	33 (23.1 to 42.8)		
Complex Partial (n= 161, 158)	37.3 (29.8 to 44.7)	36.1 (28.6 to 43.6)		
SGTC (n= 112,114)	38.4 (29.4 to 47.4)	43.9 (34.8 to 53)		

Statistical analyses

Statistical analysis title	All partial seizure
Statistical analysis description: p-value was calculated from the 2-sided Fisher's exact test.	
Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9232
Method	Fisher exact

Statistical analysis title	Simple Partial
Statistical analysis description: p-value was calculated from the 2-sided Fisher's exact test.	
Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6361
Method	Fisher exact

Statistical analysis title	Complex partial
Statistical analysis description: p-value was calculated from the 2-sided Fisher's exact test.	
Comparison groups	Pregabalin v Gabapentin

Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9075
Method	Fisher exact

Statistical analysis title	SGTC seizure
Statistical analysis description:	
p-value was calculated from the 2-sided Fisher's exact test.	
Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4203
Method	Fisher exact

Secondary: Percentage of Subjects Without Seizures

End point title	Percentage of Subjects Without Seizures

End point description:

Seizure free for 28 days was defined as subjects who have not experienced any seizure (simple partial, complex partial and SGTC) for at least 28 consecutive days from their last seizure until the end of the MP. Same subject could be seizure free for a specific type of seizure but not necessarily for the other types of seizure. FAS included all randomized subjects who had received at least 1 blinded dose of study drug and had at least 1 Baseline and post Baseline primary efficacy evaluation. n= is the number of subjects that can be analyzed for each treatment group.

End point type	Secondary

End point timeframe:

6 weeks Baseline, 21 weeks through End of MP for 27 weeks

End point values	Pregabalin	Gabapentin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189[1]	182[2]		
Units: percentage of subjects				
number (confidence interval 95%)				
All Partial Seizure (n= 189, 182)	30.7 (24.1 to 37.3)	34.1 (27.2 to 41)		
Simple Partial (n=74, 66)	29.7 (19.3 to 40.1)	36.4 (24.8 to 48)		
Complex Partial (n=126, 123)	37.3 (28.9 to 45.8)	40.7 (32 to 49.3)		
SGTC (n=95, 91)	46.3 (36.3 to 56.3)	42.9 (32.7 to 53)		

Notes:
[1] - Number of subjects analyzed 'N' signifies those subjects who were evaluable for the measure.
[2] - Number of subjects analyzed 'N' signifies those subjects who were evaluable for the measure.

Statistical analyses

Statistical analysis title	All partial seizure
Statistical analysis description: p-value was calculated from the 2-sided Fisher’s exact test.	
Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	371
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5069
Method	Fisher exact

Statistical analysis title	Simple partial seizure
Statistical analysis description: p-value was calculated from the 2-sided Fisher’s exact test.	
Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	371
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4721
Method	Fisher exact

Statistical analysis title	Complex partial seizure
Statistical analysis description: p-value was calculated from the 2-sided Fisher’s exact test.	
Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	371
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6054
Method	Fisher exact

Statistical analysis title	SGTC seizure
Statistical analysis description: p-value was calculated from the 2-sided Fisher’s exact test.	
Comparison groups	Pregabalin v Gabapentin

Number of subjects included in analysis	371
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6603
Method	Fisher exact

Secondary: Change From Baseline in the 28-day Secondarily Generalized Tonic-clonic (SGTC) Seizure Frequency at Week 21

End point title	Change From Baseline in the 28-day Secondarily Generalized Tonic-clonic (SGTC) Seizure Frequency at Week 21

End point description:

Change in SGTC = (Proportion of SGTC/All Partial Seizure rate during at the double-blind phase) - (Proportion of SGTC/All Partial Seizure rate at Baseline). Negative values indicate reduction from baseline. SGTC population included all subjects who had at least 1 SGTC seizure during either Baseline or double-blind phase. n= number of subjects evaluable at specific time points for each arm group, respectively.

End point type	Secondary

End point timeframe:

6 weeks Baseline, 21 weeks through End of MP for 27 weeks

End point values	Pregabalin	Gabapentin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	114		
Units: percentage of all partial seizure/28 day				
arithmetic mean (standard deviation)				
Baseline (n=114, 114)	56.53 (± 40.856)	59.6 (± 40.571)		
Change from Baseline at Double Blind (n= 104, 98)	1.59 (± 28.164)	-2.17 (± 26.024)		

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in Proportion of the 28-day SGTC Seizure Rate Over the Total Partial Seizure Rate at Week 21

End point title	Reduction in Proportion of the 28-day SGTC Seizure Rate Over the Total Partial Seizure Rate at Week 21

End point description:

SGTC Responder is defined as a subject who shows reduction from Baseline to double-blind phase in proportion of 28-Day SGTC Seizure Rate to 28-Day All Partial Seizure Rate. SGTC population included all subjects who had at least 1 SGTC seizure during either Baseline or double-blind phase. n is the number of subjects analyzed for SGTC. Twenty-six subjects were not included in the n because they did not have a post Baseline all partial seizure, but they were included in the analysis by seizure type.

End point type	Secondary

End point timeframe:

6 weeks Baseline, 21 weeks through End of MP for 27 weeks

End point values	Pregabalin	Gabapentin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	98		
Units: percentage of responders				
number (confidence interval 95%)	30.8 (21.9 to 39.6)	39.8 (30.1 to 49.5)		

Statistical analyses

Statistical analysis title	Reduction in SGTC Seizure Rate at Week 21
Statistical analysis description: p-value is calculated using Fisher Exact Test.	
Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1881
Method	Fisher exact

Secondary: Hospital Anxiety and Depression Scale (HADS) Score

End point title	Hospital Anxiety and Depression Scale (HADS) Score
End point description: HADS: subject rated questionnaire with 2 subscales. Hospital Anxiety and Depression Scale - anxiety (HADS-A) assesses state of generalized anxiety (anxious mood, restlessness, anxious thoughts, panic attacks); Hospital Anxiety and Depression Scale - depression (HADS-D) assesses state of lost interest and diminished pleasure response (lowering of hedonic tone). Each subscale comprised of 7 items with range 0 (no presence of anxiety or depression) to 3 (severe feeling of anxiety or depression). Total score 0 to 21 for each subscale; higher score indicates greater severity of anxiety and depression symptoms. FAS included all randomized subjects who had received at least 1 blinded dose of study drug and had at least 1 baseline and post baseline primary efficacy evaluation. n= number of subjects evaluable at specific time points for each arm group, respectively.	
End point type	Secondary
End point timeframe: Baseline, Week 21	

End point values	Pregabalin	Gabapentin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	240		
Units: Units on a scale				
least squares mean (standard error)				
Baseline HADS-A (n=238, 240)	7.82 (± 0.31)	7.6 (± 0.31)		

Change at Week 21/Early Termination (n=212, 210)	-0.92 (± 0.26)	-0.83 (± 0.27)		
Baseline HADS-D (n=238, 240)	5.94 (± 0.29)	5.65 (± 0.29)		
Change at Week 21/Early Termination (n=212,210)	-0.59 (± 0.24)	-0.42 (± 0.24)		

Statistical analyses

Statistical analysis title	Baseline, HADS-A
Statistical analysis description:	
ANCOVA model was used to calculate least square (LS) mean estimates of the treatment difference along with 95% CI, with main effects of treatment and and country as covariates.	
Comparison groups	Gabapentin v Pregabalin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5643
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.97
Variability estimate	Standard error of the mean
Dispersion value	0.38

Statistical analysis title	Change at Week 21/Early Termination(ET),HADS-A
Statistical analysis description:	
ANCOVA model was used to calculate LS mean estimates of the treatment difference along with 95% CI, with main effects of treatment and country as covariates.	
Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7712
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	0.54
Variability estimate	Standard error of the mean
Dispersion value	0.32

Statistical analysis title	Baseline, HADS-D
Statistical analysis description:	
ANCOVA model was used to calculate LS mean estimates of the treatment difference along with 95% CI, with main effects of treatment and combined center, and for post-baseline assessments baseline was included as a covariate.	
Comparison groups	Gabapentin v Pregabalin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4236
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.41
upper limit	0.97
Variability estimate	Standard error of the mean
Dispersion value	0.35

Statistical analysis title	Change at Week 21/ET, HADS-D
Statistical analysis description:	
ANCOVA model was used to calculate LS mean estimates of the treatment1difference along with 95% CI, with main effects of treatment and combined center, and for post-baseline assessments baseline was included as a covariate.	
Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5492
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.29

Secondary: Medical Outcomes Study Sleep Scale (MOS-SS) Score	
End point title	Medical Outcomes Study Sleep Scale (MOS-SS) Score

End point description:

Subject-rated 12-item questionnaire to assess constructs of sleep over past week; 7 subscales: sleep disturbance, snoring, awakened short of breath, sleep adequacy, somnolence (range: 0-100); sleep quantity (range: 0-24), optimal sleep (yes/no), and 9 item index measures of sleep disturbance provide composite scores: sleep problem summary, overall sleep problem. Except adequacy, optimal sleep and quantity, higher scores= more impairment. Scores transformed (actual raw score [RS] minus lowest possible score divided by possible RS range*100); total score range: 0-100; higher score= more intensity of attribute. FAS included all randomized subjects who had received at least 1 blinded dose of study drug and had at least 1 baseline and post baseline primary efficacy evaluation. n= number of subjects evaluable at specific time points for each arm group, respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 21

End point values	Pregabalin	Gabapentin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	240		
Units: Units on a scale				
least squares mean (standard error)				
Baseline: Sleep Disturbance (n=238, 240)	29.68 (± 1.7)	26.43 (± 1.7)		
Baseline: Snoring (n=238, 240)	29.28 (± 2.31)	28.09 (± 2.31)		
Baseline: Awaken Short of Breath (n=238, 240)	23.64 (± 2.07)	19.61 (± 2.07)		
Baseline: Quantity of Sleep (n=238, 240)	7.56 (± 0.11)	7.59 (± 0.11)		
Baseline: Adequacy of Sleep (n=238, 240)	61.3 (± 2.01)	63.67 (± 2.01)		
Baseline: Somnolence (n=238, 240)	32.29 (± 1.56)	29.31 (± 1.56)		
Baseline: Sleep Problem Index (9) (n=238, 240)	31.6 (± 1.32)	28.15 (± 1.32)		
Week 21: Sleep Disturbance (n=212, 210)	24.99 (± 1.37)	25.31 (± 1.39)		
Week 21: Snoring (n=212, 210)	28.07 (± 1.89)	26.12 (± 1.9)		
Week 21: Awaken Short of Breath (n=212, 210)	16.26 (± 1.73)	18.2 (± 1.74)		
Week 21: Quantity of Sleep (n=212, 210)	8.79 (± 0.17)	8.77 (± 0.17)		
Week 21: Adequacy of Sleep (n=212, 210)	63.87 (± 1.68)	64.53 (± 1.69)		
Week 21: Somnolence (n=212, 210)	32.04 (± 1.36)	29.98 (± 1.37)		
Week 21: Sleep Problem Index (9) (n=212, 210)	27.88 (± 1.04)	27.54 (± 1.05)		

Statistical analyses

Statistical analysis title	Baseline Sleep disturbance

Statistical analysis description:

ANCOVA model was used to calculate least square (LS) mean estimates of the treatment difference along with 95% CI, with main effects of treatment and country; for post-baseline, baseline was included as a covariate.

Comparison groups	Pregabalin v Gabapentin

Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.116
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	3.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	7.31
Variability estimate	Standard error of the mean
Dispersion value	2.07

Statistical analysis title	Week 21 Sleep disturbance

Statistical analysis description:

ANCOVA model was used to calculate LS mean estimates of the treatment difference along with 95% CI, with main effects of treatment and country; for post-baseline, baseline was included as a covariate.

Comparison groups	Gabapentin v Pregabalin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.849
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.62
upper limit	2.98
Variability estimate	Standard error of the mean
Dispersion value	1.68

Statistical analysis title	Baseline snoring

Statistical analysis description:

ANCOVA model was used to calculate LS mean estimates of the treatment difference along with 95% CI, with main effects of treatment and country; for post-baseline, baseline was included as a covariate.

Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6728
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	1.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.34
upper limit	6.73
Variability estimate	Standard error of the mean
Dispersion value	2.82

Statistical analysis title	Week 21 snoring

Statistical analysis description:

ANCOVA model was used to calculate LS mean estimates of the treatment difference along with 95% CI, with main effects of treatment and country; for post-baseline, baseline was included as a covariate.

Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3954
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	1.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.56
upper limit	6.47
Variability estimate	Standard error of the mean
Dispersion value	2.3

Statistical analysis title	Baseline Awaken Short of Breath

Statistical analysis description:

ANCOVA model was used to calculate LS mean estimates of the treatment difference along with 95% CI, with main effects of treatment and country; for post-baseline, baseline was included as a covariate.

Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1106
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	4.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	8.98
Variability estimate	Standard error of the mean
Dispersion value	2.52

Statistical analysis title	Week 21 Awaken Short of Breath
Statistical analysis description:	
ANCOVA model was used to calculate LS mean estimates of the treatment difference along with 95% CI, with main effects of treatment and country; for post-baseline, baseline was included as a covariate.	
Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3603
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-1.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.09
upper limit	2.22
Variability estimate	Standard error of the mean
Dispersion value	2.11

Statistical analysis title	Baseline Quantity of Sleep
Statistical analysis description:	
ANCOVA model was used to calculate LS mean estimates of the treatment difference along with 95% CI, with main effects of treatment and country; for post-baseline, baseline was included as a covariate.	
Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8312
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.24
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Week 21 Quantity of Sleep
Statistical analysis description:	
ANCOVA model was used to calculate LS mean estimates of the treatment difference along with 95% CI, with main effects of treatment and country; for post-baseline, baseline was included as a covariate.	

Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9101
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.38
upper limit	0.42
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Baseline Adequacy of Sleep

Statistical analysis description:

ANCOVA model was used to calculate LS mean estimates of the treatment difference along with 95% CI, with main effects of treatment and country; for post-baseline, baseline was included as a covariate.

Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3346
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-2.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.19
upper limit	2.45
Variability estimate	Standard error of the mean
Dispersion value	2.45

Statistical analysis title	Week 21 Adequacy of Sleep

Statistical analysis description:

ANCOVA model was used to calculate LS mean estimates of the treatment difference along with 95% CI, with main effects of treatment and country; for post-baseline, baseline was included as a covariate.

Comparison groups	Pregabalin v Gabapentin

Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7491
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.69
upper limit	3.37
Variability estimate	Standard error of the mean
Dispersion value	2.05

Statistical analysis title	Baseline Somnolence
Statistical analysis description:	
ANCOVA model was used to calculate LS mean estimates of the treatment difference along with 95% CI, with main effects of treatment and country; for post-baseline, baseline was included as a covariate.	
Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1162
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	2.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.74
upper limit	6.71
Variability estimate	Standard error of the mean
Dispersion value	1.9

Statistical analysis title	Week 21 Somnolence
Statistical analysis description:	
ANCOVA model was used to calculate LS mean estimates of the treatment difference along with 95% CI, with main effects of treatment and country; for post-baseline, baseline was included as a covariate.	
Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2163
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	2.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.21
upper limit	5.32
Variability estimate	Standard error of the mean
Dispersion value	1.66

Statistical analysis title	Baseline Sleep Problem Index (9)
Statistical analysis description:	
ANCOVA model was used to calculate LS mean estimates of the treatment difference along with 95% CI, with main effects of treatment and country; for post-baseline, baseline was included as a covariate.	
Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0321
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	3.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	6.61
Variability estimate	Standard error of the mean
Dispersion value	1.61

Statistical analysis title	Week 21 Sleep Problem Index (9)
Statistical analysis description:	
ANCOVA model was used to calculate LS mean estimates of the treatment difference along with 95% CI, with main effects of treatment and country; for post-baseline, baseline was included as a covariate.	
Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7889
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.17
upper limit	2.85
Variability estimate	Standard error of the mean
Dispersion value	1.28

Secondary: Percentage of Subjects With Optimal Sleep Assessed Using Medical Outcomes Study-Sleep Scale (MOS-SS) Score.

End point title	Percentage of Subjects With Optimal Sleep Assessed Using Medical Outcomes Study-Sleep Scale (MOS-SS) Score.

End point description:

MOS-SS: subject-rated 12 item questionnaire to assess constructs of sleep over past week. It included 7 subscales: sleep disturbance, snoring, awakened short of breath, sleep adequacy, somnolence, sleep quantity and optimal sleep. Subjects responded whether their sleep was optimal or not by choosing yes or no. Percentage of subjects with optimal sleep are reported. FAS included all randomized subjects who had received at least 1 blinded dose of study drug and had at least 1 baseline and post baseline primary efficacy evaluation. n= number of participants evaluable at specific time points for each arm group, respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 21

End point values	Pregabalin	Gabapentin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	240		
Units: percentage of subjects				
number (not applicable)				
Baseline (n=238, 240)	49.2	58.8		
Week 21 (n=212, 210)	51.4	58.6		

Statistical analyses

Statistical analysis title	MOS-SS Score: Week 21

Statistical analysis description:

Logistic regression model was used to estimate odds ratio and corresponding 95% CI of treatment difference, with treatment as fixed effect and for post-baseline assessments baseline was included as a covariate.

Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3459
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.811
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.524
upper limit	1.254

Statistical analysis title	MOSS - score: Baseline

Statistical analysis description:

Logistic regression model was used to estimate odds ratio and corresponding 95% CI of treatment difference, with treatment as fixed effect and for post-baseline assessments baseline was included as a covariate.

Comparison groups	Pregabalin v Gabapentin
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0252
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.653
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.449
upper limit	0.948

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to end of treatment

Adverse event reporting additional description:

The same event may appear as both an adverse event (AE) and a serious adverse event (SAE). However, what is presented are distinct events. An event may be categorized as serious in one subject and as nonserious in another subject, or one subject may have experienced both a serious and nonserious event during the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Gabapentin

Reporting group description:

Gabapentin was initiated at 300 mg/day [100 mg capsules orally three times a day (TID)] followed by gabapentin 600 mg/day (200 mg TID) on Day 3. At the end of Week 1 (Day 7), the dose was increased to 1200 mg/day (400 mg TID) and remained on this dose for the next 4 weeks). Subjects who had adequate seizure control (>=50% reduction in seizure frequency) with acceptable tolerability during this initial 5-week period, remained on this dose until the end of theTP (Week 9), then entered the MP on this dose. If seizure control was inadequate, the gabapentin dose was escalated to 1500 mg/day (500 mg TID) during Weeks 5 through 9. If they had adequate seizure control with acceptable tolerability on this dose, they entered the MP on this dose. If there was inadequate seizure control at the end of Week 9, the dose was escalated a final time to 1800 mg/day (600 mg TID), at which time they entered the MP.

Reporting group title	Pregabalin

Reporting group description:

Pregabalin was initiated at 150 mg/day [50 mg capsules orally three times a day (TID)] for 1 Week followed by pregabalin 300 mg/day (100 mg TID) orally TID up to Week 5 in the Titration Phase (TP). Subjects who had adequate seizure control (adequate: >=50 percent (%) reduction in seizures) with acceptable tolerability with pregabalin 300 mg/day in TP, continued same dose until the end of TP (Week 9) and then entered the maintenance phase (MP) on this dose. If seizure control was inadequate, the pregabalin dose was escalated to 450 mg/day orally (150 mg TID) from Weeks 5 through 9. If the subjects had adequate seizure control with acceptable tolerability on this dose, then they entered the MP on this dose. If there was inadequate seizure control at the end of Week 9, the dose was escalated a final time to 600 mg/day (200 mg TID) at which time they entered the MP.

Serious adverse events	Gabapentin	Pregabalin	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 241 (5.81%)	13 / 241 (5.39%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Astrocytoma			
subjects affected / exposed	1 / 241 (0.41%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 241 (0.41%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	1 / 241 (0.41%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 241 (0.00%)	2 / 241 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 241 (0.41%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Withdrawal syndrome			

subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 241 (0.41%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face injury			
subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	1 / 241 (0.41%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	1 / 241 (0.41%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			

subjects affected / exposed	1 / 241 (0.41%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			
subjects affected / exposed	1 / 241 (0.41%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 241 (0.41%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral disorder			
subjects affected / exposed	1 / 241 (0.41%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	0 / 241 (0.00%)	3 / 241 (1.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	1 / 241 (0.41%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Grand mal convulsion			

subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	2 / 241 (0.83%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	2 / 241 (0.83%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 241 (0.41%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 241 (0.41%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Rectal haemorrhage			
subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin necrosis			
subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urogenital fistula			
subjects affected / exposed	1 / 241 (0.41%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis viral			
subjects affected / exposed	1 / 241 (0.41%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 241 (0.00%)	2 / 241 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			

subjects affected / exposed	0 / 241 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Gabapentin	Pregabalin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	74 / 241 (30.71%)	74 / 241 (30.71%)	
Investigations			
Weight increased			
subjects affected / exposed	15 / 241 (6.22%)	23 / 241 (9.54%)	
occurrences (all)	16	26	
Nervous system disorders			
Dizziness			
subjects affected / exposed	21 / 241 (8.71%)	22 / 241 (9.13%)	
occurrences (all)	24	26	
Headache			
subjects affected / exposed	25 / 241 (10.37%)	21 / 241 (8.71%)	
occurrences (all)	35	31	
Somnolence			
subjects affected / exposed	34 / 241 (14.11%)	35 / 241 (14.52%)	
occurrences (all)	45	42	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 December 2007	Added the maximum duration time of 2 years for the blinded continuation phase.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported