Clinical trial results:
A Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study of the Efficacy and Safety of Pregabalin as Adjunctive Therapy in Children 1 Month Through <4 Years of Age With Partial Onset Seizures

Summary

EudraCT number	2013-003420-37
Trial protocol	BE HU NL ES DE PL SK GR PT BG
Global end of trial date	13 March 2018

Results information

Result version number	v1 (current)
This version publication date	23 September 2018
First version publication date	23 September 2018

Trial information

Trial identification

Sponsor protocol code	A0081042

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02072824
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 ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 July 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of 2 dose levels of Pregabalin compared to placebo as an adjunctive treatment in reducing the frequency of POS in pediatric subjects 1 month to <4 years of age.

Protection of trial subjects:

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

Background therapy:

Subjects were on a stable dose of 1 to 3 antiepileptic drugs concomitant to double-blind study medication throughout the duration of the study.

Evidence for comparator: -

Actual start date of recruitment	16 September 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Bulgaria: 3
Country: Number of subjects enrolled	China: 2
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Belarus: 4
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Lebanon: 6
Country: Number of subjects enrolled	Malaysia: 2
Country: Number of subjects enrolled	Philippines: 41
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Russian Federation: 16
Country: Number of subjects enrolled	Serbia: 4
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: 4
Country: Number of subjects enrolled	Ukraine: 57
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	175
EEA total number of subjects	25

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)	65
Children (2-11 years)	110
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects received treatment in double-blind treatment phase (total duration: 21 days) which included dose escalation (5 days), fixed-dose (9 days) and taper (7 days).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pregabalin 7 mg/kg/day or 6 mg/kg/day

Arm description:

Subjects aged greater than (>) 3 months to less than (<) 4 years, received Pregabalin 3.5 milligrams per kilogram per day (mg/kg/day) (3.0 mg/kg/day for subjects 1 to 3 months of age), orally three times daily (TID) in equally divided doses for first 5 days; followed by 7 mg/kg/day (6 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for 9 days and 3.5 mg/kg/day (3.0 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for next 7 days.

Arm type	Experimental
Investigational medicinal product name	Pregabalin
Investigational medicinal product code	NO3AX16
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Pregabalin was administered as oral solution, TID, up to 21 days.

Arm title	Pregabalin 14 mg/kg/day or 12 mg/kg/day

Arm description:

Subjects aged >3 months to <4 years, received Pregabalin 3.5 mg/kg/day (3.0 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for first 2 days and 7 mg/kg/day (6 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for next 3 days; followed by 14 mg/kg/day (12 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for 9 days; and 7 mg/kg/day (6 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for next 4 days and 3.5 mg/kg/day (3.0 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for next 3 days.

Arm type	Experimental
Investigational medicinal product name	Pregabalin
Investigational medicinal product code	NO3AX16
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Pregabalin was administered as oral solution, TID, up to 21 days.

Arm title	Placebo

Arm description:

Subjects aged >3 months to <4 years received placebo matched to Pregabalin, orally TID for 21 days.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to Pregabalin was administered as oral solution, TID, up to 21 days.

Number of subjects in period 1	Pregabalin 7 mg/kg/day or 6 mg/kg/day	Pregabalin 14 mg/kg/day or 12 mg/kg/day	Placebo
Started	71	34	70
Completed	69	33	67
Not completed	2	1	3
Medication error	-	1	-
No longer willing to participate	1	-	1
Adverse Events	-	-	1
Insufficient clinical response	1	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Pregabalin 7 mg/kg/day or 6 mg/kg/day
Reporting group description:	
Subjects aged greater than (>) 3 months to less than (<) 4 years, received Pregabalin 3.5 milligrams per kilogram per day (mg/kg/day) (3.0 mg/kg/day for subjects 1 to 3 months of age), orally three times daily (TID) in equally divided doses for first 5 days; followed by 7 mg/kg/day (6 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for 9 days and 3.5 mg/kg/day (3.0 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for next 7 days.	
Reporting group title	Pregabalin 14 mg/kg/day or 12 mg/kg/day
Reporting group description:	
Subjects aged >3 months to <4 years, received Pregabalin 3.5 mg/kg/day (3.0 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for first 2 days and 7 mg/kg/day (6 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for next 3 days; followed by 14 mg/kg/day (12 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for 9 days; and 7 mg/kg/day (6 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for next 4 days and 3.5 mg/kg/day (3.0 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for next 3 days.	
Reporting group title	Placebo
Reporting group description:	
Subjects aged >3 months to <4 years received placebo matched to Pregabalin, orally TID for 21 days.	

Reporting group values	Pregabalin 7 mg/kg/day or 6 mg/kg/day	Pregabalin 14 mg/kg/day or 12 mg/kg/day	Placebo
Number of subjects	71	34	70
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)	27	12	26
Children (2-11 years)	44	22	44
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Safety population included all randomized subjects who received at least 1 dose of study drug.			
Units: months			
arithmetic mean	27.5	28.5	28.8
standard deviation	± 12.7	± 12.5	± 12.6
Sex: Female, Male			
Safety population included all randomized subjects who received at least 1 dose of study drug.			
Units: Subjects			
Female	26	14	32
Male	45	20	38
Race (NIH/OMB)			
Safety population included all randomized subjects who received at least 1 dose of study drug.			
Units: Subjects			

American Indian or Alaska Native	0	0	0
Asian	23	10	19
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	47	24	49
More than one race	0	0	0
Other	1	0	2
Weight			
Safety population included all randomized subjects who received at least 1 dose of study drug.			
Units: kilogram			
arithmetic mean	11.7	11.4	11.4
standard deviation	± 3.5	± 3.4	± 3.1

Reporting group values	Total		
Number of subjects	175		
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)	65		
Children (2-11 years)	110		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Safety population included all randomized subjects who received at least 1 dose of study drug.			
Units: months			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Safety population included all randomized subjects who received at least 1 dose of study drug.			
Units: Subjects			
Female	72		
Male	103		
Race (NIH/OMB)			
Safety population included all randomized subjects who received at least 1 dose of study drug.			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	52		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	120		
More than one race	0		
Other	3		

Weight			
Safety population included all randomized subjects who received at least 1 dose of study drug.			
Units: kilogram arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	Pregabalin 7 mg/kg/day or 6 mg/kg/day

Reporting group description:

Subjects aged greater than (>) 3 months to less than (<) 4 years, received Pregabalin 3.5 milligrams per kilogram per day (mg/kg/day) (3.0 mg/kg/day for subjects 1 to 3 months of age), orally three times daily (TID) in equally divided doses for first 5 days; followed by 7 mg/kg/day (6 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for 9 days and 3.5 mg/kg/day (3.0 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for next 7 days.

Reporting group title	Pregabalin 14 mg/kg/day or 12 mg/kg/day

Reporting group description:

Subjects aged >3 months to <4 years, received Pregabalin 3.5 mg/kg/day (3.0 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for first 2 days and 7 mg/kg/day (6 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for next 3 days; followed by 14 mg/kg/day (12 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for 9 days; and 7 mg/kg/day (6 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for next 4 days and 3.5 mg/kg/day (3.0 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for next 3 days.

Reporting group title	Placebo

Reporting group description:

Subjects aged >3 months to <4 years received placebo matched to Pregabalin, orally TID for 21 days.

Primary: Log Transformed 24-Hour Seizure Rate for All Partial Onset Seizures During the Double-Blind Treatment Phase

End point title	Log Transformed 24-Hour Seizure Rate for All Partial Onset Seizures During the Double-Blind Treatment Phase

End point description:

All partial onset seizures experienced during treatment phase were recorded by central reader during the 48 to 72 hour video-electroencephalogram (EEG). Double Blind 24 hour EEG seizure rate for all partial onset seizures = ([Number of seizures in double blind 48 to 72 hour EEG assessment] divided by [number of hours of video-EEG monitoring])*24. The EEG assessment was done at the end of the fixed dose treatment. For log-transformation, the quantity 1 was added to the double blind 24 hour EEG seizure rate for all subjects to account for any possible "0" seizure incidence. This resulted in final calculation as: log transformed (double-blind 24-hour EEG seizure rate + 1). Modified intent-to-treat (mITT) population included all randomized subjects who took at least one dose of study drug during the double-blind treatment phase, had a baseline with at least one partial onset seizure identified by video-EEG (at least 24 hours of evaluable monitoring) and a treatment phase video-EEG.

End point type	Primary

End point timeframe:

Day 1 up to Day 14

End point values	Pregabalin 7 mg/kg/day or 6 mg/kg/day	Pregabalin 14 mg/kg/day or 12 mg/kg/day	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	28	53	
Units: seizures per 24 hours				
least squares mean (standard error)	1.69 (± 0.115)	1.15 (± 0.163)	1.58 (± 0.129)	

Statistical analyses

Statistical analysis title	Pregabalin 7 mg/kg/day or 6 mg/kg/day vs. Placebo
Statistical analysis description:	
Linear model with log transformed baseline seizure rate as continuous covariate and treatment, age stratum, and geographical region as fixed factor effects.	
Comparison groups	Pregabalin 7 mg/kg/day or 6 mg/kg/day v Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4606
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	0.42
Variability estimate	Standard error of the mean
Dispersion value	0.153

Statistical analysis title	Pregabalin 14 mg/kg/day or 12 mg/kg/day vs.Placebo
Statistical analysis description:	
Linear model with log transformed baseline seizure rate as continuous covariate and treatment, age stratum, and geographical region as fixed factor effects.	
Comparison groups	Pregabalin 14 mg/kg/day or 12 mg/kg/day v Placebo
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0223
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	-0.06
Variability estimate	Standard error of the mean
Dispersion value	0.185

Secondary: Responder Rate: Percentage of Subjects With at Least 50 Percent (%) or Greater Reduction From Baseline in 24-Hour Seizure Rate for All Partial Onset Seizures During the Double-Blind Treatment Phase

End point title	Responder Rate: Percentage of Subjects With at Least 50 Percent (%) or Greater Reduction From Baseline in 24-Hour Seizure Rate for All Partial Onset Seizures During the Double-Blind Treatment Phase

End point description:

Responder Rate was defined as percentage of subjects who had a 50% or greater reduction from baseline in 24-hour seizure rate during the double-blind treatment phase. Double Blind 24 hour EEG seizure rate for all partial onset seizures = ([Number of seizures in double blind 48 to 72 hour EEG assessment] divided by [number of hours of video-EEG monitoring])*24. The EEG assessment was done at the end of the fixed dose treatment. mITT population included all randomized subjects who took at least one dose of study drug during the double-blind treatment phase, had a baseline with at least one partial onset seizure identified by video-EEG (at least 24 hours of evaluable monitoring) and a treatment phase video-EEG.

End point type	Secondary

End point timeframe:

Day 1 up to Day 14

End point values	Pregabalin 7 mg/kg/day or 6 mg/kg/day	Pregabalin 14 mg/kg/day or 12 mg/kg/day	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	28	53	
Units: percentage of subjects				
number (not applicable)	30.51	53.57	41.51	

Statistical analyses

Statistical analysis title	Pregabalin 7 mg/kg/day or 6 mg/kg/day vs.Placebo

Statistical analysis description:

The dichotomized responder variable was analyzed using a logistic regression model via maximum likelihood estimation with treatment group, age stratum, and geographical region as a fixed effect covariates.

Comparison groups	Pregabalin 7 mg/kg/day or 6 mg/kg/day v Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2418
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.625

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.284
upper limit	1.373

Statistical analysis title	Pregabalin 14 mg/kg/day or 12 mg/kg/day vs.Placebo

Statistical analysis description:

The dichotomized responder variable was analyzed using a logistic regression model via maximum likelihood estimation with treatment group, age stratum, and geographical region as a fixed effect covariates.

Comparison groups	Pregabalin 14 mg/kg/day or 12 mg/kg/day v Placebo
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.305
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.622
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.644
upper limit	4.086

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

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

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent AEs were events which occurred between first dose of study drug and up to end of study (up to Day 25) that were absent before treatment or that worsened relative to pre-treatment state. AEs included both serious and non-serious adverse events. Safety population included all randomized subjects who received at least 1 dose of study drug.

End point type	Other pre-specified

End point timeframe:

Day 1 up to End of study (EOS) (maximum Day 25)

End point values	Pregabalin 7 mg/kg/day or 6 mg/kg/day	Pregabalin 14 mg/kg/day or 12 mg/kg/day	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	34	70	
Units: subjects				
AEs	32	17	38	
SAEs	0	1	4	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Treatment-related AE was any untoward medical occurrence attributed to study drug in a subject who received study drug. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent AEs were events which occurred between first dose of study drug and up to end of study (up to Day 25) that were absent before treatment or that worsened relative to pre-treatment state. Relatedness to drug was assessed by the investigator. AEs included both serious and non-serious adverse events. Safety population included all randomized subjects who received at least 1 dose of study drug.

End point type	Other pre-specified

End point timeframe:

Day 1 up to EOS (maximum Day 25)

End point values	Pregabalin 7 mg/kg/day or 6 mg/kg/day	Pregabalin 14 mg/kg/day or 12 mg/kg/day	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	34	70	
Units: subjects				
AEs	15	8	13	
SAEs	0	0	1	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Adverse Events by Severity

End point title	Number of Adverse Events by Severity

End point description:

An AE was any untoward medical occurrence attributed to study drug in a subject who received study drug. AEs were classified according to the severity in 3 categories a) mild: AEs does not interfere with subject's usual function b) moderate: AEs interferes to some extent with subject's usual function c) severe: AEs interferes significantly with subject's usual function. Safety population included all randomized subjects who received at least 1 dose of study drug.

End point type	Other pre-specified

End point timeframe:

Day 1 up to EOS (maximum Day 25)

End point values	Pregabalin 7 mg/kg/day or 6 mg/kg/day	Pregabalin 14 mg/kg/day or 12 mg/kg/day	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	34	70	
Units: events				
Mild|	60	23	67	
Moderate|	3	13	19	
Severe|	0	0	0	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Laboratory Test Abnormalities

End point title	Number of Subjects With Laboratory Test Abnormalities

End point description:

Abnormality Criteria: hemoglobin,hematocrit,red blood cells(RBC)count:<0.8*lower limit of normal[LLN],platelets:<0.5*LLN/>1.75*upper limit of normal[ULN]; leukocytes:<0.6*LLN/>1.5*ULN; lymphocytes,neutrophils, total protein,albumin, tetraiodothyronine,thyroid stimulating hormone:<0.8*LLN/>1.2*ULN; basophils,eosinophils,monocytes:>1.2*ULN; prothrombin [PT],PT international ratio:>1.1*ULN; aspartate aminotransferase,alanine aminotransferase,alkaline phosphatase,gamma glutamyl transferase:>0.3*ULN; bilirubin:>1.5*ULN; blood urea nitrogen,creatinine, cholesterol,triglycerides:>1.3*ULN; sodium: <0.95*LLN/>1.05*ULN; potassium,chloride,calcium,bicarbonate:<0.9*LLN/>1.1*ULN; glucose fasting:<0.6*LLN/>1.5*ULN; creatine kinase:>2*ULN;urine glucose,ketone,protein:>=1;urine WBC,RBC:>= 20/High Power Field[HPF]; urine casts,hyaline casts:>1/Low Power Field; urine bacteria:>20/HPF. Analysis was performed on safety population.Here,number of subject analyzed=subjects evaluable for this endpoint.

End point type	Other pre-specified

End point timeframe:

From Baseline up to EOS (maximum Day 25)

End point values	Pregabalin 7 mg/kg/day or 6 mg/kg/day	Pregabalin 14 mg/kg/day or 12 mg/kg/day	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	34	69	
Units: subjects	65	29	61	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Subjects With Vital Signs Abnormalities

End point description:

Criteria for abnormalities in vital signs included: sitting/supine systolic blood pressure (SBP) values: maximum increase and decrease of greater than or equal to (>=) 30 millimeter of mercury (mmHg) from baseline; sitting/supine diastolic blood pressure (DBP) value: maximum increase and decrease of >=20 mmHg from baseline. Safety population included all randomized subjects who received at least 1 dose of study drug.

End point type	Other pre-specified

End point timeframe:

From Baseline (BL) up to EOS (maximum Day 25)

End point values	Pregabalin 7 mg/kg/day or 6 mg/kg/day	Pregabalin 14 mg/kg/day or 12 mg/kg/day	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	34	70	
Units: subjects				
Maximum Increase from BL(>=30):sitting/supine SBP	2	0	1	
Maximum Increase from BL(>=20):sitting/supine DBP	7	1	3	
Maximum Decrease from BL(>=30):sitting/supine SBP	1	0	1	
Maximum Decrease from BL(>=20):sitting/supine DBP	2	2	1	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Abnormal Physical Examination Findings at Screening and End of Study

End point title	Percentage of Subjects With Abnormal Physical Examination Findings at Screening and End of Study

End point description:

Physical examinations evaluated the following body systems/organs: abdomen; ears; extremities; eyes;

general appearance; head; heart; lungs; lymph nodes; mouth; musculoskeletal; nose; skin and throat. Abnormalities in physical examination were based on investigator's discretion. Safety population included all randomized subjects who received at least 1 dose of study drug. Here, "n" signifies number of subjects who were evaluable for the specified category for each arm respectively.

End point type	Other pre-specified

End point timeframe:

Screening and EOS (maximum Day 25)

End point values	Pregabalin 7 mg/kg/day or 6 mg/kg/day	Pregabalin 14 mg/kg/day or 12 mg/kg/day	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	34	70	
Units: percentage of subjects				
number (not applicable)				
Abdomen: Screening (n=71,34,70)	4.2	5.9	2.9	
Abdomen: EOS (n=71,34,69)	4.2	5.9	1.4	
Ears: Screening (n=71,34,70)	1.4	0	1.4	
Ears: EOS (n=70,34,69)	1.4	0	1.4	
Extremities: Screening (n=71,34,70)	14.1	26.5	15.7	
Extremities: EOS (n=71,34,69)	14.1	26.5	18.8	
Eyes: Screening (n=71,34,70)	9.9	20.6	17.1	
Eyes: EOS (n=71,34,69)	9.9	20.6	18.8	
General appearance: Screening (n=71,34,70)	15.5	26.5	15.7	
General appearance: EOS (n=71,34,69)	15.5	23.5	15.9	
Head: Screening (n=71,34,70)	31.0	47.1	31.4	
Head: EOS (n=71,34,69)	33.8	47.1	31.9	
Heart: Screening (n=71,34,70)	1.4	8.8	4.3	
Heart: EOS (n=71,34,69)	1.4	5.9	4.3	
Lungs: Screening (n=71,34,70)	2.8	8.8	4.3	
Lungs: EOS (n=71,34,69)	2.8	8.8	5.8	
Lymph nodes: Screening (n=71,34,70)	0	8.8	0	
Lymph nodes: EOS (n=70,34,69)	0	2.9	0	
Mouth: Screening (n=71,34,70)	9.9	2.9	5.7	
Mouth: EOS (n=70,34,69)	7.1	2.9	5.8	
Musculoskeletal: Screening (n=71,34,70)	31.0	38.2	35.7	
Musculoskeletal: EOS (n=71,34,69)	33.8	38.2	37.7	
Nose: Screening (n=71,34,70)	0	2.9	0	
Nose: EOS (n=70,34,69)	0	0	5.8	
Skin: Screening (n=71,34,70)	9.9	14.7	21.4	
Skin: EOS (n=71,34,69)	8.5	14.7	21.7	
Throat: Screening (n=71,34,70)	1.4	2.9	0	
Throat: EOS (n=70,34,68)	0	5.9	2.9	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Abnormal Neurological Examination Findings at Baseline and End of Study

End point title	Percentage of Subjects With Abnormal Neurological Examination Findings at Baseline and End of Study

End point description:

Neurological examinations included: coordination; cranial nerve function (CNF); gait and station; level of consciousness (LOC); lower and upper extremity sensation; muscle strength (str.); muscle tone; nystagmus; reflexes and speech. Abnormalities in neurological examination were based on investigator's discretion and also, some components of the neurological examination were not done for certain subjects due to subject age or significant developmental impairment. Only those categories of neurological examination in which at least 10% of subjects had an abnormality in any treatment group at any time point were reported in this endpoint. Safety population included all randomized subjects who received at least 1 dose of study drug. Here, "n" signifies number of subjects who were evaluable for the specified category for each arm respectively.

End point type	Other pre-specified

End point timeframe:

Baseline (BL) and EOS (maximum Day 25)

End point values	Pregabalin 7 mg/kg/day or 6 mg/kg/day	Pregabalin 14 mg/kg/day or 12 mg/kg/day	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	34	70	
Units: percentage of subjects				
number (not applicable)				
Coordination-left hand movement(BL)(n=71,34,70)	1.4	11.8	8.6	
Coordination-left hand movement(EOS)(n=71,34,69)	1.4	8.8	10.1	
Coordination-right hand movement(EOS)(n=71,34,69)	2.8	5.9	10.1	
Coordination romberg test (BL)(n=71,34,70)	2.8	8.8	10.0	
Coordination-romberg test (EOS)(n=71,34,69)	2.8	5.9	11.6	
CNF-left eye visual field(BL)(n=71,34,70)	12.7	8.8	10.0	
CNF-left eye visual field(EOS)(n=71,34,69)	12.7	8.8	10.1	
CNF-right eye visual field (BL)(n=71,34,70)	12.7	5.9	10.0	
CNF- right eye visual field (EOS)(n=71,34,69)	12.7	5.9	10.1	
CNF-left fundoscopic exam(BL)(n=71,34,70)	12.7	26.5	12.9	
CNF-left fundoscopic exam(EOS)(n=71,34,69)	12.7	23.5	14.5	
CNF-right fundoscopic exam(BL)(n=71,34,70)	11.3	20.6	14.3	
CNF-right fundoscopic exam(EOS)(n=71,34,69)	11.3	17.6	14.5	
CNF-left visual acuity(BL)(n=71,34,70)	11.3	11.8	12.9	
CNF-left visual acuity(EOS)(n=71,34,69)	11.3	11.8	13.0	

CNF-right visual acuity(BL)(n=71,34,70)	11.3	11.8	11.4	
CNF-right visual acuity(EOS)(n=71,34,69)	11.3	11.8	11.6	
CNF-finger tracking(BL)(n=71,34,70)	22.5	26.5	24.3	
CNF-finger tracking (EOS)(n=71,34,69)	21.1	23.5	26.1	
CNF-swallowing(BL)(n=71,34,70)	14.1	14.7	14.3	
CNF-swallowing (EOS)(n=71,34,69)	14.1	14.7	14.5	
CNF-Leftshoulder,headturn str.(BL)(n=71,34,70)	11.3	2.9	7.1	
CNF-Leftshoulder,headturn str.(EOS)(n=71,34,69)	11.3	2.9	10.1	
Gait and station–gait (BL)(n=71,34,70)	52.1	50.0	45.7	
Gait and station–gait (EOS)(n=71,34,69)	52.1	52.9	46.4	
Level of consciousness(BL)(n=71,34,70)	5.6	20.6	5.7	
Level of consciousness(EOS)(n=71,34,69)	7.0	20.6	2.9	
Muscle str.-lower extremities (BL)(n=71,34,70)	49.3	58.8	51.4	
Muscle str.-lower extremities(EOS)(n=71,34,69)	49.3	58.8	53.6	
Muscle strength-upper extremities (BL)(n=71,34,70)	47.9	58.8	50.0	
Muscle strength-upper extremities(EOS)n=71,34,69	49.3	58.8	52.2	
Muscle strength-trunk(BL)(n=71,34,70)	43.7	38.2	44.3	
Muscle strength-trunk(EOS)(n=71,34,69)	39.4	38.2	42.0	
Muscle tone-lower extremities(BL)(n=70,34,69)	64.3	73.5	63.8	
Muscle tone-lower extremities(EOS)(n=71,34,68)	64.8	73.5	66.2	
Muscle tone-upper extremities(BL)(n=71,34,69)	64.8	73.5	63.8	
Muscle tone-upper extremities (EOS)(n=71,34,68)	64.8	73.5	66.2	
Nystagmus-horizontal(BL)(n=71,34,70)	9.9	11.8	7.1	
Nystagmus-horizontal(EOS)(n=71,34,69)	8.5	11.8	5.8	
Reflexes-left ankle(BL)(n=71,34,70)	46.5	52.9	47.1	
Reflexes-left ankle(EOS)(n=71,34,69)	46.5	52.9	46.4	
Reflexes-right ankle(BL)(n=71,34,70)	46.5	58.8	47.1	
Reflexes-right ankle (EOS)(n=71,34,69)	45.1	58.8	46.4	
Reflexes-left babinski(BL)(n=71,34,70)	42.3	47.1	47.1	
Reflexes-left babinski(EOS)(n=71,34,69)	40.8	47.1	47.8	
Reflexes-right babinski(BL)(n=71,34,70)	42.3	55.9	50.0	
Reflexes-right babinski(EOS)(n=71,34,69)	40.8	55.9	50.7	
Reflexes-left biceps(BL)(n=71,34,70)	47.9	52.9	50.0	
Reflexes-left biceps(EOS)(n=71,34,69)	47.9	52.9	49.3	
Reflexes-right biceps(BL)(n=71,34,70)	46.5	58.8	52.9	
Reflexes-right biceps(EOS)(n=71,34,69)	46.5	58.8	52.2	
Reflexes-left brachioradialis(BL)(n=71,34,70)	45.1	52.9	48.6	
Reflexes-left brachioradialis(EOS)(n=71,34,69)	45.1	52.9	47.8	

Reflexes-right brachioradialis(BL)(n=71,34,70)	43.7	58.8	50.0	
Reflexes-right brachioradialis(EOS)(n=71,34,69)	43.7	58.8	50.7	
Reflexes-left knee(BL)(n=71,34,70)	53.5	55.9	57.1	
Reflexes-left knee(EOS)(n=71,34,69)	52.1	58.8	56.5	
Reflexes-right knee(BL)(n=71,34,70)	52.1	61.8	61.4	
Reflexes-right knee (EOS)(n=71,34,69)	50.7	64.7	59.4	
Reflexes-left triceps(BL)(n=71,34,70)	46.5	52.9	45.7	
Reflexes-left triceps(EOS)(n=71,34,69)	46.5	52.9	44.9	
Reflexes-right triceps(BL)(n=71,34,70)	45.1	58.8	48.6	
Reflexes-right triceps(EOS)(n=71,34,69)	45.1	58.8	47.8	
Speech-articulation(BL)(n=71,34,70)	53.5	47.1	45.7	
Speech-articulation(EOS)(n=71,34,69)	54.9	44.1	47.8	
Speech-language(BL)(n=71,34,70)	69.0	76.5	65.7	
Speech-language(EOS)(n=71,34,68)	69.0	73.5	66.7	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Subjects With Electrocardiogram (ECG) Abnormalities

End point description:

Criteria for abnormalities in ECG findings: 1) Time from ECG Q wave to the end of the S wave corresponding to ventricle depolarization (QRS complex): >=140 milliseconds (msec); 2) The interval between the start of the P wave and the start of the QRS complex, corresponding to the time between the onset of the atrial depolarization and onset of ventricular depolarization (PR interval): >=200 msec; 3) Time from ECG Q wave to the end of the T wave corresponding to electrical systole corrected for heart rate using Fridericia's formula (QTCF interval): absolute value 450 to <480 msec, 480 to <500 msec, >=500 msec; 4) Maximum QT interval: >=500 msec; 5) Maximum QTCB interval (Bazett's correction): 450 to< 480 msec, 480 to <500 msec, >=500 msec. Only those categories of ECG abnormalities in which subjects were found abnormal (maximum QTCB interval 450-<480 msec), were reported in this endpoint. Safety population included all randomized subjects who received at least 1 dose of study drug.

End point type	Other pre-specified

End point timeframe:

From screening up to EOS (maximum Day 25)

End point values	Pregabalin 7 mg/kg/day or 6 mg/kg/day	Pregabalin 14 mg/kg/day or 12 mg/kg/day	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	34	70	
Units: subjects	0	2	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 up to End of Study (maximum Day 25)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	v20.1

Reporting groups	
Reporting group title	Pregabalin 7 mg/kg/day or 6 mg/kg/day
Reporting group description:	
Subjects aged > 3 months to < 4 years, received Pregabalin 3.5 mg/kg/day (3.0 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for first 5 days; followed by 7 mg/kg/day (6 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for 9 days and 3.5 mg/kg/day (3.0 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for next 7 days.	
Reporting group title	Placebo
Reporting group description:	
Subjects aged >3 months to <4 years received placebo matched to Pregabalin, orally TID for 21 days.	
Reporting group title	Pregabalin 14 mg/kg/day or 12 mg/kg/day
Reporting group description:	
Subjects aged >3 months to <4 years, received Pregabalin 3.5 mg/kg/day (3.0 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for first 2 days and 7 mg/kg/day (6 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for next 3 days; followed by 14 mg/kg/day (12 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for 9 days; and 7 mg/kg/day (6 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for next 4 days and 3.5 mg/kg/day (3.0 mg/kg/day for subjects 1 to 3 months of age), orally TID in equally divided doses for next 3 days.	

Serious adverse events	Pregabalin 7 mg/kg/day or 6 mg/kg/day	Placebo	Pregabalin 14 mg/kg/day or 12 mg/kg/day
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 71 (0.00%)	4 / 70 (5.71%)	1 / 34 (2.94%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (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, thoracic and mediastinal disorders			
Choking			

subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Pregabalin 7 mg/kg/day or 6 mg/kg/day	Placebo	Pregabalin 14 mg/kg/day or 12 mg/kg/day
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 71 (45.07%)	37 / 70 (52.86%)	16 / 34 (47.06%)
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 71 (1.41%)	2 / 70 (2.86%)	0 / 34 (0.00%)
occurrences (all)	1	2	0
General disorders and administration site conditions			
Application site irritation			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	2
Asthenia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Hyperthermia			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	4 / 71 (5.63%)	4 / 70 (5.71%)	2 / 34 (5.88%)
occurrences (all)	4	5	2
Sluggishness			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Feeling hot			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Bronchial hyperreactivity			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Cough			
subjects affected / exposed	1 / 71 (1.41%)	3 / 70 (4.29%)	0 / 34 (0.00%)
occurrences (all)	1	3	0
Rhinitis allergic			
subjects affected / exposed	2 / 71 (2.82%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	3	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Enuresis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Irritability			

subjects affected / exposed	3 / 71 (4.23%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	3	2	0
Sleep disorder			
subjects affected / exposed	2 / 71 (2.82%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	2	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Electrocardiogram repolarisation abnormality			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Lymphocyte morphology abnormal			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Lymphocyte percentage increased			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Neutrophil percentage decreased			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Platelet count increased			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Fall			

subjects affected / exposed	2 / 71 (2.82%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	2	1	0
Skin abrasion			
subjects affected / exposed	0 / 71 (0.00%)	2 / 70 (2.86%)	0 / 34 (0.00%)
occurrences (all)	0	2	0
Cardiac disorders			
Bradyarrhythmia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Dysarthria			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Epilepsy			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Hypersomnia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Lethargy			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Myoclonic epilepsy			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Psychomotor hyperactivity			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Seizure			

subjects affected / exposed	1 / 71 (1.41%)	3 / 70 (4.29%)	2 / 34 (5.88%)
occurrences (all)	1	3	2
Somnolence			
subjects affected / exposed	8 / 71 (11.27%)	4 / 70 (5.71%)	6 / 34 (17.65%)
occurrences (all)	9	4	6
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 71 (0.00%)	2 / 70 (2.86%)	1 / 34 (2.94%)
occurrences (all)	0	2	1
Eye disorders			
Chalazion			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Mydriasis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	2
Diarrhoea			
subjects affected / exposed	3 / 71 (4.23%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	4	0	0
Dry mouth			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	1	1	0
Gingival bleeding			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Oral contusion			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Regurgitation			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Salivary hypersecretion			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	1 / 71 (1.41%)	6 / 70 (8.57%)	0 / 34 (0.00%)
occurrences (all)	1	6	0
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Dermatitis atopic			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Dermatitis diaper			
subjects affected / exposed	0 / 71 (0.00%)	3 / 70 (4.29%)	0 / 34 (0.00%)
occurrences (all)	0	3	0
Eczema			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 71 (0.00%)	2 / 70 (2.86%)	0 / 34 (0.00%)
occurrences (all)	0	2	0
Rash			
subjects affected / exposed	0 / 71 (0.00%)	3 / 70 (4.29%)	0 / 34 (0.00%)
occurrences (all)	0	3	0
Skin irritation			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Vesicoureteric reflux			

subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Bronchitis viral			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Fungal infection			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Impetigo			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Lice infestation			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 71 (1.41%)	3 / 70 (4.29%)	2 / 34 (5.88%)
occurrences (all)	1	3	2
Otitis media			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Pneumonia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	2 / 34 (5.88%)
occurrences (all)	1	0	2
Respiratory tract infection viral			
subjects affected / exposed	2 / 71 (2.82%)	1 / 70 (1.43%)	1 / 34 (2.94%)
occurrences (all)	2	2	1

Rhinitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Tracheitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Upper respiratory tract infection			
subjects affected / exposed	5 / 71 (7.04%)	8 / 70 (11.43%)	4 / 34 (11.76%)
occurrences (all)	5	8	5
Urinary tract infection			
subjects affected / exposed	0 / 71 (0.00%)	2 / 70 (2.86%)	0 / 34 (0.00%)
occurrences (all)	0	2	0
Viral infection			
subjects affected / exposed	2 / 71 (2.82%)	2 / 70 (2.86%)	2 / 34 (5.88%)
occurrences (all)	3	2	2
Viral rash			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 71 (0.00%)	3 / 70 (4.29%)	0 / 34 (0.00%)
occurrences (all)	0	3	0
Hypokalaemia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Hyponatraemia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Increased appetite			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	0 / 34 (0.00%)
occurrences (all)	1	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported