Clinical trial results:
A Multicenter, Open, Long-term Follow-up Study to Evaluate the Safety and Efficacy of L059 (Levetiracetam) at Individual Optimal Dose Ranging From 500 to 3000 mg/Day in Twice Daily Administration in Subjects From 16 to 65 Years With Epilepsy Suffering From Partial Onset Seizures Whether or Not Secondarily Generalized Who Completed in a Previous Study

Summary

EudraCT number	2014-004334-26
Trial protocol	Outside EU/EEA
Global end of trial date	28 December 2010

Results information

Result version number	v1 (current)
This version publication date	30 June 2016
First version publication date	17 April 2015

Trial information

Trial identification

Sponsor protocol code	N01222

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00367432
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Japan Co. Ltd.
Sponsor organisation address	8-17-1 Nishi-Shinjuku, Tokyo, Japan, 160-0023
Public contact	Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, 0049 2173 4815 15, clinicaltrials@ucb.com
Scientific contact	Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, 0049 2173 48 15 15, clinicaltrials@ucb.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	03 June 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 December 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to continuously evaluate the safety of long-term administration at the dose range from LEV 500 mg/day to LEV 3000 mg/day in subjects who completed N01221 or N01020.

Protection of trial subjects:

Not applicable

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	12 July 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 398
Worldwide total number of subjects	398
EEA total number of subjects	0

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)	19
Adults (18-64 years)	379
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The Full Analysis Set (FAS) includes all subjects to whom the investigational products are assigned after registration, excluding those with serious Good Clinical Practice violations , subjects not administered the investigational products and subjects for whom no data is available after assignment of the investigational products.

Pre-assignment

Screening details:

Eligible subjects from preceding study N01221 [NCT00280696] entered the First Period of this study and those subjects from N01221 [NCT00280696] who completed the First Period and subjects from the study N01020 [NCT00160615] entered the Second Period.
Participant Flow refers to the FAS.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Levetiracetam

Arm description:

Levetiracetam 500 mg/day to 3000 mg/day , tablets twice daily (morning and evening orally) during the study period (until the time of approval granted).

Arm type	Experimental
Investigational medicinal product name	Levetiracetam
Investigational medicinal product code	ucb L059
Other name	Keppra
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Levetiracetam 500 mg/day to 3000 mg/day , tablets twice daily (morning and evening orally) during the study period (until the time of approval granted).

Number of subjects in period 1	Levetiracetam
Started	398
Completed	257
Not completed	141
AE, serious fatal	3
Consent withdrawn by subject	19
Other Reason	10
AE, non-serious non-fatal	14
Lost to follow-up	1
SAE, non-fatal	6
Lack of efficacy	88

Baseline characteristics

Reporting groups	
Reporting group title	Levetiracetam
Reporting group description:	
Levetiracetam 500 mg/day to 3000 mg/day , tablets twice daily (morning and evening orally) during the study period (until the time of approval granted).	

Reporting group values	Levetiracetam	Total	
Number of subjects	398	398	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	19	19	
Adults (18-64 years)	379	379	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	33.68		
standard deviation	± 11.18	-	
Gender Categorical Units: Subjects			
Female	196	196	
Male	202	202	
Race/Ethnicity, Customized Units: Subjects			
Japanese	396	396	
Asian (other than Japanese)	2	2	
Region of Enrollment Units: Subjects			
Japan	398	398	
Weight Units: Kilogram (kg)			
arithmetic mean	60.39		
standard deviation	± 13.64	-	

End points

End points reporting groups

Reporting group title	Levetiracetam

Reporting group description:

Levetiracetam 500 mg/day to 3000 mg/day , tablets twice daily (morning and evening orally) during the study period (until the time of approval granted).

Primary: Occurrence of treatment-emergent adverse events during the study period (until the time of approval granted)

End point title	Occurrence of treatment-emergent adverse events during the study period (until the time of approval granted)[1]

End point description:

An Adverse Event (AE) is any untoward medical occurrence in a clinical investigation subject administered a pharmaceutical product which does not necessarily have a causal relationship with the pharmaceutical product.
Occurrence of treatment-emergent AEs is reported by the number of subjects with at least one treatment-emergent AE.

End point type	Primary

End point timeframe:

During the study period from Visit 1 (Week 0) to the Follow-up Visit (up to Month 60) until the time of approval granted

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There was no statistical analysis for this endpoint in this open-label study.

End point values	Levetiracetam			
Subject group type	Reporting group			
Number of subjects analysed	398			
Units: participants				
number	381			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in N01221 [NCT00280696] in partial (type 1) seizure frequency per week during the first 16-week period in this study

End point title	Change from Baseline in N01221 [NCT00280696] in partial (type 1) seizure frequency per week during the first 16-week period in this study

End point description:

The change in partial (type 1) seizure frequency from Baseline is given as a percent reduction computed as:
[Weekly partial seizure frequency (Baseline)- Weekly partial seizure frequency (Evaluation Period)]/ [Weekly partial seizure frequency (Baseline)] x 100.
Positive values in percent reduction means that the value has decreased from Baseline during the first 16-week Period.
Partial (Type I) seizures can be classified into one of the following three groups: Simple partial seizures, Complex partial seizures, Partial seizures evolving to secondarily generalized seizures.

End point type	Secondary

End point timeframe:

Baseline in N01221 [NCT00280696], the First 16-week Evaluation Period from Visit 1 (Week 0) to Visit 5 (Week 16) in this study

End point values	Levetiracetam			
Subject group type	Reporting group			
Number of subjects analysed	313			
Units: Percent Reduction				
median (inter-quartile range (Q1-Q3))				
median (inter-quartile-range)	22 (-11 to 46.71)			

Statistical analyses

No statistical analyses for this end point

Secondary: Seizure frequency per week in partial seizures during the first 16-week period in this study

End point title	Seizure frequency per week in partial seizures during the first 16-week period in this study

End point description:

Partial (Type I) seizures can be classified into one of the following three groups: Simple partial seizures, Complex partial seizures, Partial seizures evolving to secondarily generalized seizures.

End point type	Secondary

End point timeframe:

First 16-week Evaluation Period from Visit 1 (Week 0) to Visit 5 (Week 16)

End point values	Levetiracetam			
Subject group type	Reporting group			
Number of subjects analysed	313			
Units: Seizures Per Week				
median (inter-quartile range (Q1-Q3))				
median (inter-quartile-range)	2.13 (1.06 to 5.23)			

Statistical analyses

No statistical analyses for this end point

Secondary: Response status (patients with a percent reduction in partial seizure frequency of at least 50% During the First 16-week Period in This Study From

Baseline in N01221)	
End point title	Response status (patients with a percent reduction in partial seizure frequency of at least 50% During the First 16-week Period in This Study From Baseline in N01221)

End point description:

The percent reduction from Baseline was computed as:
[Weekly seizure frequency (Baseline)- Weekly seizure frequency (Evaluation Period)]/ [Weekly seizure frequency (Baseline)] x 100.
Responders are those patients with a percent reduction in partial seizure frequency of at least 50% from Baseline to first Evaluation Period in partial seizure frequency per week.
Partial (Type I) seizures can be classified into one of the following three groups: Simple partial seizures, Complex partial seizures, Partial seizures evolving to secondarily generalized seizures.

End point type	Secondary

End point timeframe:

Baseline in N01221 [NCT00280696], the First 16-week Evaluation Period from Visit 1 (Week 0) to Visit 5 (Week 16) in this study

End point values	Levetiracetam			
Subject group type	Reporting group			
Number of subjects analysed	313			
Units: Participants				
Responders	74			
Non-responders	239			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in N01221 [NCT00280696] in simple partial seizure frequency per week during the first 16-week period in this study	
End point title	Change from Baseline in N01221 [NCT00280696] in simple partial seizure frequency per week during the first 16-week period in this study

End point description:

Change in simple partial seizure frequency is given as a percent reduction computed as:
[Weekly simple partial seizure frequency (Baseline)- Weekly simple partial seizure frequency (Evaluation Period)]/ [Weekly simple partial seizure frequency (Baseline)] x 100.
Positive values in percent reduction means that the value has decreased from Baseline during the first 16-week Period.
Partial (Type I) seizures can be classified into one of the following three groups: Simple partial seizures, Complex partial seizures, Partial seizures evolving to secondarily generalized seizures.

End point type	Secondary

End point timeframe:

Baseline in N01221 [NCT00280696], the First 16-week Evaluation Period from Visit 1 (Week 0) to Visit 5 (Week 16) in this study

End point values	Levetiracetam			
Subject group type	Reporting group			
Number of subjects analysed	173			
Units: Percent Reduction				
median (inter-quartile range (Q1-Q3))				
median (inter-quartile-range)	39.84 (-17.19 to 94.96)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in N01221 [NCT00280696] in complex partial seizure frequency per week during the first 16-week period in this study

End point title	Change from Baseline in N01221 [NCT00280696] in complex partial seizure frequency per week during the first 16-week period in this study

End point description:

Change in complex partial seizure frequency is given as a percent reduction computed as:
[Weekly complex partial seizure frequency (Baseline)- Weekly complex partial seizure frequency (Evaluation Period)]/ [Weekly complex partial seizure frequency (Baseline)] x 100.
Positive values in percent reduction means that the value has decreased from Baseline during the first 16-week Period.
Partial (Type I) seizures can be classified into one of the following three groups: Simple partial seizures, Complex partial seizures, Partial seizures evolving to secondarily generalized seizures.

End point type	Secondary

End point timeframe:

Baseline in N01221 [NCT00280696], the First 16-week Evaluation Period from Visit 1 (Week 0) to Visit 5 (Week 16) in this study

End point values	Levetiracetam			
Subject group type	Reporting group			
Number of subjects analysed	285			
Units: Percent Reduction				
median (inter-quartile range (Q1-Q3))				
median (inter-quartile-range)	20.59 (-15.24 to 52.94)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in N01221 [NCT00280696] in secondary generalized seizure frequency per week during the first 16-week period in this study

End point title	Change from Baseline in N01221 [NCT00280696] in secondary generalized seizure frequency per week during the first 16-

	week period in this study

End point description:

Change in secondary generalized seizure frequency is given as a percent reduction computed as:
[Weekly sec. generalized seizure frequency (Baseline)- Weekly sec. generalized seizure frequency (Evaluation Period)]/ [Weekly sec. generalized seizure frequency (Baseline)] x 100.
Positive values in reduction means the value decreased from Baseline during the first 16-week Period.
Secondary generalized seizures belong to one of the 3 groups:
- Simple partial sz evolving to gen sz
- Complex partial sz evolving to gen sz
- Simple partial sz evolving to Complex partial sz evolving to gen sz

End point type	Secondary

End point timeframe:

Baseline in N01221 [NCT00280696], the First 16-week Evaluation Period from Visit 1 (Week 0) to Visit 5 (Week 16) in this study

End point values	Levetiracetam			
Subject group type	Reporting group			
Number of subjects analysed	87			
Units: Percent Reduction				
median (inter-quartile range (Q1-Q3))				
median (inter-quartile-range)	76.56 (23.11 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in N01221 [NCT00280696] in simple and complex partial seizure frequency per week during the first 16-week period in this study

End point title	Change from Baseline in N01221 [NCT00280696] in simple and complex partial seizure frequency per week during the first 16-week period in this study

End point description:

Change in simple and complex partial seizure frequency is given as a percent reduction computed as (simple and complex partial seizure frequency := A):
[Weekly A (Baseline)- Weekly A (Evaluation Period)]/ [Weekly A (Baseline)] x 100.
Positive values in percent reduction means that the value has decreased from Baseline during the first 16-week Period.
Partial (Type I) seizures can be classified into one of the following three groups: Simple partial seizures, Complex partial seizures, Partial seizures evolving to secondarily generalized seizures.

End point type	Secondary

End point timeframe:

Baseline in N01221 [NCT00280696], the First 16-week Evaluation Period from Visit 1 (Week 0) to Visit 5 (Week 16) in this study

End point values	Levetiracetam			
Subject group type	Reporting group			
Number of subjects analysed	308			
Units: Percent Reduction				
median (inter-quartile range (Q1-Q3))				
median (inter-quartile-range)	20.71 (-13.17 to 47.42)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in N01221 [NCT00280696] in other types of seizure frequency per week during the first 16-week period in this study

End point title	Change from Baseline in N01221 [NCT00280696] in other types of seizure frequency per week during the first 16-week period in this study

End point description:

Change in other types of seizure frequency is given as a percent reduction computed as (other types of seizure frequency:= B):
[Weekly B (Baseline)- Weekly B (Evaluation Period)]/ [Weekly B (Baseline)] x 100.
Positive values in percent reduction means that the value has decreased from Baseline during the first 16-week Period.
Other types of Seizures are all seizures except Partial Seizures (Type 1).

End point type	Secondary

End point timeframe:

Baseline in N01221 [NCT00280696], the First 16-week Evaluation Period from Visit 1 (Week 0) to Visit 5 (Week 16) in this study

End point values	Levetiracetam			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Percent Reduction				
median (inter-quartile range (Q1-Q3))				
median (inter-quartile-range)	66.47 (7.48 to 100)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were collected up to 60 months from Visit 1 (Week 0) over the First and Second Period until Down-titration and Follow up.

Adverse event reporting additional description:

Adverse Events refer to the Safety Set (SS). SS includes all subjects from studies N01221 [NCT00280696] and N01020 [NCT00160615] administered the investigational products at least once.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	Levetiracetam

Reporting group description:

Levetiracetam 500 mg/day to 3000 mg/day , tablets twice daily (morning and evening orally) during the study period (until the time of approval granted).

Serious adverse events	Levetiracetam		
Total subjects affected by serious adverse events			
subjects affected / exposed	64 / 398 (16.08%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Meningioma			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small Intestine Carcinoma			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Abortion Induced			
subjects affected / exposed	2 / 398 (0.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Brain Operation			

subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Medical Diet			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wisdom Teeth Removal			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion Complete			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	2 / 398 (0.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Sudden Unexplained Death in Epilepsy			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Immune system disorders			
Drug Hypersensitivity			

subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Lactation Disorder			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Choking			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumonia Aspiration			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Acute Psychosis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hallucination			

subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Ideas of Reference				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Mental Disorder				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Morose				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Suicide Attempt				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Anticonvulsant Drug Level Increased				
subjects affected / exposed	2 / 398 (0.50%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Electrocardiogram ST Segment Elevation				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Anticonvulsant Toxicity				
subjects affected / exposed	3 / 398 (0.75%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			

Burns Second Degree				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cervical Vertebral Fracture				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Femoral Neck Fracture				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Head Injury				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lumbar Vertebral Fracture				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Patella Fracture				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Rib Fracture				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Road Traffic Accident				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin Laceration				

subjects affected / exposed	3 / 398 (0.75%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Skull Fracture				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subdural Haematoma				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Palpitations				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebral Infarction				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Complex Partial Seizures				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Convulsion				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	1 / 398 (0.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Drug Withdrawal Convulsions				

subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	5 / 398 (1.26%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Head Titubation			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuropathy Peripheral			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postictal State			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Status Epilepticus			
subjects affected / exposed	5 / 398 (1.26%)		
occurrences causally related to treatment / all	5 / 9		
deaths causally related to treatment / all	0 / 1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Eyelid Ptosis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Enterocolitis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal Obstruction			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Irritable Bowel Syndrome			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal Ulcer Haemorrhage			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colonic Polyp			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urethral Stenosis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Haemarthrosis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Jaw Disorder			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal Column Stenosis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Acute Sinusitis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis Escherichia Coli			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infected Epidermal Cyst			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injection Site Infection			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lobar Pneumonia			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			

subjects affected / exposed	4 / 398 (1.01%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Pneumonia Mycoplasmal			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory Tract Infection			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Levetiracetam		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	369 / 398 (92.71%)		
Investigations			
Weight Decreased			
subjects affected / exposed	28 / 398 (7.04%)		
occurrences (all)	33		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	110 / 398 (27.64%)		
occurrences (all)	237		
Excoriation			

subjects affected / exposed	52 / 398 (13.07%)		
occurrences (all)	85		
Injury			
subjects affected / exposed	33 / 398 (8.29%)		
occurrences (all)	39		
Joint Sprain			
subjects affected / exposed	27 / 398 (6.78%)		
occurrences (all)	37		
Laceration			
subjects affected / exposed	20 / 398 (5.03%)		
occurrences (all)	23		
Skin Laceration			
subjects affected / exposed	31 / 398 (7.79%)		
occurrences (all)	53		
Thermal Burn			
subjects affected / exposed	36 / 398 (9.05%)		
occurrences (all)	43		
Nervous system disorders			
Dizziness			
subjects affected / exposed	63 / 398 (15.83%)		
occurrences (all)	92		
Epilepsy			
subjects affected / exposed	31 / 398 (7.79%)		
occurrences (all)	37		
Headache			
subjects affected / exposed	96 / 398 (24.12%)		
occurrences (all)	261		
Somnolence			
subjects affected / exposed	159 / 398 (39.95%)		
occurrences (all)	226		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	52 / 398 (13.07%)		
occurrences (all)	95		
Immune system disorders			

Seasonal Allergy			
subjects affected / exposed	29 / 398 (7.29%)		
occurrences (all)	43		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	38 / 398 (9.55%)		
occurrences (all)	67		
Abdominal Pain Upper			
subjects affected / exposed	20 / 398 (5.03%)		
occurrences (all)	40		
Constipation			
subjects affected / exposed	45 / 398 (11.31%)		
occurrences (all)	70		
Diarrhoea			
subjects affected / exposed	69 / 398 (17.34%)		
occurrences (all)	128		
Nausea			
subjects affected / exposed	44 / 398 (11.06%)		
occurrences (all)	53		
Stomatitis			
subjects affected / exposed	42 / 398 (10.55%)		
occurrences (all)	75		
Toothache			
subjects affected / exposed	21 / 398 (5.28%)		
occurrences (all)	32		
Vomiting			
subjects affected / exposed	40 / 398 (10.05%)		
occurrences (all)	85		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	21 / 398 (5.28%)		
occurrences (all)	25		
Pharyngolaryngeal Pain			
subjects affected / exposed	32 / 398 (8.04%)		
occurrences (all)	60		
Rhinitis Allergic			

subjects affected / exposed	20 / 398 (5.03%)		
occurrences (all)	26		
Upper Respiratory Tract Inflammation			
subjects affected / exposed	33 / 398 (8.29%)		
occurrences (all)	46		
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	47 / 398 (11.81%)		
occurrences (all)	61		
Pruritus			
subjects affected / exposed	21 / 398 (5.28%)		
occurrences (all)	25		
Rash			
subjects affected / exposed	26 / 398 (6.53%)		
occurrences (all)	37		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	24 / 398 (6.03%)		
occurrences (all)	26		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	31 / 398 (7.79%)		
occurrences (all)	34		
Back Pain			
subjects affected / exposed	45 / 398 (11.31%)		
occurrences (all)	70		
Myalgia			
subjects affected / exposed	21 / 398 (5.28%)		
occurrences (all)	27		
Infections and infestations			
Dental Caries			
subjects affected / exposed	42 / 398 (10.55%)		
occurrences (all)	49		
Gastroenteritis			
subjects affected / exposed	27 / 398 (6.78%)		
occurrences (all)	34		

Influenza			
subjects affected / exposed	32 / 398 (8.04%)		
occurrences (all)	32		
Nasopharyngitis			
subjects affected / exposed	308 / 398 (77.39%)		
occurrences (all)	1360		
Pharyngitis			
subjects affected / exposed	25 / 398 (6.28%)		
occurrences (all)	38		
Rhinitis			
subjects affected / exposed	22 / 398 (5.53%)		
occurrences (all)	26		

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