Clinical trial results:
An Open-label, Randomized, Multicenter Study to Evaluate the Efficacy and Safety of Levetiracetam Used as Monotherapy in Newly or Recently Diagnosed Epilepsy Patients Aged Older Than or Equal to 16 Years With Partial Seizures

Summary

EudraCT number	2014-004377-16
Trial protocol	Outside EU/EEA
Global end of trial date	14 April 2015

Results information

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

Trial information

Trial identification

Sponsor protocol code	N01375

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01506882
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, +49 2173 4815 15, clinicaltrials@ucb.com
Scientific contact	Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, +49 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	21 May 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy of LEV used as monotherapy, with efficacy measured as 6-month seizure freedom at the last evaluated dose in the LEV 1000 mg/day to 2000 mg/day group, in newly or recently diagnosed epilepsy subjects.

Protection of trial subjects:

N01375 was continued until the Ministry of Health, Labor and Welfare (Japan) approved the use of Levetiracetam (LEV) monotherapy for Partial Onset Seizures (POS) in adults and until all subjects who were taking LEV as investigational medicinal product (IMP) had a the option to switch to commercial LEV in Japan.
Antidepressant use was allowed if the medication and dose were stable for at least 6 months prior to Visit 1 and the medication and dose were to be kept stable for the entire study duration.
The following medications were used as rescue medications at the investigator's discretion to maintain the subject's safety:
- Diazepam (suppository, injection)
- Phenobarbital sodium (suppository, injection)
- Chloral hydrate (enema preparation, suppository)
- Phenytoin sodium (injection)
- Fosphenytoin sodium hydrate (injection)

Background therapy:

Not applicable

Evidence for comparator:

Based on the controlled studies that evaluated Anti-Epileptic Drugs (AEDs) in the past, the magnitude of the clinical effects of conventional AEDs as the percentage of subjects who achieved 6-month seizure freedom was expected to be approximately 50 % in subjects with newly or recently diagnosed Partial Onset Seizures (POS).The ILAE Treatment Guidelines (Glauser, 2006) stated that non-inferiority outcomes with any relative difference >20 % in the efficacy evaluation had to be regarded as clinically important. According to this, a threshold level of 40 % (50 % − 0.2 × 50 %) in efficacy of Levetiracetam (LEV) monotherapy was defined for the percentage of the subjects who would achieve seizure freedom for 6 months by detecting the statistically significant difference between the defined threshold level and the study result to be obtained. The primary efficacy evaluation was to be performed on the LEV 1000 mg/day to 2000 mg/day groups.

Actual start date of recruitment	15 December 2011
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: 71
Worldwide total number of subjects	71
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)	6
Adults (18-64 years)	58
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This multicenter study started to enroll subjects in December 2011 in order to end up with 27 centers with enrolled subjects in Japan.

Pre-assignment

Screening details:

Participant Flow refers to the Randomized Set (RS). RS consists of all subjects who were randomized to the study groups.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Levetiracetam 1000 mg/day to 2000 mg/day group

Arm description:

- Formulation: Tablet- Strength: LEV 250 mg, LEV 500 mg- Dosage: First study dose is 1000 mg/day and if a seizure occurs, the dose will be increased to 2000 mg/day. Max dose in the Follow Up Period is 3000 mg/day.- Frequency: Twice daily

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

Dosage and administration details:

- Active Substance: Levetiracetam
- Pharmaceutical Form: Film-coated tablet
- Concentration: 250 mg and 500 mg
- Route of Administration: Oral use

Arm title	Levetiracetam 3000 mg/day group

Arm description:

- Formulation: Tablet- Strength: LEV 250 mg, LEV 500 mg- Dosage: 1000 mg/day for first two weeks, then 2000 mg/day for two weeks then 3000 mg/day by the end of the trial. - Frequency: Twice daily

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

Dosage and administration details:

- Active Substance: Levetiracetam
- Pharmaceutical Form: Film-coated tablet
- Concentration: 250 mg and 500 mg
- Route of Administration: Oral use

Number of subjects in period 1	Levetiracetam 1000 mg/day to 2000 mg/day group	Levetiracetam 3000 mg/day group
Started	61	10
Completed	39	3
Not completed	22	7
Consent withdrawn by subject	9	3
AE, non-serious non-fatal	3	1
Other Reason	2	-
Lost to follow-up	1	-
SAE, non-fatal	2	-
Lack of efficacy	4	3
SAE, non-fatal + AE, non-serious non-fatal	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Levetiracetam 1000 mg/day to 2000 mg/day group
Reporting group description:	
- Formulation: Tablet- Strength: LEV 250 mg, LEV 500 mg- Dosage: First study dose is 1000 mg/day and if a seizure occurs, the dose will be increased to 2000 mg/day. Max dose in the Follow Up Period is 3000 mg/day.- Frequency: Twice daily	
Reporting group title	Levetiracetam 3000 mg/day group
Reporting group description:	
- Formulation: Tablet- Strength: LEV 250 mg, LEV 500 mg- Dosage: 1000 mg/day for first two weeks, then 2000 mg/day for two weeks then 3000 mg/day by the end of the trial. - Frequency: Twice daily	

Reporting group values	Levetiracetam 1000 mg/day to 2000 mg/day group	Levetiracetam 3000 mg/day group	Total
Number of subjects	61	10	71
Age Categorical Units: Subjects			
<=18 years	10	1	11
Between 18 and 65 years	45	8	53
>=65 years	6	1	7
Age Continuous Units: years			
arithmetic mean	36.5	37	
standard deviation	± 18	± 18.6	-
Gender Categorical Units: Subjects			
Female	34	4	38
Male	27	6	33
Region of Enrollment Units: Subjects			
Japan	61	10	71
Weight Units: kilogram (kg)			
arithmetic mean	58.98	62.58	
standard deviation	± 12.3	± 15.11	-
Height Units: centimeter (cm)			
arithmetic mean	161.96	166.07	
standard deviation	± 8.77	± 10.21	-

End points

End points reporting groups

Reporting group title	Levetiracetam 1000 mg/day to 2000 mg/day group

Reporting group description:

- Formulation: Tablet- Strength: LEV 250 mg, LEV 500 mg- Dosage: First study dose is 1000 mg/day and if a seizure occurs, the dose will be increased to 2000 mg/day. Max dose in the Follow Up Period is 3000 mg/day.- Frequency: Twice daily

Reporting group title	Levetiracetam 3000 mg/day group

Reporting group description:

- Formulation: Tablet- Strength: LEV 250 mg, LEV 500 mg- Dosage: 1000 mg/day for first two weeks, then 2000 mg/day for two weeks then 3000 mg/day by the end of the trial. - Frequency: Twice daily

Subject analysis set title	Full Analysis Set (LEV 1000 mg/day to 2000 mg/day group)
Subject analysis set type	Full analysis

Subject analysis set description:

FAS includes all subjects in the Safety Set who had at least 1 treatment day in the Evaluation Period. This means that subjects in LEV 1000 to 2000 mg/day group had to have at least 1 treatment day in the Evaluation Period on their final evaluated dose.

- Formulation: Tablet
- Strength: LEV 250 mg, LEV 500 mg
- Dosage: First study dose is 1000 mg/day and if a seizure occurs, the dose will be increased to 2000 mg/day. Max dose in the Follow Up Period is 3000 mg/day.
- Frequency: Twice daily

Subject analysis set title	Full Analysis Set (LEV 3000 mg/day group)
Subject analysis set type	Full analysis

Subject analysis set description:

FAS includes all subjects in the Safety Set who had at least 1 treatment day in the Evaluation Period. This means that subjects in LEV 1000 to 2000 mg/day group had to have at least 1 treatment day in the Evaluation Period on their final evaluated dose.

- Formulation: Tablet
- Strength: LEV 250 mg, LEV 500 mg
- Dosage: 1000 mg/day for first two weeks, then 2000 mg/day for two weeks then 3000 mg/day by the end of the trial.
- Frequency: Twice daily

Primary: Percentage of subjects in the Levetiracetam (LEV) 1000 mg/day to 2000 mg/day group who are seizure free for 26 consecutive weeks of treatment during the Evaluation Period

End point title	Percentage of subjects in the Levetiracetam (LEV) 1000 mg/day to 2000 mg/day group who are seizure free for 26 consecutive weeks of treatment during the Evaluation Period[1]

End point description:

A subject was considered seizure free, if no seizure occurred during the 6 consecutive months (26 weeks) in the Evaluation Period. If one of the following occurred, the subject was not considered seizure free:
- A documented seizure during 6 consecutive months of the Evaluation Analysis Period
- Subject discontinued the study prematurely during the Evaluation Analysis Period
- Missing Seizure Count Case Report Forms (CRFs) prior to completing the Evaluation Analysis Period.

End point type	Primary

End point timeframe:

From the end of the 1-week Stabilization Period over the 26-weeks Evaluation Period

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: Values presented below are from the statistical analysis of this Primary Endpoint. The lower limit of the two-sided 95% CI for the estimate of Percentage of subjects in the Levetiracetam (LEV) 1000 mg/day to 2000 mg/day group who are seizure free for 26 consecutive weeks of treatment during

the Evaluation Period, 60.9%, was greater than the reference value 40%.

End point values	Levetiracetam 1000 mg/day to 2000 mg/day group	Levetiracetam 3000 mg/day group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	0[2]		
Units: percentage of participants				
number (confidence interval 95%)				
percentage of participants	73.8 (60.9 to 84.2)	(to)		

Notes:

[2] - Primary Efficacy analysis was conducted for the 1000 mg/day - 2000 mg/day group only

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects in the Levetiracetam (LEV) 1000 mg/day to 2000 mg/day group who are seizure free for 52 consecutive weeks of treatment during the Evaluation Period and the Maintenance Period

End point title	Percentage of subjects in the Levetiracetam (LEV) 1000 mg/day to 2000 mg/day group who are seizure free for 52 consecutive weeks of treatment during the Evaluation Period and the Maintenance Period

End point description:

Subjects who complete the 26-weeks Evaluation Period without having a seizure will continue receiving the same dose of LEV as in the Evaluation Period during the 26-weeks Maintenance Period unless a seizure occurs.

End point type	Secondary

End point timeframe:

From entry in the 26-weeks Evaluation Period to the end of the 26-weeks Maintenance Period

End point values	Full Analysis Set (LEV 1000 mg/day to 2000 mg/day group)			
Subject group type	Subject analysis set			
Number of subjects analysed	61			
Units: percentage of participants				
number (confidence interval 95%)				
percentage of participants	59 (45.7 to 71.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects in the Levetiracetam (LEV) 3000 mg/day group who are seizure free for 26 consecutive weeks of treatment during the Evaluation Period

End point title	Percentage of subjects in the Levetiracetam (LEV) 3000 mg/day group who are seizure free for 26 consecutive weeks of treatment during the Evaluation Period[3]

End point description:

A subject was considered seizure free, if no seizure occurred during the 6 consecutive months (26 weeks) in the Evaluation Period. If one of the following occurred, the subject was not considered seizure free:
- A documented seizure during 6 consecutive months of the Evaluation Analysis Period
- Subject discontinued the study prematurely during the Evaluation Analysis Period
- Missing Seizure Count Case Report Forms (CRFs) prior to completing the Evaluation Analysis Period.

End point type	Secondary

End point timeframe:

From the end of the 1-week Stabilization Period over the 26-weeks Evaluation Period

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics for the 1000 mg/day to 2000 mg/day group are not reported here as this group was not part of this secondary Endpoint.

End point values	Levetiracetam 3000 mg/day group			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percentage of participants				
number (confidence interval 95%)				
percentage of participants	22.2 (2.8 to 60)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects in the Levetiracetam (LEV) 3000 mg/day group who are seizure free for 52 consecutive weeks of treatment during the Evaluation Period and the Maintenance Period

End point title	Percentage of subjects in the Levetiracetam (LEV) 3000 mg/day group who are seizure free for 52 consecutive weeks of treatment during the Evaluation Period and the Maintenance Period

End point description:

Subjects who complete the 26-weeks Evaluation Period without having a seizure will continue receiving LEV 3000 mg/day during the 26-weeks Maintenance Period unless a seizure occurs.

End point type	Secondary

End point timeframe:

From entry in the 26-weeks Evaluation Period to the end of the 26-weeks Maintenance Period

End point values	Full Analysis Set (LEV 3000 mg/day group)			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: percentage of participants				
number (confidence interval 95%)				
percentage of participants	11.1 (0.3 to 48.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first seizure at the last evaluated dose in subjects in the Levetiracetam (LEV) 1000 mg/day to 2000 mg/day group

End point title	Time to first seizure at the last evaluated dose in subjects in the Levetiracetam (LEV) 1000 mg/day to 2000 mg/day group

End point description:

Time was measured from first day of last evaluated dose. Seizures during Stabilization were not considered.
The Median time to first seizure will be estimated from the Kaplan-Meier curve.

End point type	Secondary

End point timeframe:

During Evaluation, Maintenance and Safety Follow Up Period after 1-week Stabilization Period, assessed up to 1 year

End point values	Full Analysis Set (LEV 1000 mg/day to 2000 mg/day group)			
Subject group type	Subject analysis set			
Number of subjects analysed	61[4]			
Units: days				
median (confidence interval 95%)				
Median Time to First Seizure (95 % CI)	999 (359 to 9999)			

Notes:

[4] - 999/9999= Median Time and upper limit of the 95 % CI were not estimable.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to withdrawal at the last evaluated dose in subjects in the

Levetiracetam (LEV) 1000 mg/day to 2000 mg/day group

End point title	Time to withdrawal at the last evaluated dose in subjects in the Levetiracetam (LEV) 1000 mg/day to 2000 mg/day group

End point description:

Median time to withdrawal will be estimated from the Kaplan-Meier curve.

End point type	Secondary

End point timeframe:

During 1-week Stabilization Period, Evaluation, Maintenance and Safety Follow Up Period, assessed up to 1 year

End point values	Full Analysis Set (LEV 1000 mg/day to 2000 mg/day group)			
Subject group type	Subject analysis set			
Number of subjects analysed	61[5]			
Units: days				
median (confidence interval 95%)				
Median Time to Withdrawal (95 % CI)	999 (99 to 9999)			

Notes:

[5] - 99/999/9999= Median Time and upper and lower limit of the 95 % CI were not estimable.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first seizure in subjects in the Levetiracetam (LEV) 3000 mg/day group

End point title	Time to first seizure in subjects in the Levetiracetam (LEV) 3000 mg/day group

End point description:

Time was measured from first day of last evaluated dose. Seizures during Stabilization were not considered.
The Median time to first seizure will be estimated from the Kaplan-Meier curve.

End point type	Secondary

End point timeframe:

During Evaluation, Maintenance and Safety Follow Up Period after 1-week Stabilization Period, assessed up to 1 year

End point values	Full Analysis Set (LEV 3000 mg/day group)			
Subject group type	Subject analysis set			
Number of subjects analysed	9[6]			
Units: days				
median (confidence interval 95%)				
Median Time to First Seizure (95 % CI)	106 (9 to 999)			

Notes:

[6] - 999= Upper limit of the 95 % CI was not estimable.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to withdrawal in subjects in the Levetiracetam (LEV) 3000 mg/day group

End point title	Time to withdrawal in subjects in the Levetiracetam (LEV) 3000 mg/day group[7]

End point description:

Median time to withdrawal will be estimated from the Kaplan-Meier curve.

End point type	Secondary

End point timeframe:

During 1-week Stabilization Period, Evaluation, Maintenance and Safety Follow Up Period, assessed up to 1 year

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics for the 1000 mg/day to 2000 mg/day group are not reported here as this group was not part of this secondary Endpoint.

End point values	Levetiracetam 3000 mg/day group			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: days				
median (confidence interval 95%)				
Median Time to Withdrawal (95 % CI)	91 (21 to 197)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent Adverse Events were collected from Screening (Week 0) over the Evaluation and Maintenance Period (Week 4 to Week 53) until the last Follow-up Visit or Withdrawal Visit.

Adverse event reporting additional description:

Adverse Events refer to the Safety Set including all subjects in the Enrolled Set who received at least 1 dose of the Investigational Medicinal Product.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Levetiracetam 1000 mg/day to 2000 mg/day group

Reporting group description:

- Formulation: Tablet
- Strength: LEV 250 mg, LEV 500 mg
- Dosage: First study dose is 1000 mg/day and if a seizure occurs, the dose will be increased to 2000 mg/day. Max dose in the Follow Up Period is 3000 mg/day.
- Frequency: Twice daily

Reporting group title	Levetiracetam 3000 mg/day group

Reporting group description:

- Formulation: Tablet
- Strength: LEV 250 mg, LEV 500 mg
- Dosage: 1000 mg/day for first two weeks, then 2000 mg/day for two weeks then 3000 mg/day by the end of the trial.
- Frequency: Twice daily

Serious adverse events	Levetiracetam 1000 mg/day to 2000 mg/day group	Levetiracetam 3000 mg/day group	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 61 (13.11%)	2 / 10 (20.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Surgical and medical procedures			
Meniscus removal			
subjects affected / exposed	0 / 61 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Status epilepticus			
subjects affected / exposed	3 / 61 (4.92%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Postictal state			
subjects affected / exposed	2 / 61 (3.28%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	1 / 61 (1.64%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 61 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 61 (1.64%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Irritability			
subjects affected / exposed	1 / 61 (1.64%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 61 (1.64%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 61 (1.64%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol withdrawal syndrome			

subjects affected / exposed	1 / 61 (1.64%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postictal psychosis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 61 (1.64%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cystitis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kaposi's varicelliform eruption			
subjects affected / exposed	1 / 61 (1.64%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Levetiracetam 1000 mg/day to 2000 mg/day group	Levetiracetam 3000 mg/day group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 61 (95.08%)	10 / 10 (100.00%)	
General disorders and administration site conditions			
Malaise			

subjects affected / exposed	12 / 61 (19.67%)	0 / 10 (0.00%)	
occurrences (all)	13	0	
Pyrexia			
subjects affected / exposed	5 / 61 (8.20%)	1 / 10 (10.00%)	
occurrences (all)	6	2	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	5 / 61 (8.20%)	0 / 10 (0.00%)	
occurrences (all)	8	0	
Acquired phimosis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	5 / 61 (8.20%)	0 / 10 (0.00%)	
occurrences (all)	6	0	
Rhinitis allergic			
subjects affected / exposed	1 / 61 (1.64%)	1 / 10 (10.00%)	
occurrences (all)	1	3	
Upper respiratory tract inflammation			
subjects affected / exposed	1 / 61 (1.64%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 61 (1.64%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 61 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 61 (3.28%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Weight increased			

subjects affected / exposed	2 / 61 (3.28%)	2 / 10 (20.00%)	
occurrences (all)	2	2	
Urine ketone body present			
subjects affected / exposed	2 / 61 (3.28%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Blood urine present			
subjects affected / exposed	1 / 61 (1.64%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Neutrophil count increased			
subjects affected / exposed	0 / 61 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	5 / 61 (8.20%)	0 / 10 (0.00%)	
occurrences (all)	6	0	
Head injury			
subjects affected / exposed	1 / 61 (1.64%)	2 / 10 (20.00%)	
occurrences (all)	1	2	
Ligament sprain			
subjects affected / exposed	1 / 61 (1.64%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Arthropod sting			
subjects affected / exposed	0 / 61 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Mouth injury			
subjects affected / exposed	0 / 61 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	0 / 61 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Nervous system disorders			
Somnolence			
subjects affected / exposed	25 / 61 (40.98%)	2 / 10 (20.00%)	
occurrences (all)	32	2	
Dizziness			

subjects affected / exposed	8 / 61 (13.11%)	1 / 10 (10.00%)	
occurrences (all)	9	1	
Headache			
subjects affected / exposed	10 / 61 (16.39%)	1 / 10 (10.00%)	
occurrences (all)	14	1	
Dizziness postural			
subjects affected / exposed	1 / 61 (1.64%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Amnestic disorder			
subjects affected / exposed	0 / 61 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 61 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	8 / 61 (13.11%)	2 / 10 (20.00%)	
occurrences (all)	18	2	
Nausea			
subjects affected / exposed	6 / 61 (9.84%)	1 / 10 (10.00%)	
occurrences (all)	14	1	
Dental caries			
subjects affected / exposed	6 / 61 (9.84%)	0 / 10 (0.00%)	
occurrences (all)	7	0	
Abdominal discomfort			
subjects affected / exposed	4 / 61 (6.56%)	1 / 10 (10.00%)	
occurrences (all)	4	1	
Abdominal pain upper			
subjects affected / exposed	4 / 61 (6.56%)	0 / 10 (0.00%)	
occurrences (all)	17	0	
Gastritis			
subjects affected / exposed	4 / 61 (6.56%)	0 / 10 (0.00%)	
occurrences (all)	4	0	
Vomiting			

subjects affected / exposed	4 / 61 (6.56%)	0 / 10 (0.00%)	
occurrences (all)	5	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 61 (1.64%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Lip ulceration			
subjects affected / exposed	0 / 61 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	0 / 61 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 61 (1.64%)	1 / 10 (10.00%)	
occurrences (all)	1	2	
Dry skin			
subjects affected / exposed	0 / 61 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Ketonuria			
subjects affected / exposed	0 / 61 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 61 (9.84%)	0 / 10 (0.00%)	
occurrences (all)	7	0	
Musculoskeletal pain			
subjects affected / exposed	1 / 61 (1.64%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	47 / 61 (77.05%)	4 / 10 (40.00%)	
occurrences (all)	155	7	
Influenza			
subjects affected / exposed	7 / 61 (11.48%)	0 / 10 (0.00%)	
occurrences (all)	8	0	

Gastroenteritis			
subjects affected / exposed	3 / 61 (4.92%)	1 / 10 (10.00%)	
occurrences (all)	3	1	
Cystitis			
subjects affected / exposed	4 / 61 (6.56%)	0 / 10 (0.00%)	
occurrences (all)	5	0	
Gingivitis			
subjects affected / exposed	1 / 61 (1.64%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Rhinitis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	

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