Clinical trial results:
An open-label, multicenter, follow-up study to evaluate the safety and efficacy of levetiracetam (LEV) (oral tablets of 166, 250 or 500 mg b.i.d.), at individualized doses up to a maximum of 4000 mg/day (or 80 mg/kg/day for children and adolescents less than 50 kg), in children (4 years old), adolescents and adults suffering from primary generalized seizures

Summary

EudraCT number	2004-001997-13
Trial protocol	AT EE
Global end of trial date	10 July 2007

Results information

Result version number	v1 (current)
This version publication date	30 June 2016
First version publication date	11 July 2015

Trial information

Trial identification

Sponsor protocol code	N167

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00150748
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Pharma SA
Sponsor organisation address	Chemin du Foriest, Braine l'Alleud, Belgium, B - 1420
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	14 March 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 July 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of N167 was to evaluate the safety and efficacy of LEV at individualized doses with a maximum dose of 4000 mg/day (or 80 mg/kg/day for children and adolescents less than 50 kg), in reducing seizures in children, adolescents, and adults suffering from Primary generalized (type II) seizures.

Protection of trial subjects:

Not applicable

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	01 November 2001
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Canada: 38
Country: Number of subjects enrolled	Estonia: 5
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Ireland: 2
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Mexico: 46
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	Poland: 41
Country: Number of subjects enrolled	Russian Federation: 21

Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	United Kingdom: 19
Country: Number of subjects enrolled	United States: 21
Worldwide total number of subjects	237
EEA total number of subjects	103

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)	10
Adolescents (12-17 years)	23
Adults (18-64 years)	204
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study started to enroll subjects in November 2001. 217 subjects were enrolled from studies N01057 and N166, which are defined as the ITT Population, and 20 subjects ere enrolled from studies N129 and N164.

Pre-assignment

Screening details:

Participant Flow shows all enrolled subjects.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Levetiracetam (subjects from N01057 and N166)

Arm description:

Subjects received treatment up to 1764 days during the Evaluation Period. Up to 4000 mg/day (or 80 mg/kg/day for children and adolescents less than 50 kg). Oral tablets of 166, 250, or 500 mg Levetiracetam twice daily (b.i.d.).

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:

All subjects received open-label Levetiracetam during this study. Investigational product consisted of film-coated tablets of 166, 250, or 500 mg Levetiracetam to be taken orally with or without food.

Arm title	Levetiracetam (subjects from N129 and N164)

Arm description:

Subjects received treatment up to 1764 days during the Evaluation Period. Up to 4000 mg/day (or 80 mg/kg/day for children and adolescents less than 50 kg). Oral tablets of 166, 250, or 500 mg Levetiracetam twice daily (b.i.d.).

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:

All subjects received open-label Levetiracetam during this study. Investigational product consisted of film-coated tablets of 166, 250, or 500 mg Levetiracetam to be taken orally with or without food.

Number of subjects in period 1	Levetiracetam (subjects from N01057 and N166)	Levetiracetam (subjects from N129 and N164)
Started	217	20
Completed	125	3
Not completed	92	17
AE, serious fatal	1	-
Consent withdrawn by subject	11	3
Loss of efficacy	2	-
Other Reason	20	11
AE, non-serious non-fatal	9	-
Lost to follow-up	10	2
SAE, non-fatal	10	-
Lack of efficacy	26	-
Protocol deviation	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Levetiracetam (subjects from N01057 and N166)
Reporting group description:	
Subjects received treatment up to 1764 days during the Evaluation Period. Up to 4000 mg/day (or 80 mg/kg/day for children and adolescents less than 50 kg). Oral tablets of 166, 250, or 500 mg Levetiracetam twice daily (b.i.d.).	
Reporting group title	Levetiracetam (subjects from N129 and N164)
Reporting group description:	
Subjects received treatment up to 1764 days during the Evaluation Period. Up to 4000 mg/day (or 80 mg/kg/day for children and adolescents less than 50 kg). Oral tablets of 166, 250, or 500 mg Levetiracetam twice daily (b.i.d.).	

Reporting group values	Levetiracetam (subjects from N01057 and N166)	Levetiracetam (subjects from N129 and N164)	Total
Number of subjects	217	20	237
Age Categorical			
Units: Subjects			
Children (2-11 years)	7	3	10
Adolescents (12-17 years)	23	0	23
Adults (18-64 years)	187	17	204
Age Continuous			
Units: years			
arithmetic mean	27.99	31.1	
standard deviation	± 10.88	± 12.28	-
Gender Categorical			
Units: Subjects			
Male	91	9	100
Female	126	11	137

End points

End points reporting groups

Reporting group title	Levetiracetam (subjects from N01057 and N166)
Reporting group description:	
Subjects received treatment up to 1764 days during the Evaluation Period. Up to 4000 mg/day (or 80 mg/kg/day for children and adolescents less than 50 kg). Oral tablets of 166, 250, or 500 mg Levetiracetam twice daily (b.i.d.).	
Reporting group title	Levetiracetam (subjects from N129 and N164)
Reporting group description:	
Subjects received treatment up to 1764 days during the Evaluation Period. Up to 4000 mg/day (or 80 mg/kg/day for children and adolescents less than 50 kg). Oral tablets of 166, 250, or 500 mg Levetiracetam twice daily (b.i.d.).	
Subject analysis set title	All intent-to-treat (ITT) population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The All intent-to-treat (ITT) Population was defined as all subjects coming from study N01057 or N166 who had recorded intake of at least 1 dose of N167 study medication.	
Subject analysis set title	Tonic-Clonic subpopulation
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Any N166/N01057 ITT subject with a Tonic-Clonic seizure frequency per week >0 at N166 (prospective) or N01057 (combined) Baseline.	
Subject analysis set title	Myoclonic subpopulation
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Any N166/N01057 ITT subject with Myoclonic seizure days per week >0 at N166 (prospective) or N01057 (combined) Baseline.	
Subject analysis set title	Absence subpopulation
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Any N166/N01057 ITT subject with a IIA seizure days per week >0 at N166 (prospective) or N01057 (combined) Baseline.	

Primary: Number of subjects having at least 6 months of seizure freedom at any time during the Evaluation Period

End point title	Number of subjects having at least 6 months of seizure freedom at any time during the Evaluation Period[1]
End point description:	
End point type	Primary
End point timeframe:	
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: No formal statistical hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

End point values	Levetiracetam (subjects from N01057 and N166)	Levetiracetam (subjects from N129 and N164)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	20		
Units: Subjects				
Number of subjects	122	12		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects having at least 6 months of seizure freedom at any time during the Evaluation Period

End point title	Percentage of subjects having at least 6 months of seizure freedom at any time during the Evaluation Period[2]

End point description:

End point type	Primary

End point timeframe:

Evaluation Period

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

End point values	Levetiracetam (subjects from N01057 and N166)	Levetiracetam (subjects from N129 and N164)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	20		
Units: Percentage of subjects				
number (not applicable)				
percentage of subjects	56.2	60		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects remaining seizure-free, for the All intent-to-treat (ITT) population, and Tonic-Clonic, Myoclonic, and Absence subpopulations since the beginning of this study N167 (Visit 1) during the Evaluation Period

End point title	Number of subjects remaining seizure-free, for the All intent-to-treat (ITT) population, and Tonic-Clonic, Myoclonic, and Absence subpopulations since the beginning of this study N167 (Visit 1) during the Evaluation Period

End point description:

End point type	Secondary

End point timeframe:

From Visit 1 to the end of the Evaluation Period

End point values	All intent-to-treat (ITT) population	Tonic-Clonic subpopulation	Myoclonic subpopulation	Absence subpopulation
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	217	152	121	70
Units: Subjects				
Number of seizure-free subjects	49	42	33	24

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects remaining seizure-free, for the All intent-to-treat (ITT) population, and Tonic-Clonic, Myoclonic, and Absence subpopulations since the beginning of this study N167 (Visit 1) during the Evaluation Period

End point title	Percentage of subjects remaining seizure-free, for the All intent-to-treat (ITT) population, and Tonic-Clonic, Myoclonic, and Absence subpopulations since the beginning of this study N167 (Visit 1) during the Evaluation Period

End point description:

End point type	Secondary

End point timeframe:

From Visit 1 to the end of the Evaluation Period

End point values	All intent-to-treat (ITT) population	Tonic-Clonic subpopulation	Myoclonic subpopulation	Absence subpopulation
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	217	152	121	70
Units: Percentage of subjects				
number (not applicable)				
Percentage of seizure-free subjects	22.6	27.6	27.3	34.3

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction from N01057 or N166 Baseline to the Evaluation Period in seizure frequency per week for Tonic-Clonic subpopulation seizures types

End point title	Reduction from N01057 or N166 Baseline to the Evaluation Period in seizure frequency per week for Tonic-Clonic subpopulation seizures types

End point description:

A positive value for Reduction of seizure frequency indicates an improvement from Baseline.

End point type	Secondary

End point timeframe:

From N01057 or N166 Baseline to the Evaluation Period

End point values	Tonic-Clonic subpopulation			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: Reduction of Seizure Frequency				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	0.8 (± 1.51)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage reduction from N01057 or N166 Baseline to the Evaluation Period in seizure frequency per week for Tonic-Clonic subpopulation seizures types

End point title	Percentage reduction from N01057 or N166 Baseline to the Evaluation Period in seizure frequency per week for Tonic-Clonic subpopulation seizures types

End point description:

A positive value for Percentage reduction of seizure frequency indicates an improvement from Baseline.

End point type	Secondary

End point timeframe:

From N01057 or N166 Baseline to the Evaluation Period

End point values	Tonic-Clonic subpopulation			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: Percentage of Seizure Frequency				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	66.84 (± 88.31)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction from N01057 or N166 Baseline to the Evaluation Period in seizure days per week for the ITT population, and Absence and Myoclonic subpopulations

End point title	Reduction from N01057 or N166 Baseline to the Evaluation Period in seizure days per week for the ITT population, and Absence and Myoclonic subpopulations

End point description:

A positive value for Reduction of seizure days per week indicates an improvement from Baseline.

End point type	Secondary

End point timeframe:

From N01057 or N166 Baseline to the Evaluation Period

End point values	All intent-to-treat (ITT) population	Myoclonic subpopulation	Absence subpopulation	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	217	121	70	
Units: Reduction of Seizure Days				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	1.44 (± 1.69)	1.48 (± 1.69)	1.31 (± 2.24)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage reduction from N01057 or N166 Baseline to the Evaluation Period in seizure days per week for the ITT population, and Absence and Myoclonic subpopulations

End point title	Percentage reduction from N01057 or N166 Baseline to the Evaluation Period in seizure days per week for the ITT population, and Absence and Myoclonic subpopulations

End point description:

A positive value for Percentage reduction of seizure days per week indicates an improvement from Baseline.

End point type	Secondary

End point timeframe:

From N01057 or N166 Baseline to the Evaluation Period

End point values	All intent-to-treat (ITT) population	Myoclonic subpopulation	Absence subpopulation	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	217	121	70	
Units: Percentage reduction of Seizure Days				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	73.06 (± 39.62)	71.67 (± 70.58)	60.13 (± 72.26)	

Statistical analyses

No statistical analyses for this end point

Secondary: Categorical percentage reduction from Baseline to the Evaluation Period in seizure days per week for the ITT population, and Absence and Myoclonic subpopulations

End point title	Categorical percentage reduction from Baseline to the Evaluation Period in seizure days per week for the ITT population, and Absence and Myoclonic subpopulations

End point description:

End point type	Secondary

End point timeframe:

Evaluation Period

End point values	All intent-to-treat (ITT) population	Myoclonic subpopulation	Absence subpopulation	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	217	121	70	
Units: Subjects				
< -25 %	8	6	8	
-25 % to < 25 %	12	6	3	
25 % to < 50 %	24	7	6	
50 % to < 75 %	32	13	6	
75 % to < 100 %	89	51	18	
100 %	52	38	29	

Statistical analyses

No statistical analyses for this end point

Secondary: Categorical percentage reduction from Baseline to the Evaluation Period in seizure frequency per week for Tonic-Clonic subpopulation seizures types

End point title	Categorical percentage reduction from Baseline to the

	Evaluation Period in seizure frequency per week for Tonic-Clonic subpopulation seizures types

End point description:

End point type	Secondary

End point timeframe:

Evaluation Period

End point values	Tonic-Clonic subpopulation			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: Subjects				
< - 25 %	4			
-25 % to < 25 %	10			
25 % to < 50 %	12			
50 % to < 75 %	33			
75 % to < 100 %	48			
100 %	45			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected from Visit 1 (Week 0) until the end of study (up to 1764 days).

Adverse event reporting additional description:

Adverse Events refer to the Intent-to-Treat (ITT) Population, including all subjects who had recorded intake of at least 1 dose of N167 study drug.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	7.0

Reporting groups

Reporting group title	Levetiracetam (subjects from N01057 and N166)

Reporting group description:

Subjects received treatment up to 1764 days during the Evaluation Period. Up to 4000 mg/day (or 80 mg/kg/day for children and adolescents less than 50 kg). Oral tablets of 166, 250, or 500 mg Levetiracetam twice daily (b.i.d.).

Reporting group title	Levetiracetam (subjects from N129 and N164)

Reporting group description:

Subjects received treatment up to 1764 days during the Evaluation Period. Up to 4000 mg/day (or 80 mg/kg/day for children and adolescents less than 50 kg). Oral tablets of 166, 250, or 500 mg Levetiracetam twice daily (b.i.d.).

Serious adverse events	Levetiracetam (subjects from N01057 and N166)	Levetiracetam (subjects from N129 and N164)	
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 217 (14.29%)	4 / 20 (20.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye injury			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			

subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scapula fracture			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Convulsion			
subjects affected / exposed	7 / 217 (3.23%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	1 / 9	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Grand mal convulsion			
subjects affected / exposed	2 / 217 (0.92%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	2 / 217 (0.92%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (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	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postictal state			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myoclonus			
subjects affected / exposed	0 / 217 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal			

conditions			
Pregnancy			
subjects affected / exposed	4 / 217 (1.84%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Unintended pregnancy			
subjects affected / exposed	2 / 217 (0.92%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-uterine death			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature baby			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion spontaneous			
subjects affected / exposed	0 / 217 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Multi-organ failure			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ulcer			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 217 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash erythematous			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychotic disorder			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Suicidal ideation			

subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scoliosis			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 217 (0.46%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site infection			
subjects affected / exposed	0 / 217 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Levetiracetam (subjects from N01057 and N166)	Levetiracetam (subjects from N129 and N164)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	106 / 217 (48.85%)	16 / 20 (80.00%)	
Investigations			
Weight increased			
subjects affected / exposed	17 / 217 (7.83%)	2 / 20 (10.00%)	
occurrences (all)	17	2	
Injury, poisoning and procedural complications			

Contusion			
subjects affected / exposed	0 / 217 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 217 (0.00%)	5 / 20 (25.00%)	
occurrences (all)	0	5	
Headache			
subjects affected / exposed	40 / 217 (18.43%)	2 / 20 (10.00%)	
occurrences (all)	93	5	
Tremor			
subjects affected / exposed	15 / 217 (6.91%)	0 / 20 (0.00%)	
occurrences (all)	17	0	
Dizziness			
subjects affected / exposed	18 / 217 (8.29%)	2 / 20 (10.00%)	
occurrences (all)	25	2	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	13 / 217 (5.99%)	0 / 20 (0.00%)	
occurrences (all)	15	0	
Constipation			
subjects affected / exposed	0 / 217 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	4	
Diarrhoea			
subjects affected / exposed	0 / 217 (0.00%)	3 / 20 (15.00%)	
occurrences (all)	0	6	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 217 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Sinus pain			
subjects affected / exposed	0 / 217 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Psychiatric disorders			

Depression			
subjects affected / exposed	15 / 217 (6.91%)	0 / 20 (0.00%)	
occurrences (all)	16	0	
Sleep disorder			
subjects affected / exposed	0 / 217 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Stress symptoms			
subjects affected / exposed	0 / 217 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Infections and infestations			
Influenza			
subjects affected / exposed	20 / 217 (9.22%)	2 / 20 (10.00%)	
occurrences (all)	30	2	
Nasopharyngitis			
subjects affected / exposed	24 / 217 (11.06%)	2 / 20 (10.00%)	
occurrences (all)	43	2	
Ear infection			
subjects affected / exposed	0 / 217 (0.00%)	3 / 20 (15.00%)	
occurrences (all)	0	3	
Urinary tract infection			
subjects affected / exposed	13 / 217 (5.99%)	2 / 20 (10.00%)	
occurrences (all)	16	3	
Respiratory tract infection			
subjects affected / exposed	0 / 217 (0.00%)	3 / 20 (15.00%)	
occurrences (all)	0	5	
Bronchitis			
subjects affected / exposed	0 / 217 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 217 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Gastroenteritis			
subjects affected / exposed	0 / 217 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 September 2003	The core protocol amendment was issued on 08 Sep 2003 and concerned the following: • The number of participating sites and countries was extended due to a delay in recruitment in the prior N166 and N01057 studies. • Adverse events reported in postmarketing experience were added to protocol Section 2.2.4, Adverse Events in Clinical Studies (Section 16.1.1). • Some administrative changes were made to the protocol that did not alter the conduct of the study (eg, emergency contacts were updated and various edits made to sentences for clarification only).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported