Clinical trial results:
A therapeutic confirmatory, open-label, multi-center, randomized 2 parallel groups, community-based trial studying the efficacy and safety of levetiracetam (1000 to 3000 mg/day oral tablets 250-500 mg b.i.d.) compared to sodium valproate (1000 to 2000 mg/day oral ER tablets 300-500 mg b.i.d.) and carbamazepine (600 to 1600 mg/day oral CR tablets 200-400 mg b.i.d.) as monotherapy in subjects with newly diagnosed epilepsy.

Summary

EudraCT number	2004-001339-41
Trial protocol	AT FI SE SK IE CZ GB DE BE ES IT HU PT DK
Global end of trial date	13 October 2007

Results information

Result version number	v1 (current)
This version publication date	08 July 2016
First version publication date	30 July 2015

Trial information

Trial identification

Sponsor protocol code	N01175

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00175903
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Pharma SA
Sponsor organisation address	Chemin du Foriest, Braine, Belgium, 1420 Braine-L'Alleud
Public contact	Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, 0049 2173 48 15 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 December 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 October 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effectiveness of levetiracetam (LEV) in monotherapy compared to the older antiepileptic drugs (sodium valproate (VPA-ER) or carbamazepine (CBZ-CR).

Protection of trial subjects:

All pertinent aspects of the trial were explained and all questions answered to the satisfaction of the subject or subject's legally acceptable representative before collecting written informed consent.

The consent of both the subject and/or the legally acceptable representative were obtained for subjects under 18 years of age (i.e. in this trial, subjects of 16 years or older where legally permitted). For mentally retarded subjects, the consent of the legally acceptable representative only was obtained.

The subject was free to withdraw from the trial at any time without penalty or loss of benefits to which he/she was otherwise entitled.

Background therapy:

Not applicable.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	09 February 2005
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 98
Country: Number of subjects enrolled	Austria: 64
Country: Number of subjects enrolled	Belgium: 70
Country: Number of subjects enrolled	Czech Republic: 39
Country: Number of subjects enrolled	Denmark: 18
Country: Number of subjects enrolled	Finland: 31
Country: Number of subjects enrolled	France: 72
Country: Number of subjects enrolled	Germany: 262
Country: Number of subjects enrolled	Greece: 47

Country: Number of subjects enrolled	Hungary: 17
Country: Number of subjects enrolled	Ireland: 4
Country: Number of subjects enrolled	Italy: 165
Country: Number of subjects enrolled	Netherlands: 41
Country: Number of subjects enrolled	Norway: 56
Country: Number of subjects enrolled	Poland: 148
Country: Number of subjects enrolled	Romania: 23
Country: Number of subjects enrolled	Russian Federation: 55
Country: Number of subjects enrolled	Slovakia: 37
Country: Number of subjects enrolled	Spain: 69
Country: Number of subjects enrolled	Sweden: 36
Country: Number of subjects enrolled	Switzerland: 68
Country: Number of subjects enrolled	Turkey: 40
Country: Number of subjects enrolled	United Kingdom: 101
Country: Number of subjects enrolled	Bulgaria: 127
Worldwide total number of subjects	1688
EEA total number of subjects	1427

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)	1441
From 65 to 84 years	223
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

The N01175 study began enrollment in February 2005 and concluded in October 2007. Recruitment took place in 24 countries.

Pre-assignment

Screening details:

Participant flow and baseline characteristics consist of the Intent-to-Treat (ITT) population, which consists of all randomized subjects regardless of actual intake.

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

Arm description:

Daily dose of 1000 to 3000 mg film-coated oral tablets, 250-500 mg twice daily.

Arm type	Experimental
Investigational medicinal product name	Levetiracetam
Investigational medicinal product code	LEV
Other name	Keppra
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Daily dose of 1000 to 3000 mg film-coated oral tablets, 250-500 mg twice daily.

Arm title	Older Antiepileptic Drugs

Arm description:

Older AEDs consist of CBZ-CR 200 mg and 400 mg and VPA-ER 300 mg and 500 mg.

Arm type	Active comparator
Investigational medicinal product name	Valproate Extended Release
Investigational medicinal product code	VER
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Daily dose of 1000-2000 mg ER oral tablets, 300 mg and 500 mg twice daily.

Investigational medicinal product name	Carbamazepine Controlled Release
Investigational medicinal product code	CBZ-CR
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Daily dose of 600-1600 mg CR oral tablets, 200 mg and 400 mg twice daily.

Number of subjects in period 1	Levetiracetam	Older Antiepileptic Drugs
Started	841	847
Completed	639	627
Not completed	202	220
AE, serious fatal	4	3
Consent withdrawn by subject	38	36
Unknown AE	2	1
Other Reason	22	15
AE, non-serious non-fatal	50	90
Lost to follow-up	36	34
SAE, non-fatal	13	14
Lack of efficacy	35	25
SAE, non-fatal + AE, non-serious non-fatal	2	2

Baseline characteristics

Reporting groups	
Reporting group title	Levetiracetam
Reporting group description:	
Daily dose of 1000 to 3000 mg film-coated oral tablets, 250-500 mg twice daily.	
Reporting group title	Older Antiepileptic Drugs
Reporting group description:	
Older AEDs consist of CBZ-CR 200 mg and 400 mg and VPA-ER 300 mg and 500 mg.	

Reporting group values	Levetiracetam	Older Antiepileptic Drugs	Total
Number of subjects	841	847	1688
Age Categorical Units: Subjects			
Adolescents (12 - <18 years)	8	11	19
Adults (18 - <65 years)	718	723	1441
Elderly (65 - <85 years)	112	111	223
>=85 years	3	2	5
Age Continuous Units: years			
arithmetic mean	40.61	40.87	
standard deviation	± 17.76	± 17.8	-
Gender Categorical Units: Subjects			
Female	375	371	746
Male	466	476	942
Race Units: Subjects			
Caucasian	818	826	1644
African-american	8	5	13
Asian/pacific islander	8	6	14
Hispanic	2	5	7
Indian/pakistani	3	2	5
Other/mixed race	2	3	5
Weight Units: kg			
arithmetic mean	73.08	74.31	
standard deviation	± 15.52	± 16.16	-
BMI Units: kg/m^2			
arithmetic mean	25.04	25.31	
standard deviation	± 4.68	± 4.6	-
Height Units: cm			
arithmetic mean	170.7	171.1	
standard deviation	± 10	± 9.7	-

End points

End points reporting groups

Reporting group title	Levetiracetam
Reporting group description:	
Daily dose of 1000 to 3000 mg film-coated oral tablets, 250-500 mg twice daily.	
Reporting group title	Older Antiepileptic Drugs
Reporting group description:	
Older AEDs consist of CBZ-CR 200 mg and 400 mg and VPA-ER 300 mg and 500 mg.	

Primary: Time to withdrawal from study medication (starting at V1) as a measure of combined efficacy and safety

End point title	Time to withdrawal from study medication (starting at V1) as a measure of combined efficacy and safety
End point description:	
End point type	Primary
End point timeframe:	
Visit 1 to End of Study (approximately 52 weeks)	

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	841[1]	847[2]		
Units: Time to Withdrawal				
median (inter-quartile range (Q1-Q3))				
median (inter-quartile range)	999 (999 to 999)	999 (999 to 999)		

Notes:

[1] - For this analysis, the value of 999 indicates Not Estimable.

[2] - For this analysis, the value of 999 indicates Not Estimable.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Older Antiepileptic Drugs v Levetiracetam
Number of subjects included in analysis	1688
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.258
Method	Chi-squared
Parameter estimate	Cox proportional hazard
Point estimate	0.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.08

Secondary: The time to withdrawal comparing Levetiracetam versus the older Antiepileptic Drugs based on the subset of subjects whose best recommended treatment was Carbamazepine Controlled Release

End point title	The time to withdrawal comparing Levetiracetam versus the older Antiepileptic Drugs based on the subset of subjects whose best recommended treatment was Carbamazepine Controlled Release

End point description:

End point type	Secondary

End point timeframe:

Visit 1 to End of Study (approximately 52 weeks)

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	492[3]	500[4]		
Units: Time to Withdrawal				
median (inter-quartile range (Q1-Q3))				
median (inter-quartile range)	999 (999 to 999)	999 (999 to 999)		

Notes:

[3] - For this analysis, the value of 999 indicates Not Estimable.

[4] - For this analysis, the value of 999 indicates Not Estimable.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs
Number of subjects included in analysis	992
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.161
Method	Chi-squared
Parameter estimate	Cox proportional hazard
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.07

Secondary: The time to withdrawal comparing Levetiracetam versus the older Antiepileptic Drugs based on the subset of subjects whose best recommended treatment was Sodium Valproate Extended Release

End point title	The time to withdrawal comparing Levetiracetam versus the older Antiepileptic Drugs based on the subset of subjects whose best recommended treatment was Sodium Valproate Extended Release

End point description:

End point type	Secondary

End point timeframe:

Visit 1 to End of Study (approximately 52 weeks)

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	349[5]	347[6]		
Units: Time to Withdrawal				
median (inter-quartile range (Q1-Q3))				
median (inter-quartile range)	999 (999 to 999)	999 (999 to 999)		

Notes:

[5] - For this analysis, the value of 999 indicates Not Estimable.

[6] - For this analysis, the value of 999 indicates Not Estimable.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs
Number of subjects included in analysis	696
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.882
Method	Chi-squared
Parameter estimate	Cox proportional hazard
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.41

Secondary: The retention rate after 6 months comparing Levetiracetam versus the older Antiepileptic Drugs

End point title	The retention rate after 6 months comparing Levetiracetam versus the older Antiepileptic Drugs

End point description:

End point type	Secondary

End point timeframe:

Visit 1 to Visit 4 (approximately 26 weeks)

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	841	847		
Units: participants				
Number	691	677		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs
Number of subjects included in analysis	1688
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2422
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.157
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.906
upper limit	1.477

Secondary: The retention rate after 12 months comparing Levetiracetam versus the older Antiepileptic Drugs

End point title	The retention rate after 12 months comparing Levetiracetam versus the older Antiepileptic Drugs

End point description:

End point type	Secondary

End point timeframe:

Visit 1 to Visit 5 (approximately 52 weeks)

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	841	847		
Units: participants				
number	408	380		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs
Number of subjects included in analysis	1688
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1402
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.155
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.954
upper limit	1.4

Secondary: The retention rate after 6 months comparing Levetiracetam versus older Antiepileptic Drugs based on the subset of subjects whose best recommended treatment was Carbamazepine Controlled Release

End point title	The retention rate after 6 months comparing Levetiracetam versus older Antiepileptic Drugs based on the subset of subjects whose best recommended treatment was Carbamazepine Controlled Release
End point description:	
End point type	Secondary
End point timeframe:	
Visit 1 to Visit 4 (approximately 26 weeks)	

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	492	500		
Units: participants				
number	402	388		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs
Number of subjects included in analysis	992
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1229
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.277
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.936
upper limit	1.743

Secondary: The retention rate after 6 months comparing Levetiracetam versus older Antiepileptic Drugs based on the subset of subjects whose best recommended treatment was Sodium Valproate Extended Release

End point title	The retention rate after 6 months comparing Levetiracetam versus older Antiepileptic Drugs based on the subset of subjects whose best recommended treatment was Sodium Valproate Extended Release

End point description:

End point type	Secondary

End point timeframe:

Visit 1 to Visit 4 (approximately 26 weeks)

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	349	347		
Units: participants				
number	289	289		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs
Number of subjects included in analysis	696
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8269
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.957
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.643
upper limit	1.423

Secondary: The retention rate after 12 months comparing Levetiracetam versus older Antiepileptic Drugs based on the subset of subjects whose best recommended treatment was Carbamazepine Controlled Release

End point title	The retention rate after 12 months comparing Levetiracetam versus older Antiepileptic Drugs based on the subset of subjects whose best recommended treatment was Carbamazepine Controlled Release

End point description:

End point type	Secondary

End point timeframe:

Visit 1 to Visit 5 (approximately 52 weeks)

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	492	500		
Units: participant				
number	229	203		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs
Number of subjects included in analysis	992
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0725
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.979
upper limit	1.621

Secondary: The retention rate after 12 months comparing Levetiracetam versus older Antiepileptic Drugs based on the subset of subjects whose best recommended treatment was Sodium Valproate Extended Release

End point title	The retention rate after 12 months comparing Levetiracetam versus older Antiepileptic Drugs based on the subset of subjects whose best recommended treatment was Sodium Valproate Extended Release

End point description:

End point type	Secondary

End point timeframe:

Visit 1 to Visit 5 (approximately 52 weeks)

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	349	347		
Units: participants				
number	179	177		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs

Number of subjects included in analysis	696
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9436
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.011
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.751
upper limit	1.361

Secondary: Seizure freedom at 6 months comparing Levetiracetam versus older Antiepileptic Drugs

End point title	Seizure freedom at 6 months comparing Levetiracetam versus older Antiepileptic Drugs

End point description:

End point type	Secondary

End point timeframe:

Visit 1 to Visit 4 (approximately 26 weeks)

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	841	847		
Units: participants				
number	431	449		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs
Number of subjects included in analysis	1688
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4409
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.927

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.765
upper limit	1.124

Secondary: Seizure freedom at 12 months comparing Levetiracetam versus older Antiepileptic Drugs

End point title	Seizure freedom at 12 months comparing Levetiracetam versus older Antiepileptic Drugs

End point description:

End point type	Secondary

End point timeframe:

Visit 1 to Visit 5 (approximately 52 weeks)

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	841	847		
Units: participants				
number	238	225		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs
Number of subjects included in analysis	1688
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4469
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.087
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.876
upper limit	1.349

Secondary: Seizure freedom at 6 months comparing Levetiracetam versus older

Antiepileptic Drugs based on based on the subset of subjects whose best recommended treatment was Carbamazepine Controlled Release

End point title	Seizure freedom at 6 months comparing Levetiracetam versus older Antiepileptic Drugs based on based on the subset of subjects whose best recommended treatment was Carbamazepine Controlled Release

End point description:

End point type	Secondary

End point timeframe:

Visit 1 to Visit 4 (approximately 26 weeks)

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	492	500		
Units: participants				
number	240	244		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs
Number of subjects included in analysis	992
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9051
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.985
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.767
upper limit	1.265

Secondary: Seizure freedom at 6 months comparing Levetiracetam versus older Antiepileptic Drugs based on based on the subset of subjects whose best recommended treatment was Sodium Valproate Extended Release

End point title	Seizure freedom at 6 months comparing Levetiracetam versus older Antiepileptic Drugs based on based on the subset of subjects whose best recommended treatment was Sodium Valproate Extended Release

End point description:

End point type	Secondary

End point timeframe:

Visit 1 to Visit 4 (approximately 26 weeks)

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	349	347		
Units: participants				
number	191	205		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs
Number of subjects included in analysis	696
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2518
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.839
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.621
upper limit	1.133

Secondary: Seizure freedom at 12 months comparing Levetiracetam versus older Antiepileptic Drugs based on based on the subset of subjects whose best recommended treatment was Carbamazepine Controlled Release

End point title	Seizure freedom at 12 months comparing Levetiracetam versus older Antiepileptic Drugs based on based on the subset of subjects whose best recommended treatment was Carbamazepine Controlled Release

End point description:

End point type	Secondary

End point timeframe:

Visit 1 to Visit 5 (approximately 52 weeks)

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	492	500		
Units: participants				
number	125	108		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs
Number of subjects included in analysis	992
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1853
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.221
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.909
upper limit	1.64

Secondary: Seizure freedom at 12 months comparing Levetiracetam versus older Antiepileptic Drugs based on based on the subset of subjects whose best recommended treatment was Sodium Valproate Extended Release

End point title	Seizure freedom at 12 months comparing Levetiracetam versus older Antiepileptic Drugs based on based on the subset of subjects whose best recommended treatment was Sodium Valproate Extended Release

End point description:

End point type	Secondary

End point timeframe:

Visit 1 to Visit 5 (approximately 52 weeks)

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	349	347		
Units: participants				
number	113	117		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs
Number of subjects included in analysis	696
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7257
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.945
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.689
upper limit	1.296

Secondary: Time to first seizure comparing Levetiracetam versus older Antiepileptic Drugs

End point title	Time to first seizure comparing Levetiracetam versus older Antiepileptic Drugs

End point description:

End point type	Secondary

End point timeframe:

Visit 1 to End of Study (approximately 52 weeks)

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	841[7]	847[8]		
Units: days				
median (inter-quartile range (Q1-Q3))				
median (inter-quartile range)	999 (999 to 999)	999 (999 to 999)		

Notes:

[7] - For this analysis, the value of 999 indicates Not Estimable.

[8] - For this analysis, the value of 999 indicates Not Estimable.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs
Number of subjects included in analysis	1688
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.022
Method	Chi-squared
Parameter estimate	Cox proportional hazard
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	1.39

Secondary: Time to first seizure comparing Levetiracetam versus older Antiepileptic Drugs based on the subset of subjects whose best recommended treatment was Carbamazepine Controlled Release

End point title	Time to first seizure comparing Levetiracetam versus older Antiepileptic Drugs based on the subset of subjects whose best recommended treatment was Carbamazepine Controlled Release

End point description:

End point type	Secondary

End point timeframe:

Visit 1 to End of Study (approximately 52 weeks)

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	492[9]	500[10]		
Units: days				
median (inter-quartile range (Q1-Q3))				
median (inter-quartile range)	999 (999 to 999)	999 (999 to 999)		

Notes:

[9] - For this analysis, the value of 999 indicates Not Estimable.

[10] - For this analysis, the value of 999 indicates Not Estimable.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs

Number of subjects included in analysis	992
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.061
Method	Chi-squared
Parameter estimate	Cox proportional hazard
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.46

Secondary: Time to first seizure comparing Levetiracetam versus older Antiepileptic Drugs based on the subset of subjects whose best recommended treatment was Sodium Valproate Extended Release

End point title	Time to first seizure comparing Levetiracetam versus older Antiepileptic Drugs based on the subset of subjects whose best recommended treatment was Sodium Valproate Extended Release

End point description:

End point type	Secondary

End point timeframe:

Visit 1 to End of Study (approximately 52 weeks)

End point values	Levetiracetam	Older Antiepileptic Drugs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	349[11]	347[12]		
Units: days				
median (inter-quartile range (Q1-Q3))				
median (inter-quartile range)	999 (999 to 999)	999 (999 to 999)		

Notes:

[11] - For this analysis, the value of 999 indicates Not Estimable.

[12] - For this analysis, the value of 999 indicates Not Estimable.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Levetiracetam v Older Antiepileptic Drugs

Number of subjects included in analysis	696
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.167
Method	Chi-squared
Parameter estimate	Cox proportional hazard
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.54

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent Adverse Events (TEAEs) were recorded during the study, which began in February 2005 and concluded in October 2007.

Adverse event reporting additional description:

TEAES consists of the Intent-to-Treat (ITT) population group, which consists of all randomized subjects regardless of actual intake.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	Older Antiepileptic Drugs

Reporting group description:

Older AEDs consist of CBZ-CR 200 mg and 400 mg and VPA-ER 300 mg and 500 mg.

Reporting group title	Levetiracetam

Reporting group description:

Daily dose of 1000 to 3000 mg film-coated oral tablets, 250-500 mg twice daily.

Serious adverse events	Older Antiepileptic Drugs	Levetiracetam	
Total subjects affected by serious adverse events			
subjects affected / exposed	61 / 841 (7.25%)	106 / 835 (12.69%)	
number of deaths (all causes)	3	5	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain neoplasm			
subjects affected / exposed	0 / 841 (0.00%)	3 / 835 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Breast neoplasm			
subjects affected / exposed	1 / 841 (0.12%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemangioma			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Glioblastoma multiforme			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Insulinoma			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mixed oligo-astrocytoma			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer stage III			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioma			
subjects affected / exposed	2 / 841 (0.24%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			

Hypertension			
subjects affected / exposed	1 / 841 (0.12%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitis			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cardiac operation			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess drainage			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neoplasm surgery			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder operation			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hospitalisation			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal			

conditions			
Pregnancy			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
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			
Chest pain			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 841 (0.24%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden unexplained death in epilepsy			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 841 (0.12%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			

Depression			
subjects affected / exposed	1 / 841 (0.12%)	2 / 835 (0.24%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abnormal behaviour			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholism			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychosomatic disease			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Restlessness			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somatoform disorder			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			

subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conversion disorder			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental disorder			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Body temperature increased			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monocyte morphology abnormal			

subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 841 (0.12%)	2 / 835 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Road traffic accident			
subjects affected / exposed	0 / 841 (0.00%)	2 / 835 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol poisoning			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 841 (0.12%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body trauma			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			

subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus lesion			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation injury			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skull fracture			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			

subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Concussion			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug toxicity			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic brain injury			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Exomphalos			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous malformation			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 841 (0.00%)	2 / 835 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Angina pectoris			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	1 / 841 (0.12%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Coronary artery disease			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			

subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (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			
Grand mal convulsion			
subjects affected / exposed	2 / 841 (0.24%)	6 / 835 (0.72%)	
occurrences causally related to treatment / all	1 / 2	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	7 / 841 (0.83%)	16 / 835 (1.92%)	
occurrences causally related to treatment / all	3 / 8	4 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	6 / 841 (0.71%)	4 / 835 (0.48%)	
occurrences causally related to treatment / all	1 / 6	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	1 / 841 (0.12%)	4 / 835 (0.48%)	
occurrences causally related to treatment / all	1 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures with secondary generalisation			
subjects affected / exposed	1 / 841 (0.12%)	3 / 835 (0.36%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complex partial seizures			
subjects affected / exposed	0 / 841 (0.00%)	2 / 835 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	0 / 841 (0.00%)	2 / 835 (0.24%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haematoma			

subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Encephalitis			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Simple partial seizures			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 841 (0.12%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope vasovagal			

subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thalamic infarction			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIIIth nerve lesion			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar infarction			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	2 / 841 (0.24%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed level of consciousness			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			

subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tonic convulsion			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal vein thrombosis			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diplopia			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heterophoria			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (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 hernia			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	2 / 841 (0.24%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer			

subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 841 (0.24%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 841 (0.00%)	2 / 835 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Generalised erythema			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	1 / 841 (0.12%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug eruption			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin haemorrhage			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Renal impairment			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 841 (0.00%)	2 / 835 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle tightness			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (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			
Abscess			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Borrelia infection			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lung infection			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 841 (0.12%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethritis			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pilonidal cyst			
subjects affected / exposed	1 / 841 (0.12%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	2 / 841 (0.24%)	0 / 835 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 841 (0.00%)	1 / 835 (0.12%)	
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	Older Antiepileptic Drugs	Levetiracetam	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	441 / 841 (52.44%)	402 / 835 (48.14%)	
Investigations			
Weight increased			
subjects affected / exposed	98 / 841 (11.65%)	47 / 835 (5.63%)	
occurrences (all)	102	47	
Nervous system disorders			
Headache			
subjects affected / exposed	170 / 841 (20.21%)	161 / 835 (19.28%)	
occurrences (all)	335	378	
Dizziness			
subjects affected / exposed	70 / 841 (8.32%)	68 / 835 (8.14%)	
occurrences (all)	89	98	
Somnolence			
subjects affected / exposed	48 / 841 (5.71%)	68 / 835 (8.14%)	
occurrences (all)	53	83	
Tremor			
subjects affected / exposed	43 / 841 (5.11%)	14 / 835 (1.68%)	
occurrences (all)	43	14	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	134 / 841 (15.93%)	120 / 835 (14.37%)	
occurrences (all)	156	135	
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	36 / 841 (4.28%)	39 / 835 (4.67%)	
occurrences (all)	47	53	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	57 / 841 (6.78%)	44 / 835 (5.27%)	
occurrences (all)	78	56	
Diarrhoea			
subjects affected / exposed	39 / 841 (4.64%)	38 / 835 (4.55%)	
occurrences (all)	42	48	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	23 / 841 (2.73%)	11 / 835 (1.32%)	
occurrences (all)	23	11	
Rash			
subjects affected / exposed	28 / 841 (3.33%)	8 / 835 (0.96%)	
occurrences (all)	29	11	
Psychiatric disorders			
Depression			
subjects affected / exposed	20 / 841 (2.38%)	42 / 835 (5.03%)	
occurrences (all)	24	46	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	46 / 841 (5.47%)	40 / 835 (4.79%)	
occurrences (all)	56	65	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 December 2005	The purpose of the amendment was as follows: 1. To correct erroneous information such as the fax number of the Clinical Trial Manager. 2. To correct new staff functions. 3. To extend enrollment.
29 September 2006	This amendment introduced the collection of a new blood sample in order to retrieve pharmacogenomic data on SV2A. This data was to be collected in order to investigate the potential influence of specific polymorphisms in the protein on therapeutic response to LEV, CBZ-CR or VPA-ER. The analysis plan as well as the results of pharmacogenomic data are presented in this amended CSR.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported