Clinical trial results:
A Multicenter, Open-label, Follow-up Trial Evaluating the Long-term Safety of Levetiracetam, for Patients Suffering From Epilepsy and Coming From the Study N01175 (NCT00175903)

Summary

EudraCT number	2006-000173-29
Trial protocol	FI BE
Global end of trial date	29 April 2008

Results information

Result version number	v1 (current)
This version publication date	30 June 2016
First version publication date	10 July 2015

Trial information

Trial identification

Sponsor protocol code	N01237

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00291655
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB S.A.
Sponsor organisation address	Allée de la Recherche, 60, Brussels, Belgium, B – 1070
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 June 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 April 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

For ethical reasons to give opportunity for adult subjects (≥16 or 18 years) suffering from newly diagnosed epilepsy who completed the therapeutic confirmatory, open-label trial N01175 conducted with levetiracetam in monotherapy and who benefited from the treatment, to receive treatment with levetiracetam until the monotherapy indication for levetiracetam is granted in Europe.

Protection of trial subjects:

Adequate information was provided to the subject in both oral and written form and consent was obtained in writing prior to performance of any study specific procedure. The content and process of obtaining informed consent was in accordance with all applicable regulatory and IEC/IRB requirements.

If the subject was unable to provide informed consent, the subject's legally acceptable representative was informed of all pertinent aspects of the trial including the written information which had been previously submitted to the IEC/IRB.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	26 June 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 9
Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Poland: 32
Country: Number of subjects enrolled	Belgium: 25
Country: Number of subjects enrolled	Bulgaria: 31
Country: Number of subjects enrolled	Switzerland: 15
Worldwide total number of subjects	130
EEA total number of subjects	115

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)	0
Adults (18-64 years)	111
From 65 to 84 years	16
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

This study began recruiting in June 2006 and concluded in April 2008.

Pre-assignment

Screening details:

Baseline demographics consists of the Intent-to-Treat (ITT) population, which is defined as all subjects who took at least one dose of study medication in N01237 trial.

Period 1

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

Arms

Arm title	Levetiracetam Open-label Treatment

Arm description:

Open-label treatment with Levetiracetam 500 mg oral tablets in monotherapy, 1000 - 3000 mg/day bid over up to 18 months.

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:

500 mg oral tablets, 1000 - 3000 mg/day, twice a day (bid), duration of the study.

Number of subjects in period 1	Levetiracetam Open-label Treatment
Started	130
Completed	115
Not completed	15
Consent withdrawn by subject	7
AE, non-serious non-fatal	1
Other Reason	2
Lost to follow-up	2
Lack of efficacy	3

Baseline characteristics

Reporting groups	
Reporting group title	Levetiracetam Open-label Treatment
Reporting group description:	
Open-label treatment with Levetiracetam 500 mg oral tablets in monotherapy, 1000 - 3000 mg/day bid over up to 18 months.	

Reporting group values	Levetiracetam Open-label Treatment	Total	
Number of subjects	130	130	
Age categorical Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	 40.68 ± 18.35	 -	
Gender Categorical Units: Subjects			
Female	58	58	
Male	72	72	
Region of Enrollment Units: Subjects			
France	18	18	
Finland	9	9	
Poland	32	32	
Belgium	25	25	
Bulgaria	31	31	
Switzerland	15	15	

End points

End points reporting groups

Reporting group title	Levetiracetam Open-label Treatment

Reporting group description:

Open-label treatment with Levetiracetam 500 mg oral tablets in monotherapy, 1000 - 3000 mg/day bid over up to 18 months.

Primary: Assessment of safety of levetiracetam as per adverse event (AE) reporting in open-label therapy phase

End point title	Assessment of safety of levetiracetam as per adverse event (AE) reporting in open-label therapy phase[1]

End point description:

Summarization for occurrence of adverse events like number of subjects with any adverse events or drug related adverse events is provided (see categories).

End point type	Primary

End point timeframe:

During open-label therapy phase of 18 months

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: The primary objective was to give opportunity for adult subjects suffering from newly diagnosed epilepsy, who completed study N01175 conducted with levetiracetam (LEV) in monotherapy and who benefited from the treatment, to receive treatment with LEV until the monotherapy indication for LEV has been granted in Europe. The safety profile of LEV was summarized descriptively across several safety variables. Therefore, no inferential statistics were performed in this safety study.

End point values	Levetiracetam Open-label Treatment			
Subject group type	Reporting group			
Number of subjects analysed	130			
Units: participants				
Subjects with at least one AE	40			
Subjects with AEs leading to dose change	8			
Subjects with AEs leading to trial discontinuation	1			
Subjects with drug-related AEs	16			
Subjects with AEs of severe intensity	4			
Subjects with serious AEs	6			
Subjects with study drug-related serious AEs	0			
Number of deaths	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in body weight to withdrawal or end of study after

18 months

End point title	Change from baseline in body weight to withdrawal or end of study after 18 months

End point description:

End point type	Secondary

End point timeframe:

Start of open-label therapy (Baseline) to withdrawal or end of study after 18 months

End point values	Levetiracetam Open-label Treatment			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: kg				
arithmetic mean (standard deviation)				
mean (standard deviation)	0.71 (± 3.16)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Open-label treatment over 18 months.

Adverse event reporting additional description:

Treatment-emergent Adverse Events consist of the Safety Set, which is all subjects who took at least one dose of study medication in N01237 trial.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	Levetiracetam Open- Label Treatment

Reporting group description:

Open-label treatment with Levetiracetam 500 mg oral tablets in monotherapy, 1000 - 3000 mg/day bid over up to 18 months

Serious adverse events	Levetiracetam Open-Label Treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 130 (4.62%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Skin laceration			
subjects affected / exposed	1 / 130 (0.77%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Foot fracture			
subjects affected / exposed	1 / 130 (0.77%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 130 (0.77%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Grand mal convulsion			
subjects affected / exposed	1 / 130 (0.77%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic cirrhosis			
subjects affected / exposed	1 / 130 (0.77%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Alcoholism			
subjects affected / exposed	1 / 130 (0.77%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Tonsillitis			
subjects affected / exposed	1 / 130 (0.77%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Levetiracetam Open-Label Treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 130 (5.38%)		
Investigations			
Weight increased			
subjects affected / exposed	7 / 130 (5.38%)		
occurrences (all)	7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported