Clinical trial results:
Open-label, Single-arm, Multi-center, Pharmacokinetic, Safety and Tolerability Study of Levetiracetam Intravenous Infusion in Children (4 - 16 Years Old) With Epilepsy

Summary

EudraCT number	2006-005722-23
Trial protocol	BE DE FR
Global end of trial date	02 February 2010

Results information

Result version number	v1 (current)
This version publication date	30 June 2016
First version publication date	12 July 2015

Trial information

Trial identification

Sponsor protocol code	N01274

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00535392
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Pharma S.A.
Sponsor organisation address	B-1420 Braine-l'Alleud, 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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 March 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 February 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of the Levetiracetam IV 15-minute infusion administered every 12 hours, either as adjunctive treatment or monotherapy in children (4 to 16 years old) with epilepsy (except status epilepticus), either after switching from the equivalent LEV oral dose administration or as a new antiepileptic treatment.

Protection of trial subjects:

Adequate information was provided to the subject's parents/legally acceptable representative in both oral and written form and consent was obtained from the parents/legally acceptable representative in writing prior to performance of any study specific procedure. In addition, it was recommended that the subject's assent was also obtained, according to the child's age/competence and the IEC/IRB requirements. The content and process of obtaining informed consent was in accordance with all applicable regulatory and IEC/IRB requirements.

Background therapy:

Not applicable.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	10 September 2007
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	France: 4
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Turkey: 6
Country: Number of subjects enrolled	Mexico: 10
Country: Number of subjects enrolled	United States: 7
Worldwide total number of subjects	33
EEA total number of subjects	10

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

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from sites in the United States, Belgium, Germany, France, Mexico, and Turkey. The study began in September 2007 and continued until February 2010, with the last subject's visit occurring in February of 2010.

Pre-assignment

Screening details:

The Intent-to-Treat (ITT) population was used for results posting. The ITT consists of all subjects who received at least one dose of study medication.

Period 1

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

Arms

Arm title	Levetiracetam

Arm description:

Intravenous 100 mg/mL, twice a day, maximum of 4 days. Subjects on oral levetiracetam at study entry receive the same intravenous (IV) dosage (mg-for-mg) to their oral dose. Dosage for subjects not on levetiracetam at study entry was based on weight: if <50 kg, the dose was 20 mg/kg/day (10 mg/kg/day twice daily); if weight ≥ 50 kg, the dose of levetiracetam intravenous (LEV IV) was 1000 mg/day (500 mg twice daily).

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

Dosage and administration details:

Subjects on oral Levetiracetam at study entry received the same intravenous (IV) dosage (mg-for-mg) to their oral dose.

Investigational medicinal product name	Levetiracetam injection
Investigational medicinal product code	LEV Injection
Other name	Keppra
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mg/mL, twice a day, maximum of 4 days.

Number of subjects in period 1	Levetiracetam
Started	33
Completed	33

Baseline characteristics

Reporting groups

Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	33	33	
Age Categorical Units: Subjects			
<=18 years	33	33	
Between 18 and 65 years	0	0	
>=65 years	0	0	
Age Continuous Units: years			
arithmetic mean	9.71		
standard deviation	± 3.38	-	
Gender Categorical Units: Subjects			
Female	14	14	
Male	19	19	
Region of Enrollment Units: Subjects			
France	4	4	
United States	7	7	
Mexico	10	10	
Belgium	5	5	
Turkey	6	6	
Germany	1	1	

End points

End points reporting groups

Reporting group title	Levetiracetam

Reporting group description:

Intravenous 100 mg/mL, twice a day, maximum of 4 days. Subjects on oral levetiracetam at study entry receive the same intravenous (IV) dosage (mg-for-mg) to their oral dose. Dosage for subjects not on levetiracetam at study entry was based on weight: if <50 kg, the dose was 20 mg/kg/day (10 mg/kg/day twice daily); if weight ≥ 50 kg, the dose of levetiracetam intravenous (LEV IV) was 1000 mg/day (500 mg twice daily).

Primary: Number of subjects reporting at least 1 Treatment-Emergent Adverse Event (TEAE) during the treatment period (up to 4 days)

End point title	Number of subjects reporting at least 1 Treatment-Emergent Adverse Event (TEAE) during the treatment period (up to 4 days)[1]

End point description:

End point type	Primary

End point timeframe:

Treatment period (up to 4 days)

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 evaluate the safety and tolerability of the LEV IV 15-minute infusion administered every 12 hours, either as adjunctive treatment or monotherapy in children with epilepsy, either after switching from the equivalent LEV oral dose administration or as a new antiepileptic treatment.

The safety profile of levocetirizine was summarized descriptively across several safety variables. Therefore, no inferential statistics were performed in this safety study.

End point values	Levetiracetam			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: Subjects				
number	21			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects who received high-dose levetiracetam intravenous (LEV IV) (more than 40 mg/kg/day) during the treatment period (up to 4 days)

End point title	Number of subjects who received high-dose levetiracetam intravenous (LEV IV) (more than 40 mg/kg/day) during the treatment period (up to 4 days)

End point description:

End point type	Secondary

End point timeframe:

Treatment period (up to 4 days)

End point values	Levetiracetam			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: Subjects				
number	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of consecutive levetiracetam intravenous (LEV IV) doses received

End point title	Number of consecutive levetiracetam intravenous (LEV IV) doses received

End point description:

End point type	Secondary

End point timeframe:

Treatment period (up to 4 days)

End point values	Levetiracetam			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: Consecutive doses				
arithmetic mean (standard deviation)				
mean (standard deviation)	3.73 (± 1.61)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 4 days.

Adverse event reporting additional description:

Treatment-emergent Adverse Events represents the Intent-to-Treat population (ITT), which consists of all subjects who received at least one dose of study medication.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	Levetiracetam

Reporting group description:

Intravenous 100 mg/mL, twice a day, maximum of 4 days

Subjects on oral levetiracetam at study entry receive the same intravenous (IV) dosage (mg-for-mg) to their oral dose.
Dosage for subjects not on levetiracetam at study entry was based on weight: if <50 kg, the dose was 20 mg/kg/day (10 mg/kg/day twice daily); if weight ≥ 50 kg, the dose of levetiracetam intravenous (LEV IV) was 1000 mg/day (500 mg twice daily).

Serious adverse events	Levetiracetam		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 33 (9.09%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
CONVULSION			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
VOMITING			

subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Levetiracetam		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 33 (36.36%)		
Investigations			
WEIGHT DECREASED			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	3 / 33 (9.09%)		
occurrences (all)	4		
Nervous system disorders			
CONVULSION			
subjects affected / exposed	3 / 33 (9.09%)		
occurrences (all)	5		
SOMNOLENCE			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	7		
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	3		
Gastrointestinal disorders			
NAUSEA			
subjects affected / exposed	3 / 33 (9.09%)		
occurrences (all)	3		
VOMITING			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	3		
DRY MOUTH			

subjects affected / exposed occurrences (all)	3 / 33 (9.09%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 May 2007	Clarification of the procedure for the administration of Levetiracetam (LEV) and of the number of mandatory infusion days.
01 June 2007	Allowed for the adjustment of the LEV dose for subjects with moderate renal insufficiency, based on their CLCR value (compliance with French Competent Authorities).
04 April 2008	Clarified the exclusion criterion for clinically significant acute or chronic illness and deleted the exclusion criteria for intake of 2 or more concomitant AEDs as well as vigabatrine. Revised the schedule of PK assessment. The predose time point was replaced by a time point at 3 to 10 minutes after the start of the infusion. Some logistical aspects of the study procedures were revised in order to facilitate the recruitment of subjects.
18 September 2008	Clarified the objectives following the 16 May 2008 teleconference with the FDA, confirming that the main goal of the study was safety and tolerability of the use of LEV IV in pediatrics, with a lesser emphasis on PK. This amendment also provided for the addition of FDA requests: - Approximately one half of the subjects exposed to at least 3 consecutive LEV IV doses - At least one third of the subjects should be in the high-dose range (≥40mg/kg/day) Additionally, this amendment provided an addition of an exclusion criterion: "The subject presents current depressive symptoms, current suicidal ideation and/or behavior."
12 November 2009	Clarified the use of local laboratory results for the evaluation of subjects' eligibility, and updated study team members' information.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported