Clinical trial results:
A Multicenter, Open-label Trial to Assess the Safety and Tolerability of a Single Intravenous Loading Dose of Lacosamide Followed by Oral Lacosamide Maintenance as Adjunctive Therapy in Subjects With Partial-onset Seizures

Summary

EudraCT number	2014-004378-40
Trial protocol	Outside EU/EEA
Global end of trial date	23 September 2009

Results information

Result version number	v1 (current)
This version publication date	28 June 2016
First version publication date	17 May 2015

Trial information

Trial identification

Sponsor protocol code	SP0925

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00655551
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB BIOSCIENCES Inc.
Sponsor organisation address	8010 Arco Corporate Drive, Raleigh, United States, 27517
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	18 November 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 September 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to evaluate the safety and tolerability of the rapid initiation of adjunctive lacosamide (LCM) via a single intravenous (iv) loading dose (iv LCM 200 mg, 300 mg, or 400 mg) and oral LCM maintenance treatment in adult subjects with partial-onset seizures.

Protection of trial subjects:

Subject’s informed consent was obtained and documented in accordance with local regulations, ICH-GCP requirements, and the ethical principles that have their origin in the
principles of the Declaration of Helsinki.

Prior to obtaining informed consent, information was given, in a language and at a level of complexity understandable to the subject, in both oral and written form by the investigator
or designee. Each subject had the opportunity to discuss the trial and its alternatives with the investigator.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	08 April 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 100
Worldwide total number of subjects	100
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	1
Adults (18-64 years)	99
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The SP0925 study began recruitment in April 2008. Recruitment took place in the United States. 100 participants entered the study, which concluded in September 2009.

Pre-assignment

Screening details:

N/A

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

Are arms mutually exclusive?	Yes
Arm title	Lacosamide (200 mg)

Arm description:

Single loading dose of intravenous (iv) lacosamide 200 mg followed by 6.5 days of oral lacosamide 100 mg twice daily

Arm type	Experimental
Investigational medicinal product name	Lacosamide
Investigational medicinal product code	SPM 927
Other name	Vimpat
Pharmaceutical forms	Infusion, Coated tablet
Routes of administration	Intravenous drip use

Dosage and administration details:

Single loading intravenous (iv) Lacosamide 200 mg dose administered over a 15 minute infusion duration followed by oral Lacosamide 200 mg/day (100 mg twice daily) for 6.5 days.

Arm title	Lacosamide (300 mg)

Arm description:

Single loading dose of intravenous (iv) lacosamide 300 mg dose followed by 6.5 days of oral lacosamide 150 mg twice daily

Arm type	Experimental
Investigational medicinal product name	Lacosamide
Investigational medicinal product code	SPM 927
Other name	Vimpat
Pharmaceutical forms	Infusion, Coated tablet
Routes of administration	Intravenous drip use

Dosage and administration details:

Single loading intravenous (iv) Lacosamide 200 mg dose administered over a 15 minute infusion duration followed by oral Lacosamide 200 mg/day (100 mg twice daily) for 6.5 days.

Arm title	Lacosamide (400 mg)

Arm description:

Single loading dose of intravenous (iv) lacosamide 400 mg followed by 6.5 days of oral lacosamide 200 mg twice daily

Arm type	Experimental

Investigational medicinal product name	Lacosamide
Investigational medicinal product code	SPM 927
Other name	Vimpat
Pharmaceutical forms	Infusion, Coated tablet
Routes of administration	Intravenous drip use

Dosage and administration details:

Single loading intravenous (iv) Lacosamide 200 mg dose administered over a 15 minute infusion duration followed by oral Lacosamide 200 mg/day (100 mg twice daily) for 6.5 days.

Number of subjects in period 1	Lacosamide (200 mg)	Lacosamide (300 mg)	Lacosamide (400 mg)
Started	25	50	25
Completed	25	47	21
Not completed	0	3	4
Non-Fatal, Non-Serious AE	-	3	4

Baseline characteristics

Reporting groups	
Reporting group title	Lacosamide (200 mg)
Reporting group description:	
Single loading dose of intravenous (iv) lacosamide 200 mg followed by 6.5 days of oral lacosamide 100 mg twice daily	
Reporting group title	Lacosamide (300 mg)
Reporting group description:	
Single loading dose of intravenous (iv) lacosamide 300 mg dose followed by 6.5 days of oral lacosamide 150 mg twice daily	
Reporting group title	Lacosamide (400 mg)
Reporting group description:	
Single loading dose of intravenous (iv) lacosamide 400 mg followed by 6.5 days of oral lacosamide 200 mg twice daily	

Reporting group values	Lacosamide (200 mg)	Lacosamide (300 mg)	Lacosamide (400 mg)
Number of subjects	25	50	25
Age Categorical Units: Subjects			
<=18 years	0	2	0
Between 18 and 65 years	25	48	25
Age Continuous Units: years			
arithmetic mean	39.1	38.6	39.6
standard deviation	± 11.8	± 11.5	± 12.2
Gender categorical Units: Subjects			
Female	14	26	9
Male	11	24	16

Reporting group values	Total		
Number of subjects	100		
Age Categorical Units: Subjects			
<=18 years	2		
Between 18 and 65 years	98		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	49		
Male	51		

End points

End points reporting groups

Reporting group title	Lacosamide (200 mg)
Reporting group description:	
Single loading dose of intravenous (iv) lacosamide 200 mg followed by 6.5 days of oral lacosamide 100 mg twice daily	
Reporting group title	Lacosamide (300 mg)
Reporting group description:	
Single loading dose of intravenous (iv) lacosamide 300 mg dose followed by 6.5 days of oral lacosamide 150 mg twice daily	
Reporting group title	Lacosamide (400 mg)
Reporting group description:	
Single loading dose of intravenous (iv) lacosamide 400 mg followed by 6.5 days of oral lacosamide 200 mg twice daily	

Primary: Number of subjects with at least one adverse event during the treatment period (up to 7 days)

End point title	Number of subjects with at least one adverse event during the treatment period (up to 7 days)[1]
End point description:	
An Adverse Event (AE) is any untoward medical occurrence (eg, noxious or pathological changes) in a subject or clinical investigation subject compared with pre-existing conditions, that occurs during any period of a clinical trial including Pre-treatment, Run-In, Wash-Out, or Follow-Up Periods. An AE is defined as being independent of assumption of any causality (eg, to study or concomitant medication, primary or concomitant disease, or study design).	
End point type	Primary
End point timeframe:	
Treatment period (up to 7 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 of this open-label study was to evaluate the safety and tolerability of a single iv loading dose of lacosamide in subjects aged 16 to 60 years. The purpose of the study was to provide a description of the safety profile of a single iv loading dose of lacosamide across several safety variables. Therefore no statistical comparisons were applied in this safety study.

End point values	Lacosamide (200 mg)	Lacosamide (300 mg)	Lacosamide (400 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	50	25	
Units: subjects				
number	17	42	20	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects who withdrew from the trial due to an adverse event

End point title	Number of subjects who withdrew from the trial due to an

	adverse event[2]

End point description:

An Adverse Event (AE) is any untoward medical occurrence (eg, noxious or pathological changes) in a subject or clinical investigation subject compared with pre-existing conditions, that occurs during any period of a clinical trial including Pre-treatment, Run-In, Wash-Out, or Follow-Up Periods. An AE is defined as being independent of assumption of any causality (eg, to study or concomitant medication, primary or concomitant disease, or study design).

End point type	Primary

End point timeframe:

Entire trial period (up to 6 weeks), screening through safety follow-up period (2 weeks post last medication)

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: The primary objective of this open-label study was to evaluate the safety and tolerability of a single iv loading dose of lacosamide in subjects aged 16 to 60 years. The purpose of the study was to provide a description of the safety profile of a single iv loading dose of lacosamide across several safety variables. Therefore no statistical comparisons were applied in this safety study.

End point values	Lacosamide (200 mg)	Lacosamide (300 mg)	Lacosamide (400 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	50	25	
Units: subjects				
number	0	3	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with at least one adverse event with an onset within 4 hours of start of infusion

End point title	Number of subjects with at least one adverse event with an onset within 4 hours of start of infusion

End point description:

An Adverse Event (AE) is any untoward medical occurrence (eg, noxious or pathological changes) in a subject or clinical investigation subject compared with pre-existing conditions, that occurs during any period of a clinical trial including Pre-treatment, Run-In, Wash-Out, or Follow-Up Periods. An AE is defined as being independent of assumption of any causality (eg, to study or concomitant medication, primary or concomitant disease, or study design).

End point type	Secondary

End point timeframe:

0-4 hours post start of the infusion

End point values	Lacosamide (200 mg)	Lacosamide (300 mg)	Lacosamide (400 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	50	25	
Units: subjects				
number	5	24	16	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: up to 7 days	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	9.1
Reporting groups	
Reporting group title	Lacosamide (200 mg)
Reporting group description: Single loading dose of intravenous (iv) lacosamide 200 mg followed by 6.5 days of oral lacosamide 100 mg twice daily	
Reporting group title	Lacosamide (400 mg)
Reporting group description: Single loading dose of intravenous (iv) lacosamide 400 mg followed by 6.5 days of oral lacosamide 200 mg twice daily	
Reporting group title	Lacosamide (300 mg)
Reporting group description: Single loading dose of intravenous (iv) lacosamide 300 mg dose followed by 6.5 days of oral lacosamide 150 mg twice daily	

Serious adverse events	Lacosamide (200 mg)	Lacosamide (400 mg)	Lacosamide (300 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)	1 / 25 (4.00%)	0 / 50 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 25 (0.00%)	1 / 25 (4.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Lacosamide (200 mg)	Lacosamide (400 mg)	Lacosamide (300 mg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 25 (28.00%)	20 / 25 (80.00%)	37 / 50 (74.00%)
Nervous system disorders			

Dizziness			
subjects affected / exposed	5 / 25 (20.00%)	15 / 25 (60.00%)	23 / 50 (46.00%)
occurrences (all)	6	19	27
Somnolence			
subjects affected / exposed	0 / 25 (0.00%)	9 / 25 (36.00%)	17 / 50 (34.00%)
occurrences (all)	0	9	18
Headache			
subjects affected / exposed	2 / 25 (8.00%)	4 / 25 (16.00%)	2 / 50 (4.00%)
occurrences (all)	2	4	2
Paraesthesia			
subjects affected / exposed	2 / 25 (8.00%)	1 / 25 (4.00%)	3 / 50 (6.00%)
occurrences (all)	2	4	3
Tremor			
subjects affected / exposed	0 / 25 (0.00%)	1 / 25 (4.00%)	3 / 50 (6.00%)
occurrences (all)	0	1	3
Hypoaesthesia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 25 (4.00%)	2 / 50 (4.00%)
occurrences (all)	0	1	2
Coordination abnormal			
subjects affected / exposed	0 / 25 (0.00%)	0 / 25 (0.00%)	3 / 50 (6.00%)
occurrences (all)	0	0	3
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	2 / 25 (8.00%)	0 / 25 (0.00%)	1 / 50 (2.00%)
occurrences (all)	2	0	1
Fatigue			
subjects affected / exposed	0 / 25 (0.00%)	3 / 25 (12.00%)	9 / 50 (18.00%)
occurrences (all)	0	3	9
Chest pain			
subjects affected / exposed	0 / 25 (0.00%)	2 / 25 (8.00%)	0 / 50 (0.00%)
occurrences (all)	0	2	0
Feeling Drunk			
subjects affected / exposed	0 / 25 (0.00%)	0 / 25 (0.00%)	2 / 50 (4.00%)
occurrences (all)	0	0	2
Eye disorders			

Diplopia			
subjects affected / exposed	1 / 25 (4.00%)	5 / 25 (20.00%)	3 / 50 (6.00%)
occurrences (all)	1	6	3
Vision blurred			
subjects affected / exposed	0 / 25 (0.00%)	3 / 25 (12.00%)	2 / 50 (4.00%)
occurrences (all)	0	3	2
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 25 (0.00%)	6 / 25 (24.00%)	8 / 50 (16.00%)
occurrences (all)	0	8	8
Dry mouth			
subjects affected / exposed	0 / 25 (0.00%)	3 / 25 (12.00%)	3 / 50 (6.00%)
occurrences (all)	0	3	3
Paraesthesia oral			
subjects affected / exposed	1 / 25 (4.00%)	2 / 25 (8.00%)	2 / 50 (4.00%)
occurrences (all)	1	2	2
Hypoaesthesia oral			
subjects affected / exposed	0 / 25 (0.00%)	2 / 25 (8.00%)	3 / 50 (6.00%)
occurrences (all)	0	2	5
Vomiting			
subjects affected / exposed	0 / 25 (0.00%)	3 / 25 (12.00%)	2 / 50 (4.00%)
occurrences (all)	0	3	2
Diarrhoea			
subjects affected / exposed	0 / 25 (0.00%)	0 / 25 (0.00%)	4 / 50 (8.00%)
occurrences (all)	0	0	4
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 25 (0.00%)	2 / 25 (8.00%)	0 / 50 (0.00%)
occurrences (all)	0	2	0
Pruritus			
subjects affected / exposed	0 / 25 (0.00%)	1 / 25 (4.00%)	3 / 50 (6.00%)
occurrences (all)	0	1	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 October 2008	• Administrative changes including contact and title information for the Associate Clinical Program Director, the Senior Clinical Project Manager, the Clinical Trial Biostatistician, and the Associate Medical Director were incorporated in the protocol • Current information on the Central Laboratory Services, Central Electrocardiogram Services, and Central Bioanalytical Services were included in the protocol • Current information on the members of the DMC was incorporated • Text was added to permit subjects withdrawing from the LCM 300 mg group or the LCM 400 mg group, due to lack of tolerability to enter the open-label extension study at a dose as low as 100 mg/day • The exclusion criteria for heart rate and diastolic blood pressure were revised • The plasma sample collection for LCM determination at the Early Withdrawal Visit was added to Section 6.1 of the protocol and in the Schedule of Study Procedures footnote • Reference to pharmacogenomic analysis was removed from the protocol • A urine drug screen at Visit 1 was not performed. All reference to the urine drug screen was removed from the protocol • Clinical protocol text was modified to provide a realistic timeframe for ECG measurement during the iv LCM infusion which allowed for any possible future alterations by the DMC to the initial protocol-specified infusion duration of 15 minutes • Clinical protocol text was modified to provide a more realistic and acceptable timeframe for PK plasma sample collection for clinical site personnel • A window period of +3 days for Visit 3/Day 8 for all LCM dose groups was added to the protocol and AE reporting was added to the LCM 300 mg group and the LCM 400 mg group under Unscheduled Visit in the Schedule of Study Procedures • Information that the brief physical examination was to be performed after dosing was added to Section 5.4 of the protocol for consistency within the protocol

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported