Clinical trial results:
An Open-Label, Long-Term, Follow-Up Study To Determine The Safety, Tolerability, and Efficacy of Rotigotine Transdermal System As Monotherapy in Adolescents with Restless Legs Syndrome

Summary

EudraCT number	2016-000635-40
Trial protocol	Outside EU/EEA
Global end of trial date	07 December 2015

Results information

Result version number	v2 (current)
This version publication date	23 December 2016
First version publication date	19 June 2016
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	SP1005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01498120
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB BIOSCIENCES, Inc.
Sponsor organisation address	8010 Arco Corporate Drive, Raleigh, United States, NC 27617
Public contact	Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, 40789 +49 2173 4815 15, clinicaltrials@ucb.com
Scientific contact	Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, 40789 +49 2173 48 15 15, clinicaltrials@ucb.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 March 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the long-term safety and tolerability of rotigotine treatment in adolescents with idiopathic restless legs syndrome (RLS).

Protection of trial subjects:

During the conduct of the study all subjects were closely monitored.

Background therapy:

Background therapy was permitted as defined in the study protocol.

Evidence for comparator: -

Actual start date of recruitment	21 January 2012
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	United States: 14
Worldwide total number of subjects	14
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)	14
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study started to enroll subjects in USA in January 2012 and concluded in December 2015.

Pre-assignment

Screening details:

Participant Flow refers to the Safety Set (SS) which consists of all subjects who were randomized in this study and received at least 1 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	Rotigotine

Arm description:

Adolescent subjects who were previously administered rotigotine transdermal system (Neupro) in study SP1004 (NCT01495793), received the rotigotine transdermal patch in the following doses and sizes: 0.5mg/24h (2.5cm^2), 1mg/24h (5cm^2), 2mg/24h (10cm^2) and 3mg/24h (15cm^2).

Arm type	Experimental
Investigational medicinal product name	Neupro
Investigational medicinal product code	Rotigotine
Other name	
Pharmaceutical forms	Transdermal patch
Routes of administration	Transdermal use

Dosage and administration details:

Subjects received the patch according to the following schedules and doses: 0.5 mg/24 h, 1 mg/24 h, 2 mg/24 h and 3 mg/24 h.

Number of subjects in period 1	Rotigotine
Started	14
Completed	1
Not completed	13
Consent withdrawn by subject	5
AE, non-serious non-fatal	3
Unspecified	4
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Rotigotine

Reporting group description:

Adolescent subjects who were previously administered rotigotine transdermal system (Neupro) in study SP1004 (NCT01495793), received the rotigotine transdermal patch in the following doses and sizes: 0.5mg/24h (2.5cm^2), 1mg/24h (5cm^2), 2mg/24h (10cm^2) and 3mg/24h (15cm^2).

Reporting group values	Rotigotine	Total	
Number of subjects	14	14	
Age Categorical Units: Subjects			
Adolescents (12-17 years)	14	14	
Age Continuous Units: years			
arithmetic mean	15.4		
standard deviation	± 1.2	-	
Gender Categorical Units: Subjects			
Male	4	4	
Female	10	10	

End points

End points reporting groups

Reporting group title	Rotigotine

Reporting group description:

Adolescent subjects who were previously administered rotigotine transdermal system (Neupro) in study SP1004 (NCT01495793), received the rotigotine transdermal patch in the following doses and sizes: 0.5mg/24h (2.5cm^2), 1mg/24h (5cm^2), 2mg/24h (10cm^2) and 3mg/24h (15cm^2).

Subject analysis set title	Rotigotine (Safety Set)
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Set (SS) which consists of all subjects who were randomized in this study and received at least 1 dose of study medication. Adolescent subjects who were previously administered rotigotine transdermal system (Neupro) in study SP1004 (NCT01495793), received the rotigotine transdermal patch in the following doses and sizes: 0.5mg/24h (2.5cm^2), 1mg/24h (5cm^2), 2mg/24h (10cm^2) and 3mg/24h (15cm^2).

Primary: Number of subjects withdrawn Due to An Adverse Event (AE) From Visit 1 (Day 1) Through End of Study

End point title	Number of subjects withdrawn Due to An Adverse Event (AE) From Visit 1 (Day 1) Through End of Study[1]

End point description:

An Adverse Event is any untoward medical occurrences in a subject administered study treatment, whether or not these events are related to treatment.

End point type	Primary

End point timeframe:

Visit 1 (Day 1) through End of Study (approximately 2 years)

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 analysis of the primary endpoint being exploratory in nature, no statistical test was performed.

End point values	Rotigotine (Safety Set)			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: subjects				
Subjects withdrawn due to AEs	3			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with At Least One Adverse Event (AE) From Visit 1 (Day 1) to End of Study

End point title	Number of Subjects with At Least One Adverse Event (AE) From Visit 1 (Day 1) to End of Study[2]

End point description:

An Adverse Event is any untoward medical occurrences in a subject administered study treatment, whether or not these events are related to treatment.

End point type	Primary

End point timeframe:

From Visit 1 (Day 1) through End of Study (approximately 2 years)

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 analysis of the primary endpoint being exploratory in nature, no statistical test was performed.

End point values	Rotigotine (Safety Set)			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: subjects				
Subjects with AE(s)	10			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Adverse Events (AEs) were collected from Visit 1 (Week 0) until Safety Follow Up Visit (up to 25 months).

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Febrile disorders			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Non-cardiac chest pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Investigations			
Electrocardiogram QT corrected interval prolonged			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Blood sodium increased			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Toxicology laboratory analyses			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Drug screen positive			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Injury, poisoning and procedural			

complications			
Joint sprain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Road traffic accident			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Sunburn			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Sinus tachycardia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Syncope vasovagal			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	3		
Dizziness			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Sudden onset of sleep			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Gastrointestinal disorders			
Food poisoning			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	4 / 14 (28.57%)		
occurrences (all)	7		
Vomiting			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	6		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Dermal cyst			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Renal and urinary disorders			
Enuresis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Haematuria			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Infections and infestations			
Ear infection			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Streptococcal infection			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	3		
Sinusitis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 July 2011	The main purpose of this substantial amendment was to include the suicidality risk assessment (Columbia-Suicide Severity Rating Scale [C-SSRS]). In accordance with the recently issued US Food and Drug Administration (FDA) draft Guidance for Industry, which went into effect on 29 Oct 2010, the C-SSRS has been added to all ongoing and new interventional protocols in order to prospectively assess the occurrence of treatment-emergent suicidality in clinical studies of drug and biological products (FDA, Guidance for Industry, 2010). In addition, a list of Anticipated serious adverse events (SAEs) was included in this amendment in compliance with the US FDA guidance on safety reporting requirements for studies conducted under an open Investigational New Drug Application (effective 28 Mar 2011; FDA, Guidance for Industry and Investigators, 2010). The Beck Depression Inventory II and the Beck Anxiety Inventory were removed from the study assessments. Other changes included in this amendment were as follows: -Added the timeframe at which the efficacy and other variables were analyzed. -Added the version number of the Attention Deficit Hyperactivity Disorder (ADHD) Rating Scale. -Updated the storage requirements for the rotigotine patch. -Clarified the subject eligibility for SP1005 based on the dosing requirements from the previous rotigotine study (ie, SP1004). -Permitted the use of a topical anesthetic prior to the needle stick. -Added safety parameters (12-lead electrocardiogram [ECG] and laboratory tests) to be performed at the investigator's discretion at the Unscheduled Visit. -Removed reference to patch size from all sections, except in Section 7.1 of the Protocol, Description of investigational medicinal product. -Revised the preparation and handling of the blood and saliva samples and clearly identified the PK sampling visits. -Updated sponsor clinical project manager contact information. -Corrected typographic errors and made changes of an editorial nature.
02 May 2012	The main purpose of this substantial amendment was to ensure consistency between the protocol and the US FDA Pediatric Development Plan for the RLS indication in subjects 13 years and older. Since the subject's dosing was no longer dependent on body weight, the dosing schedules for each study period were revised. In addition, PK saliva sampling was removed from the study. Data from a completed PK study (RL0002) suggested that saliva concentrations of rotigotine could not be used as a surrogate for plasma concentrations of rotigotine. Other changes included in this amendment were as follows: -Updated the contact information for SAE reporting and procedures for reporting SAEs to be consistent with the current protocol template. -Updated the regulatory status of rotigotine for the treatment of RLS in adults in the US. -Clarified that the sample size may be increased if adolescent subjects with RLS were to roll over into this study from other future rotigotine studies. -Removed the requirement for PK blood samples to be centrifuged at a controlled temperature. -Corrected typographic errors and minor inconsistencies of an editorial nature.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported