Clinical trial results:
A Remote, 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	2021-003403-18
Trial protocol	Outside EU/EEA
Global end of trial date	07 April 2023

Results information

Result version number	v1 (current)
This version publication date	21 October 2023
First version publication date	21 October 2023

Trial information

Trial identification

Sponsor protocol code	RL0007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03992196
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Biopharma SRL
Sponsor organisation address	Allée de la Recherche 60, Brussels, Belgium, 1070
Public contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com
Scientific contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, 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	26 April 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 September 2022
Global end of trial reached?	Yes
Global end of trial date	07 April 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

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 participants were closely monitored.

Background therapy:

Background therapy as permitted in the protocol

Evidence for comparator:

Not applicable

Actual start date of recruitment	03 December 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Regulatory reason
Long term follow-up duration	13 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 10
Worldwide total number of subjects	10
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)	10
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in December 2019 and concluded prematurely in September 2022. Study participants entered this study from the parent rotigotine study in adolescents (SP1006) (NCT03728933).

Pre-assignment

Screening details:

10 participants were screened and considered enrolled, but only 9 participants were treated. The 10th participant was lost to follow-up prior dosing and no Adverse events were reported for this participant. Participant Flow refers to the Enrolled Set.

Period 1

Period 1 title	Enrollment
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	No Treatment

Arm description:

Participant signed the informed consent form but never received any study medication during the study.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Rotigotine Final Dose 2 mg/24 h

Arm description:

Participants in this arm were initiated on 1 milligram (mg)/24 hours (h) rotigotine and up-titrated to a maximum of 2 mg/24 h rotigotine and the same dose was continued throughout the 1 year Maintenance Period. Dose adjustment was allowed at any time during the Maintenance Period, based on the investigator’s assessment. At the end of the Maintenance Period, participants were down-titrated.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Rotigotine Final Dose 3 mg/24 h

Arm description:

Participants in this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 3 mg/24 h rotigotine and the same dose was continued throughout the 1 year Maintenance Period. Dose adjustment was allowed at any time during the Maintenance Period, based on the investigator’s assessment. At the end of the Maintenance Period, participants were down-titrated.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	No Treatment	Rotigotine Final Dose 2 mg/24 h	Rotigotine Final Dose 3 mg/24 h
Started	1	2	7
Completed	0	2	7
Not completed	1	0	0
lost to follow-up prior dosing	1	-	-

Period 2

Period 2 title	Treatment
Is this the baseline period?	Yes[1]
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Rotigotine Final Dose 2 mg/24 h

Arm description:

Participants in this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 2 mg/24 h rotigotine and the same dose was continued throughout the 1 year Maintenance Period. Dose adjustment was allowed at any time during the Maintenance Period, based on the investigator's assessment. At the end of the Maintenance Period, participants were down-titrated.

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

Dosage and administration details:

Participants in this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 2 mg/24 h rotigotine and the same dose was continued throughout the 1 year Maintenance Period. Dose adjustment was allowed at any time during the Maintenance Period, based on the investigator's assessment. At the end of the Maintenance Period, participants were down-titrated.

Arm title	Rotigotine Final Dose 3 mg/24 h

Arm description:

Participants in this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 3 mg/24 h rotigotine and the same dose was continued throughout the 1 year Maintenance Period. Dose adjustment was allowed at any time during the Maintenance Period, based on the investigator's assessment. At the end of the Maintenance Period, participants were down-titrated.

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

Dosage and administration details:

Participants in this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 3 mg/24 h rotigotine and the same dose was continued throughout the 1 year Maintenance Period. Dose adjustment was allowed at any time during the Maintenance Period, based on the investigator's assessment. At the end of the Maintenance Period, participants were down-titrated.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Data cannot be reported for a single participant due to data protection/data privacy.

Number of subjects in period 2[2]	Rotigotine Final Dose 2 mg/24 h	Rotigotine Final Dose 3 mg/24 h
Started	2	7
Completed	2	1
Not completed	0	6
Poor drug compliance withdrawn by team & sponsor	-	1
PI's decision due to IMP non-compliance	-	1
Withdrawal due to non-compliance	-	1
Withdrawal by parent/guardian	-	2
Protocol deviation	-	1

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 10 study participants were screened and enrolled, but only 9 participants were treated.

Baseline characteristics

Reporting groups	
Reporting group title	Rotigotine Final Dose 2 mg/24 h
Reporting group description:	
Participants in this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 2 mg/24 h rotigotine and the same dose was continued throughout the 1 year Maintenance Period. Dose adjustment was allowed at any time during the Maintenance Period, based on the investigator's assessment. At the end of the Maintenance Period, participants were down-titrated.	
Reporting group title	Rotigotine Final Dose 3 mg/24 h
Reporting group description:	
Participants in this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 3 mg/24 h rotigotine and the same dose was continued throughout the 1 year Maintenance Period. Dose adjustment was allowed at any time during the Maintenance Period, based on the investigator's assessment. At the end of the Maintenance Period, participants were down-titrated.	

Reporting group values	Rotigotine Final Dose 2 mg/24 h	Rotigotine Final Dose 3 mg/24 h	Total
Number of subjects	2	7	9
Age Categorical Units: Participants			
Adolescents (12-17 years)	2	7	9
Sex: Female, Male Units: Participants			
Female	2	2	4
Male	0	5	5

End points

End points reporting groups

Reporting group title	No Treatment
Reporting group description:	
Participant signed the informed consent form but never received any study medication during the study.	
Reporting group title	Rotigotine Final Dose 2 mg/24 h
Reporting group description:	
Participants in this arm were initiated on 1 milligram (mg)/24 hours (h) rotigotine and up-titrated to a maximum of 2 mg/24 h rotigotine and the same dose was continued throughout the 1 year Maintenance Period. Dose adjustment was allowed at any time during the Maintenance Period, based on the investigator's assessment. At the end of the Maintenance Period, participants were down-titrated.	
Reporting group title	Rotigotine Final Dose 3 mg/24 h
Reporting group description:	
Participants in this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 3 mg/24 h rotigotine and the same dose was continued throughout the 1 year Maintenance Period. Dose adjustment was allowed at any time during the Maintenance Period, based on the investigator's assessment. At the end of the Maintenance Period, participants were down-titrated.	
Reporting group title	Rotigotine Final Dose 2 mg/24 h
Reporting group description:	
Participants in this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 2 mg/24 h rotigotine and the same dose was continued throughout the 1 year Maintenance Period. Dose adjustment was allowed at any time during the Maintenance Period, based on the investigator's assessment. At the end of the Maintenance Period, participants were down-titrated.	
Reporting group title	Rotigotine Final Dose 3 mg/24 h
Reporting group description:	
Participants in this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 3 mg/24 h rotigotine and the same dose was continued throughout the 1 year Maintenance Period. Dose adjustment was allowed at any time during the Maintenance Period, based on the investigator's assessment. At the end of the Maintenance Period, participants were down-titrated.	

Primary: Percentage of participants with treatment-emergent adverse events (TEAEs) leading to withdrawal of study medication

End point title	Percentage of participants with treatment-emergent adverse events (TEAEs) leading to withdrawal of study medication[1]
End point description:	
An AE is any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. TEAEs were defined as events that started during the Treatment Period or within 30 days following the end of the Treatment Period (ie, on or after the date of first patch application and within 30 days following the date of last patch removal + 1 day), or those events where the intensity worsened within this time frame. The Safety Set consisted of all participants who had at least one patch (rotigotine) applied.	
End point type	Primary
End point timeframe:	
From Baseline until the Safety Follow-Up Visit (up to 14 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: No formal statistical hypothesis testing was planned due to early stopping of this study. Results were summarized in tables as descriptive statistics only.

End point values	Rotigotine Final Dose 2 mg/24 h	Rotigotine Final Dose 3 mg/24 h		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	7		
Units: percentage of participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with treatment-emergent adverse events (TEAEs)

End point title	Percentage of participants with treatment-emergent adverse events (TEAEs)[2]

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. TEAEs were defined as events that started during the Treatment Period or within 30 days following the end of the Treatment Period (ie, on or after the date of first patch application and within 30 days following the date of last patch removal + 1 day), or those events where the intensity worsened within this time frame. The Safety Set consisted of all participants who had at least one patch (rotigotine) applied.

End point type	Primary

End point timeframe:

From Baseline until the Safety Follow-Up Visit (up to 14 Months)

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: No formal statistical hypothesis testing was planned due to early stopping of this study. Results were summarized in tables as descriptive statistics only.

End point values	Rotigotine Final Dose 2 mg/24 h	Rotigotine Final Dose 3 mg/24 h		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	7		
Units: percentage of participants				
number (not applicable)	100	85.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in Clinical Global Impressions (CGI) Item 1 at Visit 9

End point title	Changes from Baseline in Clinical Global Impressions (CGI) Item 1 at Visit 9

End point description:

The Clinical Global Impressions Item 1 (Severity of Illness) score ranges from 0 to 7 as follows: 0=not assessed, 1=normal, not ill at all, 2=borderline ill, 3=mildly ill, 4=moderately ill, 5=markedly ill,

6=severely ill, 7=among the most extremely ill. The CGI Item 1 was completed during an interview between the participant and the investigator or designee. A negative change from Baseline indicates improvement. The Safety Set consisted of all participants who had at least one patch (rotigotine) applied. Here, Number of Participants analyzed signifies those who were evaluable for this outcome measure. 99999 signifies that summary statistics are not reported for N<3 due to small sample size and participant identification issues.

End point type	Secondary

End point timeframe:

Visit 9 (Month 12), compared to Baseline (in SP1006)

End point values	Rotigotine Final Dose 2 mg/24 h	Rotigotine Final Dose 3 mg/24 h		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: score on a scale				
arithmetic mean (standard deviation)	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in Restless Legs-6 Rating Scales (RLS-6) at Visit 9

End point title	Changes from Baseline in Restless Legs-6 Rating Scales (RLS-6) at Visit 9

End point description:

The RLS-6 Rating Scales was designed to assess severity of RLS and consisted of 6 subscales. The subscales assessed severity of symptoms at the following times of the day/evening: falling asleep, during the night, during the day at rest, and during the day when engaged in daytime activities (not at rest). In addition, the subscales assessed satisfaction with sleep and severity of daytime tiredness/sleepiness. Scores for each of the 6 subscales ranged from 0 (completely satisfied) to 10 (completely dissatisfied). The change from baseline was derived for each of the subscales and reported in this outcome measure. A negative change from Baseline indicates improvement. The Safety Set consisted of all participants who had at least one patch (rotigotine) applied. Here, Number of Participants analyzed signifies those who were evaluable for this outcome measure. 99999 signifies that summary statistics are not reported for N<3 due to small sample size and participant identification issues.

End point type	Secondary

End point timeframe:

Visit 9 (Month 12), compared to Baseline (in SP1006)

End point values	Rotigotine Final Dose 2 mg/24 h	Rotigotine Final Dose 3 mg/24 h		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: score on a scale				
arithmetic mean (standard deviation)				
Satisfaction with sleep	99999 (± 99999)	99999 (± 99999)		
Severity: RLS symptoms at falling asleep	99999 (± 99999)	99999 (± 99999)		
Severity: RLS symptoms during the night	99999 (± 99999)	99999 (± 99999)		
Severity: RLS symptoms during the day - at rest	99999 (± 99999)	99999 (± 99999)		
Severity: RLS symptoms during the day-not at rest	99999 (± 99999)	99999 (± 99999)		
How tired or sleepy during the day	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in International Restless Legs Rating Scale (IRLS) sum score at Visit 9

End point title	Changes from Baseline in International Restless Legs Rating Scale (IRLS) sum score at Visit 9

End point description:

The IRLS consisted of 10 questions, each scored using a 5-point scale ranging from 0=not present to 4=very severe. The IRLS sum score was calculated by summing up the single scores of all applicable questions, i.e., the total sum score ranged from 0 (no RLS symptoms present) to 40 (maximum severity in all symptoms). A score between 31 and 40, indicates very severe RLS. A score between 21 and 30 indicates severe RLS. A score between 11 and 20 indicates moderate RLS. A score between 1 and 10 indicates mild RLS and a score of 0 means no RLS. A negative change from Baseline indicates improvement. The Safety Set consisted of all participants who had at least one patch (rotigotine) applied. Here, Number of Participants analyzed signifies those who were evaluable for this outcome measure. 99999 signifies that summary statistics are not reported for N<3 due to small sample size and participant identification issues.

End point type	Secondary

End point timeframe:

Visit 9 (Month 12), compared to Baseline (in SP1006)

End point values	Rotigotine Final Dose 2 mg/24 h	Rotigotine Final Dose 3 mg/24 h		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: score on a scale				
arithmetic mean (standard deviation)	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline until the Safety Follow-Up Visit (up to 14 Months)

Adverse event reporting additional description:

TEAEs: Events started during Treatment Period (TP) or within 30 days following end of TP(i.e.,on or after date of first patch application and within 30 days following date of last patch removal + 1 day),or events where intensity worsened within this time frame. AEs are presented for 9 treated participants in the Safety Set.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Rotigotine Final Dose 3 mg/24 h

Reporting group description:

Participants in this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 3 mg/24 h rotigotine and the same dose was continued throughout the 1 year Maintenance Period. Dose adjustment was allowed at any time during the Maintenance Period, based on the investigator's assessment. At the end of the Maintenance Period, participants were down-titrated.

Reporting group title	Rotigotine Final Dose 2 mg/24 h

Reporting group description:

Participants in this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 2 mg/24 h rotigotine and the same dose was continued throughout the 1 year Maintenance Period. Dose adjustment was allowed at any time during the Maintenance Period, based on the investigator's assessment. At the end of the Maintenance Period, participants were down-titrated.

Serious adverse events	Rotigotine Final Dose 3 mg/24 h	Rotigotine Final Dose 2 mg/24 h	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Rotigotine Final Dose 3 mg/24 h	Rotigotine Final Dose 2 mg/24 h	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)	2 / 2 (100.00%)	
Injury, poisoning and procedural complications			
Procedural dizziness			

subjects affected / exposed	0 / 7 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Application site rash			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Application site erythema			
subjects affected / exposed	2 / 7 (28.57%)	2 / 2 (100.00%)	
occurrences (all)	2	2	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 7 (42.86%)	0 / 2 (0.00%)	
occurrences (all)	5	0	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Rhinitis allergic			
subjects affected / exposed	0 / 7 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Skin irritation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	1 / 7 (14.29%)	1 / 2 (50.00%)	
occurrences (all)	1	1	
Dermatitis contact			

subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Rash papular			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	1 / 2 (50.00%)	
occurrences (all)	1	1	
COVID-19			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Ear infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Pharyngitis streptococcal			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Suspected COVID-19			
subjects affected / exposed	0 / 7 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	

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