



Clinical trial results:

A Remote, Double-Blind, Randomized, Placebo-Controlled Study of Rotigotine Transdermal System in Adolescent Subjects With Idiopathic Restless Legs Syndrome

Summary

EudraCT number	2018-001445-13
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	SP1006
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03728933
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	23 July 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 demonstrate the efficacy of rotigotine against placebo in adolescent subjects with idiopathic Restless Legs Syndrome (RLS) over a 12-week Maintenance Period.

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	20 December 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Regulatory reason
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 23
Worldwide total number of subjects	23
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)	23
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in December 2018 and concluded prematurely in July 2022.

Pre-assignment

Screening details:

The Participant Flow refers to the Randomized Set.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants randomized to this arm received placebo as a comparator matched to rotigotine during 3 week titration period and is continued throughout the 12-week Maintenance Period.

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

Dosage and administration details:

Participants received placebo as a comparator matched to rotigotine during 3 week titration period and is continued throughout the 12-week Maintenance Period.

Arm title	Rotigotine 2 mg/24h
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Arm description:

Participants randomized to this arm were initiated on 1 milligram (mg)/24 hours (h) rotigotine and up-titrated to a maximum of 2 mg/24 h rotigotine during 3 week titration period and the same dose is continued throughout the 12-week Maintenance Period.

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

Dosage and administration details:

Participants randomized to this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 2 mg/24 h rotigotine during 3 week titration period and the same dose is continued throughout the 12-week Maintenance Period.

Arm title	Rotigotine 3 mg/24h
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Arm description:

Participants randomized to this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 3 mg/24 h rotigotine during 3 week titration period and the same dose is continued throughout the 12-week Maintenance Period.

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

Dosage and administration details:

Participants randomized to this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 3 mg/24 h rotigotine during 3 week titration period and the same dose is continued throughout the 12-week Maintenance Period.

Number of subjects in period 1	Placebo	Rotigotine 2 mg/24h	Rotigotine 3 mg/24h
Started	8	8	7
Completed	5	7	6
Not completed	3	1	1
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	1	-	-
Withdrawal by Parent/Guardian	2	-	-
Lost to follow-up	-	1	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants randomized to this arm received placebo as a comparator matched to rotigotine during 3 week titration period and is continued throughout the 12-week Maintenance Period.	
Reporting group title	Rotigotine 2 mg/24h
Reporting group description:	
Participants randomized to this arm were initiated on 1 milligram (mg)/24 hours (h) rotigotine and up-titrated to a maximum of 2 mg/24 h rotigotine during 3 week titration period and the same dose is continued throughout the 12-week Maintenance Period.	
Reporting group title	Rotigotine 3 mg/24h
Reporting group description:	
Participants randomized to this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 3 mg/24 h rotigotine during 3 week titration period and the same dose is continued throughout the 12-week Maintenance Period.	

Reporting group values	Placebo	Rotigotine 2 mg/24h	Rotigotine 3 mg/24h
Number of subjects	8	8	7
Age Categorical			
Units: Subjects			
Adolescents (12-17 years)	8	8	7
Age Continuous			
Units: years			
arithmetic mean	15.4	16.1	15.6
standard deviation	± 1.3	± 1.1	± 1.0
Gender Categorical			
Units: Subjects			
Female	6	6	2
Male	2	2	5

Reporting group values	Total		
Number of subjects	23		
Age Categorical			
Units: Subjects			
Adolescents (12-17 years)	23		
Age Continuous			
Units: years			
arithmetic mean	-		
standard deviation			
Gender Categorical			
Units: Subjects			
Female	14		
Male	9		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Participants randomized to this arm received placebo as a comparator matched to rotigotine during 3 week titration period and is continued throughout the 12-week Maintenance Period.	
Reporting group title	Rotigotine 2 mg/24h
Reporting group description: Participants randomized to this arm were initiated on 1 milligram (mg)/24 hours (h) rotigotine and up-titrated to a maximum of 2 mg/24 h rotigotine during 3 week titration period and the same dose is continued throughout the 12-week Maintenance Period.	
Reporting group title	Rotigotine 3 mg/24h
Reporting group description: Participants randomized to this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 3 mg/24 h rotigotine during 3 week titration period and the same dose is continued throughout the 12-week Maintenance Period.	

Primary: Change from Baseline in Clinical Global Impressions (CGI) Item 1 to the end of the Maintenance Period

End point title	Change from Baseline in Clinical Global Impressions (CGI) Item 1 to the end of the Maintenance Period ^[1]
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 FAS consisted of all participants from the Safety Set who had a valid IRLS score and a valid CGI Item 1 score at Baseline and a valid post-Baseline IRLS score and a valid post-Baseline CGI Item 1 score. Here, Number of Subjects analyzed signifies those who were evaluable for this endpoint.	
End point type	Primary
End point timeframe: From Baseline to the end of the Maintenance Period (Day 106)	

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	Placebo	Rotigotine 2 mg/24h	Rotigotine 3 mg/24h	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	7	5	
Units: score on a scale				
arithmetic mean (standard deviation)	-1.0 (± 1.4)	-1.7 (± 1.1)	-0.8 (± 0.8)	

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline to the end of the Maintenance Period in

International Restless Legs Rating Scale (IRLS) sum score

End point title	Change from Baseline to the end of the Maintenance Period in International Restless Legs Rating Scale (IRLS) sum score ^[2]
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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 Full Analysis Set (FAS) consisted of all participants from the Safety Set who had a valid IRLS score and a valid clinical global impressions (CGI) Item 1 score at Baseline and a valid post-Baseline IRLS score and a valid post-Baseline CGI Item 1 score. Here, Number of Subjects analyzed signifies those who were evaluable for this endpoint.

End point type	Primary
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End point timeframe:

From Baseline to the end of the Maintenance Period (Day 106)

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	Placebo	Rotigotine 2 mg/24h	Rotigotine 3 mg/24h	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	7	5	
Units: score on a scale				
arithmetic mean (standard deviation)	-8.2 (± 6.8)	-14.0 (± 8.2)	-6.4 (± 5.8)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of participants with treatment-emergent adverse events (TEAEs) leading to withdrawals ^[3]
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End point description:

TEAEs were defined as events that started during the Treatment Period or within 30 days following the end of the Treatment Period (i.e., 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 from the RS who had at least one patch (rotigotine or placebo) applied.

End point type	Primary
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End point timeframe:

From Baseline to Safety Follow-Up (up to Week 20)

Notes:

[3] - 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	Placebo	Rotigotine 2 mg/24h	Rotigotine 3 mg/24h	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	8	7	
Units: percentage of participants				
number (not applicable)	12.5	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) ^[4]
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End point description:

TEAEs were defined as events that started during the Treatment Period or within 30 days following the end of the Treatment Period (i.e., 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 from the Randomized Set (RS) who had at least one patch (rotigotine or placebo) applied.

End point type	Primary
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End point timeframe:

From Baseline to Safety Follow-Up (up to Week 20)

Notes:

[4] - 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	Placebo	Rotigotine 2 mg/24h	Rotigotine 3 mg/24h	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	8	7	
Units: percentage of participants				
number (not applicable)	87.5	87.5	71.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Restless Legs-6 Rating Scales (RLS-6) to the end of the Maintenance Period

End point title	Change from Baseline in Restless Legs-6 Rating Scales (RLS-6) to the end of the Maintenance Period
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End point description:

The RLS-6 Rating Scales was designed to assess the 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. 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 endpoint. A

negative change from Baseline indicates improvement. The FAS consisted of all participants from the Safety Set who had a valid IRLS score and a valid CGI Item 1 score at Baseline and a valid post-Baseline IRLS score and a valid post-Baseline CGI Item 1 score. Here, Number of Subjects analyzed signifies those who were evaluable for this endpoint.

End point type	Secondary
End point timeframe:	
From Baseline to the end of the Maintenance Period (Day 106)	

End point values	Placebo	Rotigotine 2 mg/24h	Rotigotine 3 mg/24h	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	7	5	
Units: score on a scale				
arithmetic mean (standard deviation)				
Satisfaction with sleep	-1.8 (± 4.1)	-4.7 (± 2.3)	-2.0 (± 2.8)	
Severity: RLS symptoms at falling asleep	-2.8 (± 3.6)	-5.6 (± 1.6)	-2.8 (± 1.8)	
Severity: RLS symptoms during the night	-1.0 (± 2.5)	-2.9 (± 3.0)	-2.4 (± 2.2)	
Severity: RLS symptoms during the day - at rest	-1.4 (± 1.3)	-3.6 (± 3.5)	-2.4 (± 2.6)	
Severity: RLS symptoms during the day-not at rest	-3.8 (± 1.9)	-4.3 (± 3.5)	-0.4 (± 1.1)	
How tired or sleepy during the day	-3.0 (± 2.8)	-5.6 (± 2.1)	-3.0 (± 1.9)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline to Safety Follow-Up (up to Week 20)

Adverse event reporting additional description:

TEAEs were defined as events that started during Treatment Period or within 30 days following the end of Treatment Period (i.e., 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 intensity worsened within this time frame. TEAEs were analyzed for Safety Set.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Participants randomized to this arm received placebo as a comparator matched to rotigotine during 3 week titration period and is continued throughout the 12-week Maintenance Period.

Reporting group title	Rotigotine 3 mg/24h
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Reporting group description:

Participants randomized to this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 3 mg/24 h rotigotine during 3 week titration period and the same dose is continued throughout the 12-week Maintenance Period.

Reporting group title	Rotigotine 2 mg/24h
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Reporting group description:

Participants randomized to this arm were initiated on 1 mg/24 h rotigotine and up-titrated to a maximum of 2 mg/24 h rotigotine during 3 week titration period and the same dose is continued throughout the 12-week Maintenance Period.

Serious adverse events	Placebo	Rotigotine 3 mg/24h	Rotigotine 2 mg/24h
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	0 / 8 (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	Placebo	Rotigotine 3 mg/24h	Rotigotine 2 mg/24h
Total subjects affected by non-serious adverse events subjects affected / exposed	7 / 8 (87.50%)	5 / 7 (71.43%)	7 / 8 (87.50%)
Surgical and medical procedures Wisdom teeth removal subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	1 / 8 (12.50%) 1
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Application site pain subjects affected / exposed occurrences (all) Application site irritation subjects affected / exposed occurrences (all) Application site pruritus subjects affected / exposed occurrences (all) Application site erythema subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 2 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 1 / 8 (12.50%) 1 1 / 8 (12.50%) 2	0 / 7 (0.00%) 0 0 / 7 (0.00%) 0 0 / 7 (0.00%) 1 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1	0 / 8 (0.00%) 0 1 / 8 (12.50%) 1 1 / 8 (12.50%) 3 4 / 8 (50.00%) 5
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 7 (14.29%) 1	0 / 8 (0.00%) 0
Reproductive system and breast disorders Amenorrhoea subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			

Upper-airway cough syndrome subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 7 (14.29%) 1	0 / 8 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Attention deficit hyperactivity disorder subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	1 / 8 (12.50%) 1
Investigations			
Serum ferritin decreased subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Transferrin saturation decreased subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Thyroid function test abnormal subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Injury, poisoning and procedural complications			
Wound subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	1 / 8 (12.50%) 1
Skin abrasion subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 7 (14.29%) 1	0 / 8 (0.00%) 0
Nervous system disorders			
Migraine subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 7 (14.29%) 1	0 / 8 (0.00%) 0
Dizziness			

subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2	1 / 7 (14.29%) 1	0 / 8 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 7 (14.29%) 4	1 / 8 (12.50%) 1
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Eye disorders Eye pain subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	1 / 8 (12.50%) 1
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 7 (0.00%) 0	2 / 8 (25.00%) 4
Vomiting subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 7 (0.00%) 0	2 / 8 (25.00%) 2
Diarrhoea subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	1 / 8 (12.50%) 2
Haemorrhoids subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 7 (14.29%) 1	0 / 8 (0.00%) 0
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0

Urticaria papular subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 7 (14.29%) 1	0 / 8 (0.00%) 0
Skin irritation subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	2 / 8 (25.00%) 3
Pruritus subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 7 (14.29%) 1	2 / 8 (25.00%) 2
Infections and infestations			
Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Gastroenteritis viral subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 7 (14.29%) 1	0 / 8 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	3 / 7 (42.86%) 3	0 / 8 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 March 2019	<p>The main purpose of Amendment 1 (dated 19 Mar 2019) was to update Exclusion Criterion with a change in the ferritin level at Visit 1/Screening from <50ng/mL to below the lower limit of normal. Other changes included in this amendment were as follows:</p> <ul style="list-style-type: none">• Sponsor contact information was updated.• Added headings for primary and other safety variables. Clarified that AEs are treatment emergent. Categorized occurrence of TEAEs and TEAEs leading to withdrawal as primary safety variables. The remaining safety variables were categorized as other.• Changed the eC-SSRS to the C-SSRS.• Addition of urine drug screen at Unscheduled Visits.• Clarified that the smartphone technology was to be used in combination with visits from mobile study personnel to subjects'/legal representatives' homes. Visits to local health care providers or Patient Service Centers were not conducted during this study.• Clarified that a serum pregnancy test was to be performed in females at Screening and urine pregnancy test at all other visits. A positive urine pregnancy test must have been confirmed by a serum pregnancy test.• Added a description of the Where's My Patch (WMP) app.• Removed BMI of <95th percentile for his or her age group, according to the Child and Teen BMI calculator as Inclusion Criterion.• Clarified that the washout period for supplemental iron is 1 month prior to Baseline in Exclusion Criterion.• Added secondary RLS (eg, due to renal insufficiency [uremia], iron deficiency, or rheumatoid arthritis as Exclusion Criterion.• Added a lifetime history of suicide attempts or suicidal ideation in the past 6 months as indicated by a positive response ("Yes") to either Question 4 or Question 5 of the C-SSRS at Screening as Exclusion Criterion.• Added taking a prohibited concomitant medication and the washout period as Exclusion Criterion.
19 March 2019	<p>Continuation of Amendment 1 rationale:</p> <ul style="list-style-type: none">• Clarified that subjects who have been screened but not randomized may be rescreened with the permission of the Study Physician or representative.• Added RBC indices (mean corpuscular hemoglobin; mean corpuscular hemoglobin concentration; mean cell volume; cell distribution width) to the laboratory measurements.• Typographic errors and changes of an editorial nature were made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported