



Clinical trial results:

A multi-center, randomized, double-blind, placebo-controlled, parallel group, polysomnography study to investigate safety and efficacy of the rotigotine transdermal patch in subjects with Restless Legs Syndrome and End-Stage Renal Disease requiring hemodialysis

Summary

EudraCT number	2011-003486-15
Trial protocol	DE FI AT IT
Global end of trial date	29 October 2013

Results information

Result version number	v1 (current)
This version publication date	30 June 2016
First version publication date	02 April 2015

Trial information

Trial identification

Sponsor protocol code	SP0934
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01537042
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB BIOSCIENCES GmbH
Sponsor organisation address	Alfred-Nobel-Strasse 10, Monheim, Germany, 40789
Public contact	Clinical Trial Registry & Results Disclosure, UCB BIOSCIENCES GmbH, 49 2173 48 1515, clinicaltrials@ucb.com
Scientific contact	Clinical Trial Registry & Results Disclosure, UCB BIOSCIENCES GmbH, 49 2173 48 1515, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 November 2013
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	29 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial is to demonstrate superiority of rotigotine against placebo in subjects with Restless Legs Syndrome (RLS) and End Stage Renal Disease (ESRD) requiring hemodialysis.

Protection of trial subjects:

The study was conducted under the auspices of an IRB/IEC, as defined in local regulations, ICH-GCP, and in accordance with the ethical principles that have their origin in the Declaration of Helsinki.

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.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	25 April 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	Germany: 5
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Finland: 2
Country: Number of subjects enrolled	United States: 18
Worldwide total number of subjects	30
EEA total number of subjects	12

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)	0
Adults (18-64 years)	23
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The recruitment for the SP0934 study began in April 2012. It concluded in October 2013. This was a multicenter study with subjects enrolled by 9 sites across Europe and 6 sites across the United States. The subject disposition consists of the Randomized Set (RS), which is all subjects randomized into SP0934.

Pre-assignment

Screening details:

The SP0934 study enrolled 49 patients. Out of the 49 patients, 19 were screen failures. Therefore, there were 30 patients randomized into the SP0934 study.

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	Rotigotine

Arm description:

Rotigotine Transdermal Patch

1 mg/24 h, 2 mg/24 h or 3 mg/24 h once daily depending on optimal dose; maximal dose is 3 mg/24 h.

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:

Transdermal patch; Dose: 1 mg/24 h, 2 mg/24 h or 3 mg/24 h once daily depending on optimal dose; maximal dose is 3 mg/24 h.

Subjects start with a Rotigotine dose of 1 mg/24 h for 1 week. The dose can be increased weekly during Up-Titration Period until either the optimal or the maximal dose of 3 mg/24 h has been reached.

Subjects will maintain the optimal/maximal dose during the 2-week Maintenance Period. Following the Maintenance Period, subjects will be de-escalated from their optimal dose by decreasing the dose by 1 mg/24 h every other day during Taper Period until complete withdrawal.

Arm title	Placebo
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Arm description:

Transdermal patch; Patches matching to active treatment patches in size and appearance.

Up to 3 weeks of Titration, 2 weeks of Maintenance, up to 4 days of Taper 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:

Transdermal patch; Patches matching to active treatment patches in size and appearance.

Up to 3 weeks of Titration, 2 weeks of Maintenance, up to 4 days of Taper Period.

Number of subjects in period 1	Rotigotine	Placebo
Started	20	10
Completed	15	10
Not completed	5	0
Other	1	-
AE, non-serious non-fatal	1	-
SAE, non-fatal	1	-
Lack of efficacy	1	-
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	Rotigotine
Reporting group description: Rotigotine Transdermal Patch	
1 mg/24 h, 2 mg/24 h or 3 mg/24 h once daily depending on optimal dose; maximal dose is 3 mg/24 h.	
Reporting group title	Placebo
Reporting group description: Transdermal patch; Patches matching to active treatment patches in size and appearance.	
Up to 3 weeks of Titration, 2 weeks of Maintenance, up to 4 days of Taper Period.	

Reporting group values	Rotigotine	Placebo	Total
Number of subjects	20	10	30
Age categorical			
The baseline analysis population consisted of the Safety Set (SS), which is all subjects who were randomized and had at least 1 patch applied during the Treatment Period.			
Units: Subjects			
Adults (18-64 years)	15	8	23
From 65-84 years	5	2	7
Age continuous			
The baseline analysis population consisted of the Safety Set (SS), which is all subjects who were randomized and had at least 1 patch applied during the Treatment Period.			
Units: years			
arithmetic mean	50.7	57.2	
standard deviation	± 16.3	± 12.6	-
Gender categorical			
The baseline analysis population consisted of the Safety Set (SS), which is all subjects who were randomized and had at least 1 patch applied during the Treatment Period.			
Units: Subjects			
Female	7	3	10
Male	13	7	20
Race Group			
The baseline analysis population consisted of the Safety Set (SS), which is all subjects who were randomized and had at least 1 patch applied during the Treatment Period.			
Units: Subjects			
American Indian/ Alaska Native	0	0	0
Asian	0	0	0
Black	6	2	8
Native Hawaiian or Other Pacific Islander	0	0	0
White	13	4	17
Other/mixed	0	1	1
Missing	1	3	4
Ethnicity			
The baseline analysis population consisted of the Safety Set (SS), which is all subjects who were randomized and had at least 1 patch applied during the Treatment Period.			
Units: Subjects			
Hispanic or Latino	3	2	5
Not Hispanic or Latino	16	5	21

Missing	1	3	4
Region			
The baseline analysis population consisted of the Safety Set (SS), which is all subjects who were randomized and had at least 1 patch applied during the Treatment Period.			
Units: Subjects			
US	12	6	18
EU	8	4	12
Weight			
The baseline analysis population consisted of the Safety Set (SS), which is all subjects who were randomized and had at least 1 patch applied during the Treatment Period.			
Units: kilogram(s)			
arithmetic mean	89.42	85.38	
standard deviation	± 15.34	± 20.99	-
Height			
The baseline analysis population consisted of the Safety Set (SS), which is all subjects who were randomized and had at least 1 patch applied during the Treatment Period.			
Units: Centimeters			
arithmetic mean	171.5	171.77	
standard deviation	± 11.99	± 8.59	-
BMI			
The baseline analysis population consisted of the Safety Set (SS), which is all subjects who were randomized and had at least 1 patch applied during the Treatment Period.			
Units: kilogram(s)/square meter			
arithmetic mean	30.405	28.85	
standard deviation	± 4.262	± 6.182	-

End points

End points reporting groups

Reporting group title	Rotigotine
Reporting group description: Rotigotine Transdermal Patch	
1 mg/24 h, 2 mg/24 h or 3 mg/24 h once daily depending on optimal dose; maximal dose is 3 mg/24 h.	
Reporting group title	Placebo
Reporting group description: Transdermal patch; Patches matching to active treatment patches in size and appearance.	
Up to 3 weeks of Titration, 2 weeks of Maintenance, up to 4 days of Taper Period.	

Primary: Ratio from Baseline to the end of the 2-week Maintenance Period in Periodic Limb Movement Index (PLMI)

End point title	Ratio from Baseline to the end of the 2-week Maintenance Period in Periodic Limb Movement Index (PLMI)
End point description: The PLMI is defined as Periodic Limb Movements (PLMs)/ total time in bed in hours. PLMs are measured by Polysomnography (PSG). The reduction of the PLMI is reflected in terms of the ratio from Baseline to the end of the Maintenance Period and was calculated as [PLMI at end of Maintenance Period (MP)] / [PLMI at Baseline]. A PLMI Ratio <1 indicates an improvement from Baseline to the end of the 2-week MP.	
End point type	Primary
End point timeframe: From Baseline over the Up-Titration Period (up to 3 Weeks) to the end of the 2-Week Maintenance Period.	

End point values	Rotigotine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: Ratio				
least squares mean (confidence interval 95%)	0.51 (0.33 to 0.8)	1.16 (0.68 to 1.99)		

Statistical analyses

Statistical analysis title	Primary Outcome Statistical Analysis
Comparison groups	Rotigotine v Placebo

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	= 0.0232
Method	ANCOVA
Parameter estimate	Treatment Ratio
Point estimate	0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	0.88

Notes:

[1] - An analysis of covariance (ANCOVA) was performed for the log-transformed PLMI ratio with treatment and region as factors and Baseline as a covariate.

Secondary: Change from Baseline in the Periodic Limb Movements Index (PLMI) to the end of the Maintenance Period

End point title	Change from Baseline in the Periodic Limb Movements Index (PLMI) to the end of the Maintenance Period
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End point description:

The PLMI is defined as Periodic Limb Movements (PLMs)/ total time in bed in hours. PLMs are measured by Polysomnography (PSG). A negative value in change from Baseline indicates an improvement from Baseline to the end of the Maintenance Period.

End point type	Secondary
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End point timeframe:

From Baseline over the Up-Titration Period (up to 3 Weeks) to the end of the 2-Week Maintenance Period.

End point values	Rotigotine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: movement/ hour				
arithmetic mean (standard deviation)	-23.7 (± 38.7)	10.3 (± 21)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the International Restless Legs Syndrome Study Group Rating Scale (IRLS) sum score to the end of the Maintenance Period

End point title	Change from Baseline in the International Restless Legs Syndrome Study Group Rating Scale (IRLS) sum score to the end of the Maintenance Period
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End point description:

The IRLS is a subject based scale that consists of 10 items to evaluate the severity of major RLS symptoms and the impact of the disease on subjects' functioning in daytime activities. Each of the 10 items is measured on a scale that ranges from 0 (not present) to 4 (severe). A sum score between 0 (no RLS symptoms present at all) and 40 (maximum severity in all symptoms) across all 10 items will be calculated.

A negative value in Change from Baseline indicates an improvement from Baseline in IRLS.

End point type	Secondary
End point timeframe:	
From Baseline over the Up-Titration Period (up to 3 Weeks) to the end of the 2-Week Maintenance Period.	

End point values	Rotigotine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: units on a scale				
arithmetic mean (standard deviation)	-15.9 (± 9.1)	-8.6 (± 7.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Restless Legs-6 (RLS-6) Rating Scale 1 to the end of the Maintenance Period

End point title	Change from Baseline in the Restless Legs-6 (RLS-6) Rating Scale 1 to the end of the Maintenance Period
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End point description:

The RLS-6 consists of six scales of which four scales are designed to assess severity of RLS and two scales cover sleep and daytime tiredness.

Scale 1 measures satisfaction with sleep during the last seven nights on an 11-point scale that ranges between 0 (completely satisfied) to 10 (completely dissatisfied). The ratings are given by the subjects. A negative value in Change from Baseline indicates an improvement from Baseline.

End point type	Secondary
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End point timeframe:

From Baseline over the Up-Titration Period (up to 3 Weeks) to the end of the 2-Week Maintenance Period

End point values	Rotigotine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: units on a scale				
arithmetic mean (standard deviation)	-2.8 (± 3.2)	-1.1 (± 3.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Restless Legs-6 (RLS-6) Rating Scale 2 to the end of the Maintenance Period

End point title	Change from Baseline in the Restless Legs-6 (RLS-6) Rating Scale 2 to the end of the Maintenance Period
End point description: The RLS-6 consists of six scales of which four scales are designed to assess severity of RLS and two scales cover sleep and daytime tiredness. Scale 2 measures the severity of RLS symptoms during the last 7 nights in the situation of falling asleep. This is measured on an 11-point scale that ranges between 0 (none) to 10 (very severe). The ratings are given by the subjects. A negative value in Change from Baseline indicates an improvement from Baseline.	
End point type	Secondary
End point timeframe: From Baseline over the Up-Titration Period (up to 3 Weeks) to the end of the 2-Week Maintenance Period	

End point values	Rotigotine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: units on a scale				
arithmetic mean (standard deviation)	-4.4 (± 2.9)	-2.8 (± 2.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Restless Legs-6 (RLS-6) Rating Scale 3 to the end of the Maintenance Period

End point title	Change from Baseline in the Restless Legs-6 (RLS-6) Rating Scale 3 to the end of the Maintenance Period
End point description: The RLS-6 consists of six scales of which four scales are designed to assess severity of RLS and two scales cover sleep and daytime tiredness. Scale 3 measures the severity of RLS symptoms during the last seven nights on an 11-point scale that ranges between 0 (none) to 10 (very severe). The ratings are given by the subjects. A negative value in Change from Baseline indicates an improvement from Baseline.	
End point type	Secondary
End point timeframe: From Baseline over the Up-Titration Period (up to 3 Weeks) to the end of the 2-Week Maintenance Period	

End point values	Rotigotine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: units on a scale				
arithmetic mean (standard deviation)	-4.7 (± 3.1)	-3.2 (± 2.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Restless Legs-6 (RLS-6) Rating Scale 4 to the end of the Maintenance Period

End point title	Change from Baseline in the Restless Legs-6 (RLS-6) Rating Scale 4 to the end of the Maintenance Period
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End point description:

The RLS-6 consists of six scales of which four scales are designed to assess severity of RLS and two scales cover sleep and daytime tiredness.

Scale 4 measures the severity of RLS symptoms during the last seven days at rest on an 11-point scale that ranges between 0 (none) to 10 (very severe). The ratings are given by the subjects.

A negative value in Change from Baseline indicates an improvement from Baseline.

End point type	Secondary
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End point timeframe:

From Baseline over the Up-Titration Period (up to 3 Weeks) to the end of the 2-Week Maintenance Period

End point values	Rotigotine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: units on a scale				
arithmetic mean (standard deviation)	-2.6 (± 2.2)	-1.6 (± 3.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Restless Legs-6 (RLS-6) Rating Scale 5 to the end of the Maintenance Period

End point title	Change from Baseline in the Restless Legs-6 (RLS-6) Rating Scale 5 to the end of the Maintenance Period
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End point description:

The RLS-6 consists of six scales of which four scales are designed to assess severity of RLS and two scales cover sleep and daytime tiredness.

Scale 5 measures the severity of RLS symptoms during the last seven days engaged in activities on an 11-point scale that ranges between 0 (none) to 10 (very severe). The ratings are given by the subjects.

A negative value in Change from Baseline indicates an improvement from Baseline.

End point type	Secondary
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End point timeframe:

From Baseline over the Up-Titration Period (up to 3 Weeks) to the end of the 2-Week Maintenance Period

End point values	Rotigotine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: units on a scale				
arithmetic mean (standard deviation)	-1.6 (± 2.7)	-1.6 (± 2.1)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Change from Baseline in the Restless Legs-6 (RLS-6) Rating Scale 6 to the end of the Maintenance Period
End point description: The RLS-6 consists of six scales of which four scales are designed to assess severity of RLS and two scales cover sleep and daytime tiredness. Scale 6 measures the severity of daytime tiredness/ sleepiness on an 11-point scale that ranges between 0 (not at all) to 10 (very severe). The ratings are given by the subjects. A negative value in Change from Baseline indicates an improvement from Baseline.	
End point type	Secondary
End point timeframe: From Baseline over the Up-Titration Period (up to 3 Weeks) to the end of the 2-Week Maintenance Period	

End point values	Rotigotine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: units on a scale				
arithmetic mean (standard deviation)	-3.4 (± 2.3)	-1.6 (± 2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Periodic Limb Movement during Sleep Arousal Index (PLMSAI) to the end of the Maintenance Period

End point title	Change from Baseline in the Periodic Limb Movement during Sleep Arousal Index (PLMSAI) to the end of the Maintenance Period
End point description: The Periodic Limb Movement during Sleep Arousal Index (PLMSAI) reflects the influence of the PLM on	

subject's sleep. Arousal is defined as sudden change in the Electroencephalogram (EEG) activity and the index illustrates to what degree the PLMs contribute to arousal from sleep.

A negative value in Change from Baseline indicates an improvement from Baseline.

End point type	Secondary
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End point timeframe:

From Baseline over the Up-Titration Period (up to 3 Weeks) to the end of the 2-Week Maintenance Period

End point values	Rotigotine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: movement per hour				
arithmetic mean (standard deviation)	-1.609 ($\pm$ 14.412)	4.634 ($\pm$ 7.162)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in sleep efficiency to the end of the Maintenance Period

End point title	Change from Baseline in sleep efficiency to the end of the Maintenance Period
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End point description:

Sleep stages and time spent in each sleep stage are determined from Electroencephalogram (EEG) readings. Sleep stage data will be used to calculate sleep efficiency. Sleep efficiency will be presented as percentages. Sleep efficiency is the percentage of time in bed spent asleep.

A positive value in Change from Baseline indicates an improvement from Baseline.

End point type	Secondary
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End point timeframe:

From Baseline over the Up-Titration Period (up to 3 Weeks) to the end of the 2-Week Maintenance Period

End point values	Rotigotine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: sleep time/ total time in bed				
arithmetic mean (standard deviation)	7.668 ($\pm$ 12.317)	-2.85 ($\pm$ 10.347)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Restless Legs-Quality of Life (RLS-QoL) total score to the end of the Maintenance Period

End point title	Change from Baseline in the Restless Legs-Quality of Life (RLS-QoL) total score to the end of the Maintenance Period
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End point description:

The RLS-QoL is a disease-specific questionnaire to evaluate quality of life. It consists of 12 items. A total score will be calculated from all of the 12 items. The overall sum score can be from 0 (highest QoL) to 60 (lowest QoL).

A negative value in Change from Baseline indicates an improvement from Baseline.

End point type	Secondary
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End point timeframe:

From Baseline over the Up-Titration Period (up to 3 Weeks) to the end of the 2-Week Maintenance Period

End point values	Rotigotine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	9		
Units: scores on a scale				
arithmetic mean (standard deviation)	-10.7 (± 10.9)	-10.2 (± 10.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Short-Form-36 (SF-36) item questionnaire Mental Component Summary (MCS) to the end of the Maintenance Period

End point title	Change from Baseline in the Short-Form-36 (SF-36) item questionnaire Mental Component Summary (MCS) to the end of the Maintenance Period
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End point description:

The SF-36 is a 36 item generic human research quality of life instrument that uses a recall period of 4 weeks. Items are grouped into 8 domains as follows: Physical Functioning (10 items), Role Physical (4 items), Bodily Pain (2 items), General Health (5 items), Vitality (4 items), Social Functioning (2 items), Role Emotional (3 items), Mental Health (5 items), and a further unscaled single item (question 2) for perceived stability or change in health (Health Transition) during the last year. The norm based scores (based on the US general population) were used for analysis. For the MCS, the lowest and highest possible scores are -9 and 82 (rounded).

The SF-36 domains (subscores) are scored so that a higher score indicates a better health state.

End point type	Secondary
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End point timeframe:

From Baseline over the Up-Titration Period (up to 3 Weeks) to the end of the 2-Week Maintenance Period

End point values	Rotigotine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	9		
Units: units on a scale				
arithmetic mean (standard deviation)	2.2 ($\pm$ 10.1)	6.4 ($\pm$ 6.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Short-Form-36 (SF-36) item questionnaire Physical Component Summary (PCS) to the end of the Maintenance Period

End point title	Change from Baseline in the Short-Form-36 (SF-36) item questionnaire Physical Component Summary (PCS) to the end of the Maintenance Period
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End point description:

The SF-36 is a 36 item generic human research quality of life instrument that uses a recall period of 4 weeks. Items are grouped into 8 domains as follows: Physical Functioning (10 items), Role Physical (4 items), Bodily Pain (2 items), General Health (5 items), Vitality (4 items), Social Functioning (2 items), Role Emotional (3 items), Mental Health (5 items), and a further unscaled single item (question 2) for perceived stability or change in health (Health Transition) during the last year. The norm-based scores (based on the US general population) were used for analysis. For the PCS, the lowest and highest possible scores are 1 and 81 (rounded).

The SF-36 domains (subscores) are scored so that a higher score indicates a better health state.

End point type	Secondary
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End point timeframe:

From Baseline over the Up-Titration Period (up to 3 Weeks) to the end of the 2-Week Maintenance Period

End point values	Rotigotine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	9		
Units: units on a scale				
arithmetic mean (standard deviation)	3.8 ($\pm$ 6.3)	-0.3 ($\pm$ 8.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Global Impressions (CGI) Item 1 score (Visit 2)

End point title	Change from Baseline in Clinical Global Impressions (CGI) Item 1 score (Visit 2)
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End point description:

The CGI Item 1 score measures the severity of illness on a scale that ranges from 0 (Not assessed) to 7 (Among the most extremely ill).

End point type	Secondary
End point timeframe:	
Visit 2 (Baseline)	

End point values	Rotigotine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: participants				
Not assessed	0	0		
Normal, not ill at all	0	0		
Borderline ill	0	0		
Mildly ill	0	0		
Moderately ill	3	3		
Markedly ill	5	9		
Severely ill	2	2		
Among the most extremely ill subjects	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Global Impressions (CGI) Item 1 score (Visit 6)

End point title	Change from Baseline in Clinical Global Impressions (CGI) Item 1 score (Visit 6)
End point description:	
The CGI Item 1 score measures the severity of illness on a scale that ranges from 0 (Not assessed) to 7 (Among the most extremely ill).	
End point type	Secondary
End point timeframe:	
Visit 6 (End of Maintenance Period)	

End point values	Rotigotine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: participants				
Not assessed	0	0		
Normal, not ill at all	5	1		
Borderline ill	4	1		
Mildly ill	3	3		
Moderately ill	1	5		
Markedly ill	2	0		
Severely ill	0	0		
Among the most extremely ill subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were recorded during the course of the SP0934 study, which began in April 2012 and concluded in October 2013.

Adverse event reporting additional description:

Adverse Events reporting refers to the Safety Set (SS). All subjects who are randomized and have at least 1 patch applied during the Treatment Period were included in the SS.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Rotigotine
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Reporting group description:

Adverse Event, Non-Serious Adverse Event and Serious Adverse Event reporting refers to the Safety Set (SS). All subjects who are randomized and have at least 1 patch applied during the Treatment Period were included in the SS.

Reporting group title	Placebo
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Reporting group description:

Adverse Event, Non-Serious Adverse Event and Serious Adverse Event reporting refers to the Safety Set (SS). All subjects who are randomized and have at least 1 patch applied during the Treatment Period were included in the SS.

Serious adverse events	Rotigotine	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 20 (15.00%)	1 / 10 (10.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastrointestinal infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Rotigotine	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 20 (60.00%)	4 / 10 (40.00%)	
Investigations			
Electrocardiogram PR prolongation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram ST segment abnormal			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			

Back injury subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 10 (0.00%) 0	
Dialysis device complication subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 10 (0.00%) 0	
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	0 / 10 (0.00%) 0	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 3	0 / 10 (0.00%) 0	
Paraesthesia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 10 (0.00%) 0	
Somnolence subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 10 (0.00%) 0	
General disorders and administration site conditions Application site pruritus subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 10 (0.00%) 0	
Fatigue subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 10 (10.00%) 1	
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 10 (10.00%) 1	
Eye disorders Eye haemorrhage subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 10 (0.00%) 0	
Gastrointestinal disorders			

Constipation subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 10 (0.00%) 0	
Diarrhoea subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	2 / 10 (20.00%) 2	
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 10 (0.00%) 0	
Nausea subjects affected / exposed occurrences (all)	4 / 20 (20.00%) 5	0 / 10 (0.00%) 0	
Vomiting subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3	0 / 10 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	0 / 10 (0.00%) 0	
Sleep apnoea syndrome subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 10 (0.00%) 0	
Psychiatric disorders Confusional state subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 10 (0.00%) 0	
Depression subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 10 (0.00%) 0	
Dysphoria subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 10 (0.00%) 0	
Musculoskeletal and connective tissue disorders Muscle spasms subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 10 (0.00%) 0	

Pain in extremity subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 10 (0.00%) 0	
Metabolism and nutrition disorders			
Anorexia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 10 (0.00%) 0	
Diabetic ketoacidosis subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 2	0 / 10 (0.00%) 0	
Fluid overload subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 3	0 / 10 (0.00%) 0	
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 2	0 / 10 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 October 2011	The protocol was amended in order to add the CGI Item 1 to Day 14 of the Maintenance Period (Visit 6) and to specify options for post-study treatment of RLS.
18 November 2011	The protocol was amended in order to clarify that subjects who switched to commercially available rotigotine (Neupro) or who entered the NPP would not be scheduled for a Safety Follow-Up Visit.
14 January 2013	The primary purpose of this protocol amendment was to revise the inclusion and exclusion criteria, based on the recommendations of the investigators, to make them less restrictive and to adapt them to the specific needs of the target patient population for the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

N/A

Notes: