

**Clinical trial results:**

An open-label clinical study to investigate pharmacokinetics (PK) of different doses (0.125 mg, 0.25 mg, 0.5 mg) of pramipexole administered once daily orally in pediatric patients who are individually optimized to stable pramipexole doses for the treatment of idiopathic Restless Legs Syndrome (RLS).

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2011-002774-23
Trial protocol	Outside EU/EEA
Global end of trial date	03 July 2007

Results information

Result version number	v2 (current)
This version publication date	02 July 2016
First version publication date	01 August 2015
Version creation reason	<ul style="list-style-type: none">• Correction of full data set Data correction due to system error in EudraCT

Trial information**Trial identification**

Sponsor protocol code	248.600
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02231918
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	173 Binger Strasse, Ingelheim am Rhein, Germany, 55216
Public contact	QRPE Processes and Systems Coordination Clinical Trial Information Disclosure, Boehringer Ingelheim, +1 8002430127, clintrriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination Clinical Trial Information Disclosure, Boehringer Ingelheim, +1 8002430127, clintrriage.rdg@boehringer-ingelheim.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-000041-PIP01-07
Does article 45 of REGULATION (EC) No	Yes

1901/2006 apply to this trial?	
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	11 September 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 July 2007
Global end of trial reached?	Yes
Global end of trial date	03 July 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the pharmacokinetics (PK) of pramipexole (PPX) after administration of a single dose orally (p.o.) in pediatric patients with the diagnosis of Restless Legs Syndrome (RLS).

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all patients as required.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 March 2006
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: 35
Worldwide total number of subjects	35
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)	20

Adolescents (12-17 years)	15
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

For the dose MIRAPEX (0.5 mg) , only 2 subjects (12 to <18 years) were recruited and it was not likely that patients for this dose will be fully recruited so the recruitment was stopped and terminated for this dose only.

Pre-assignment

Screening details:

All subjects were screened for eligibility to participate in the trial. Subjects attended specialist sites which would then ensure that they (the subjects) met all strictly implemented inclusion/exclusion criteria. Subjects were not to be provided the trial treatment if any one of the specific entry criteria were violated.

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This study was an open-label PK study.

Arms

Are arms mutually exclusive?	Yes
Arm title	PPX (MIRAPEX®, 0.125 mg)

Arm description:

Orally administered single daily maintenance dose of MIRAPEX® (0.125 mg) tablet per day in evening with 240 mL of water in a fasting state.

Arm type	Experimental
Investigational medicinal product name	MIRAPEX®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orally administered single daily maintenance dose of MIRAPEX® (0.125 mg) tablet per day in evening with 240 mL of water in a fasting state.

Arm title	PPX (MIRAPEX®, 0.25 mg)
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Arm description:

Orally administered single daily maintenance dose of MIRAPEX® (0.25 mg) tablet per day in evening with 240 mL of water in a fasting state.

Arm type	Experimental
Investigational medicinal product name	MIRAPEX®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orally administered single daily maintenance dose of MIRAPEX® (0.25 mg) tablet per day in evening with 240 mL of water in a fasting state.

Arm title	PPX (MIRAPEX®, 0.5 mg)
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Arm description:

Orally administered single daily maintenance dose of MIRAPEX® (0.5 mg) tablet per day in evening with

240 mL of water in a fasting state.

Arm type	Experimental
Investigational medicinal product name	MIRAPEX®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orally administered single daily maintenance dose of MIRAPEX® (0.5 mg) tablet per day in evening with 240 mL of water in a fasting state.

Number of subjects in period 1^[1]	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)
Started	9	15	2
Completed	9	14	1
Not completed	0	1	1
Consent withdrawn by subject	-	1	-
AE Other	-	-	1

Notes:

[1] - 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: Baseline characteristics are based on patients who were randomised after successfully completing the screening period and received at least one of the trial medication.

Baseline characteristics

Reporting groups

Reporting group title	PPX (MIRAPEX®, 0.125 mg)
Reporting group description:	Orally administered single daily maintenance dose of MIRAPEX® (0.125 mg) tablet per day in evening with 240 mL of water in a fasting state.
Reporting group title	PPX (MIRAPEX®, 0.25 mg)
Reporting group description:	Orally administered single daily maintenance dose of MIRAPEX® (0.25 mg) tablet per day in evening with 240 mL of water in a fasting state.
Reporting group title	PPX (MIRAPEX®, 0.5 mg)
Reporting group description:	Orally administered single daily maintenance dose of MIRAPEX® (0.5 mg) tablet per day in evening with 240 mL of water in a fasting state.

Reporting group values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)
Number of subjects	9	15	2
Age categorical Units: Subjects			

Age Continuous			
The safety analysis set was used.			
Safety analysis set : The safety population comprised all patients who provided informed consent and received at least one dose of study drug.			
Units: years			
arithmetic mean	10.6	11.4	15
standard deviation	± 4.3	± 3.4	± 0
Gender, Male/Female Units: participants			
Female	5	5	2
Male	4	10	0

Reporting group values	Total		
Number of subjects	26		
Age categorical Units: Subjects			

Age Continuous			
The safety analysis set was used.			
Safety analysis set : The safety population comprised all patients who provided informed consent and received at least one dose of study drug.			
Units: years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female Units: participants			
Female	12		
Male	14		

End points

End points reporting groups

Reporting group title	PPX (MIRAPEX®, 0.125 mg)
Reporting group description: Orally administered single daily maintenance dose of MIRAPEX® (0.125 mg) tablet per day in evening with 240 mL of water in a fasting state.	
Reporting group title	PPX (MIRAPEX®, 0.25 mg)
Reporting group description: Orally administered single daily maintenance dose of MIRAPEX® (0.25 mg) tablet per day in evening with 240 mL of water in a fasting state.	
Reporting group title	PPX (MIRAPEX®, 0.5 mg)
Reporting group description: Orally administered single daily maintenance dose of MIRAPEX® (0.5 mg) tablet per day in evening with 240 mL of water in a fasting state.	

Primary: C_{max,ss}

End point title	C _{max,ss} ^[1]
End point description: Maximum concentration of the pramipexole (PPX) in plasma at steady state over a uniform dosing interval (C _{max,ss}).	
Pharmacokinetic Set (PKS): All evaluable patients who received at least one dose of Pramipexole (PPX) between 0.125 and 0.5 mg were included in the PK analysis.	
Patients were stratified into two age groups for analysis: 6 to < 12 years and 12 to < 18 years 99999 (PPX (MIRAPEX®, 0.5 mg), 6 to < 12 years): No patients were recruited for this category. 99999 (PPX (MIRAPEX®, 0.5 mg), 12 to < 18 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the Geometric Mean (gMean) and Geometric Coefficient of Variation (gCV) are not calculated according to internal rules.	
End point type	Primary
End point timeframe: 0.25h before the drug administration on day 1 and 0.5 h, 1 h, 2 h, 3 h, 5 h, 7h, 12h and 24h after the last drug administration on day 1.	
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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.	

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[2]	15 ^[3]	2 ^[4]	
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
6 to <12 years (N=5, 9, 0)	0.633 (± 26.2)	1.13 (± 35.3)	99999 (± 99999)	
12 to <18 years(N=4, 6, 2))	0.396 (± 30)	0.677 (± 40.3)	99999 (± 99999)	

Notes:

[2] - Pharmacokinetic Set (PKS)

[3] - Pharmacokinetic Set (PKS)

[4] - Pharmacokinetic Set (PKS)

Statistical analyses

No statistical analyses for this end point

Primary: Cmin,ss

End point title | Cmin,ss^[5]

End point description:

Minimum measured concentration of the pramipexole in plasma at steady state over a uniform dosing interval (Cmin,ss).

Patients were stratified into two age groups for analysis: 6 to < 12 years and 12 to < 18 years
99999 (PPX (MIRAPEX®, 0.5 mg), 6 to < 12 years): No patients were recruited for this category.
99999 (PPX (MIRAPEX®, 0.5 mg), 12 to < 18 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the gMean and gCV are not calculated according to internal rules.

End point type | Primary

End point timeframe:

0.25 h before the drug administration on day 1 and 0.5 h, 1 h, 2 h, 3 h, 5 h, 7 h, 12 h and 24 h after the last drug administration on day 1.

Notes:

[5] - 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[6]	15 ^[7]	2 ^[8]	
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
6 to <12 years (N=5, 9, 0)	0.0872 (± 35.5)	0.136 (± 99.5)	99999 (± 99999)	
12 to <18 years(N=4, 6, 2)	0.0972 (± 37.5)	0.122 (± 53.8)	99999 (± 99999)	

Notes:

[6] - Pharmacokinetic Set (PKS)

[7] - Pharmacokinetic Set (PKS)

[8] - Pharmacokinetic Set (PKS)

Statistical analyses

No statistical analyses for this end point

Primary: Cpre,N

End point title | Cpre,N^[9]

End point description:

Predose concentration of the pramipexole in plasma at steady state immediately before administration of the next dose N (Cpre,N).

Patients were stratified into two age groups for analysis: 6 to < 12 years and 12 to < 18 years
99999 (PPX (MIRAPEX®, 0.5 mg), 6 to < 12 years): No patients were recruited for this category.
99999 (PPX (MIRAPEX®, 0.5 mg) & PPX (MIRAPEX®, 0.125 mg), 12 to < 18 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the gMean and gCV are not calculated according to internal rules.

End point type	Primary
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End point timeframe:

0.25 h before the drug administration on day 1 and 0.5 h, 1 h, 2 h, 3 h, 5 h, 7 h, 12 h and 24 h after the last drug administration on day 1.

Notes:

[9] - 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[10]	15 ^[11]	2 ^[12]	
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
6 to <12 years (N=4, 8, 0)	0.074 (± 17.3)	0.147 (± 75.3)	99999 (± 99999)	
12 to <18 years (N=1, 5, 1)	99999 (± 99999)	0.112 (± 60.7)	99999 (± 99999)	

Notes:

[10] - Pharmacokinetic Set (PKS)

4 subjects were not analysed as their data were not evaluable.

[11] - Pharmacokinetic Set (PKS)

2 subjects were not analysed as their data were not evaluable.

[12] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

Statistical analyses

No statistical analyses for this end point

Primary: Cavg

End point title	Cavg ^[13]
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End point description:

Average concentration of the pramipexole in plasma at steady state (Cavg).

Patients were stratified into two age groups for analysis: 6 to < 12 years and 12 to < 18 years
99999 (PPX (MIRAPEX®, 0.5 mg), 6 to < 12 years): No patients were recruited for this category.
99999 (PPX (MIRAPEX®, 0.5 mg), 12 to < 18 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the gMean and gCV are not calculated according to internal rules.

End point type	Primary
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End point timeframe:

0.25h before the drug administration on day 1 and 0.5 h, 1 h, 2 h, 3 h, 5 h, 7 h, 12 h and 24 h after the last drug administration on day 1.

Notes:

[13] - 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[14]	15 ^[15]	2 ^[16]	
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
6 to <12 years (N=5, 8, 0)	0.213 (± 27.4)	0.458 (± 42.8)	99999 (± 99999)	
12 to <18 years (N=4, 6, 1)	0.137 (± 21.3)	0.309 (± 35.2)	99999 (± 99999)	

Notes:

[14] - Pharmacokinetic Set (PKS)

[15] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

[16] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

Statistical analyses

No statistical analyses for this end point

Primary: tmax,ss

End point title | tmax,ss^[17]

End point description:

Time from dosing to maximum concentration at steady state (tmax,ss).

Patients were stratified into two age groups for analysis: 6 to < 12 years and 12 to < 18 years
99999 (PPX (MIRAPEX®, 0.5 mg), 6 to < 12 years): No patients were recruited for this category.
99999 (PPX (MIRAPEX®, 0.5 mg), 12 to < 18 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the median and range are not calculated according to internal rules.

End point type | Primary

End point timeframe:

0.25 h before the drug administration on day 1 and 0.5 h, 1 h, 2 h, 3 h, 5 h, 7 h, 12 h and 24 h after the last drug administration on day 1.

Notes:

[17] - 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[18]	15 ^[19]	2 ^[20]	
Units: hours				
median (full range (min-max))				
6 to <12 years (N=5, 9, 0)	2 (1 to 2)	2 (1 to 3)	99999 (99999 to 99999)	
12 to <18 years (N=4, 6, 2)	2 (0.5 to 2)	1.96 (0.5 to 5)	99999 (99999 to 99999)	

Notes:

[18] - Pharmacokinetic Set (PKS)

[19] - Pharmacokinetic Set (PKS)

[20] - Pharmacokinetic Set (PKS)

Statistical analyses

No statistical analyses for this end point

Primary: tmin,ss

End point title | tmin,ss^[21]

End point description:

Time from dosing to minimum concentration at steady state (tmin,ss).

Patients were stratified into two age groups for analysis: 6 to < 12 years and 12 to < 18 years
99999 (PPX (MIRAPEX®, 0.5 mg), 6 to < 12 years): No patients were recruited for this category.
99999 (PPX (MIRAPEX®, 0.5 mg), 12 to < 18 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the median and range are not calculated according to internal rules.

End point type | Primary

End point timeframe:

0.25 h before the drug administration on day 1 and 0.5 h, 1 h, 2 h, 3 h, 5 h, 7 h, 12 h and 24 h after the last drug administration on day 1.

Notes:

[21] - 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[22]	15 ^[23]	2 ^[24]	
Units: hours				
median (full range (min-max))				
6 to <12 years (N=5, 9, 0)	12 (0.5 to 24)	24 (0.25 to 24)	99999 (99999 to 99999)	
12 to <18 years (N=4, 6, 2)	6.25 (0.5 to 12)	23.9 (0.5 to 24)	99999 (99999 to 99999)	

Notes:

[22] - Pharmacokinetic Set (PKS)

[23] - Pharmacokinetic Set (PKS)

[24] - Pharmacokinetic Set (PKS)

Statistical analyses

No statistical analyses for this end point

Primary: AUC_{T,ss}

End point title | AUC_{T,ss}^[25]

End point description:

Area under the concentration-time curve of the pramipexole in plasma at steady state over a uniform dosing interval (AUC_{T,ss}).

Patients were stratified into two age groups for analysis: 6 to < 12 years and 12 to < 18 years

99999 (PPX (MIRAPEX®, 0.5 mg), 6 to < 12 years): No patients were recruited for this category.
 99999 (PPX (MIRAPEX®, 0.5 mg), 12 to < 18 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the gMean and gCV are not calculated according to internal rules.

End point type	Primary
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End point timeframe:

0.25 h before the drug administration on day 1 and 0.5 h, 1 h, 2 h, 3 h, 5 h, 7 h, 12 h and 24 h after the last drug administration on day 1.

Notes:

[25] - 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[26]	15 ^[27]	2 ^[28]	
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)				
6 to <12 years (N=5, 8, 0)	5.12 (± 27.4)	11 (± 42.8)	99999 (± 99999)	
12 to <18 years (N=4, 6, 1)	3.28 (± 21.3)	7.42 (± 35.2)	99999 (± 99999)	

Notes:

[26] - Pharmacokinetic Set (PKS)

[27] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

[28] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

Statistical analyses

No statistical analyses for this end point

Primary: λz,ss

End point title	λz,ss ^[29]
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End point description:

Terminal rate constant in plasma at steady state (λz,ss).

Patients were stratified into two age groups for analysis: 6 to < 12 years and 12 to < 18 years

99999 (PPX (MIRAPEX®, 0.5 mg), 6 to < 12 years): No patients were recruited for this category.

99999 (PPX (MIRAPEX®, 0.5 mg), 12 to < 18 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the gMean and gCV are not calculated according to internal rules.

End point type	Primary
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End point timeframe:

0.25h before the drug administration on day 1 and 0.5 h, 1 h, 2 h, 3 h, 5 h, 7 h, 12 h and 24 h after the last drug administration on day 1.

Notes:

[29] - 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[30]	15 ^[31]	2 ^[32]	
Units: 1/h				
geometric mean (geometric coefficient of variation)				
6 to <12 years (N=5, 8, 0)	0.132 (± 22.6)	0.107 (± 20.1)	99999 (± 99999)	
12 to <18 years (N=4, 6, 1)	0.113 (± 1.88)	0.0938 (± 25.4)	99999 (± 99999)	

Notes:

[30] - Pharmacokinetic Set (PKS)

[31] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

[32] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

Statistical analyses

No statistical analyses for this end point

Primary: t1/2,ss

End point title	t1/2,ss ^[33]
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End point description:

Terminal half-life of the pramipexole in plasma at steady state (t1/2,ss).

Patients were stratified into two age groups for analysis: 6 to < 12 years and 12 to < 18 years
99999 (PPX (MIRAPEX®, 0.5 mg), 6 to < 12 years): No patients were recruited for this category.
99999 (PPX (MIRAPEX®, 0.5 mg), 12 to < 18 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the gMean and gCV are not calculated according to internal rules.

End point type	Primary
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End point timeframe:

0.25 h before the drug administration on day 1 and 0.5 h, 1 h, 2 h, 3 h, 5 h, 7 h, 12 h and 24 h after the last drug administration on day 1.

Notes:

[33] - 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[34]	15 ^[35]	2 ^[36]	
Units: hours				
geometric mean (geometric coefficient of variation)				
6 to <12 years (N=5, 8, 0)	5.26 (± 22.6)	6.5 (± 20.1)	99999 (± 99999)	
12 to <18 years (N=4, 6, 1)	6.13 (± 1.88)	7.39 (± 25.4)	99999 (± 99999)	

Notes:

[34] - Pharmacokinetic Set (PKS)

[35] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

[36] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

Statistical analyses

No statistical analyses for this end point

Primary: MRT_{po,ss}

End point title MRT_{po,ss}^[37]

End point description:

Mean residence time of the pramipexole in the body at steady state (MRT_{po,ss}).

Patients were stratified into two age groups for analysis: 6 to < 12 years and 12 to < 18 years
99999 (PPX (MIRAPEX®, 0.5 mg), 6 to < 12 years): No patients were recruited for this category.
99999 (PPX (MIRAPEX®, 0.5 mg), 12 to < 18 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the gMean and gCV are not calculated according to internal rules.

End point type Primary

End point timeframe:

0.25 h before the drug administration on day 1 and 0.5 h, 1 h, 2 h, 3 h, 5 h, 7 h, 12 h and 24 h after the last drug administration on day 1.

Notes:

[37] - 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[38]	15 ^[39]	2 ^[40]	
Units: hours				
geometric mean (geometric coefficient of variation)				
6 to <12 years (N=5, 8, 0)	8.19 (± 13.1)	10.1 (± 19.5)	99999 (± 99999)	
12 to <18 years (N=4, 6, 1)	9.47 (± 5.3)	11.6 (± 23.3)	99999 (± 99999)	

Notes:

[38] - Pharmacokinetic Set (PKS)

[39] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

[40] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

Statistical analyses

No statistical analyses for this end point

Primary: CL/F_{ss}

End point title CL/F_{ss}^[41]

End point description:

Apparent clearance of the pramipexole in the plasma after extravascular administration at steady state; F = absolute bioavailability factor (CL/F,ss).

Patients were stratified into two age groups for analysis: 6 to < 12 years and 12 to < 18 years
99999 (PPX (MIRAPEX®, 0.5 mg), 6 to < 12 years): No patients were recruited for this category.
99999 (PPX (MIRAPEX®, 0.5 mg), 12 to < 18 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the gMean and gCV are not calculated according to internal rules.

End point type	Primary
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End point timeframe:

0.25 h before the drug administration on day 1 and 0.5 h, 1 h, 2 h, 3 h, 5 h, 7 h, 12 h and 24 h after the last drug administration on day 1.

Notes:

[41] - 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[42]	15 ^[43]	2 ^[44]	
Units: mL/min				
geometric mean (geometric coefficient of variation)				
6 to <12 years (N=5, 8, 0)	284 (± 27.4)	265 (± 42.8)	99999 (± 99999)	
12 to <18 years (N=4, 6, 1)	444 (± 21.3)	393 (± 35.2)	99999 (± 99999)	

Notes:

[42] - Pharmacokinetic Set (PKS)

[43] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

[44] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

Statistical analyses

No statistical analyses for this end point

Primary: Vz/F,ss

End point title	Vz/F,ss ^[45]
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End point description:

Apparent volume of distribution during the terminal phase λz following an extravascular dose at steady state (Vz/F,ss).

Patients were stratified into two age groups for analysis: 6 to < 12 years and 12 to < 18 years
99999 (PPX (MIRAPEX®, 0.5 mg), 6 to < 12 years): No patients were recruited for this category.
99999 (PPX (MIRAPEX®, 0.5 mg), 12 to < 18 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the gMean and gCV are not calculated according to internal rules.

End point type	Primary
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End point timeframe:

0.25 h before the drug administration on day 1 and 0.5 h, 1 h, 2 h, 3 h, 5 h, 7 h, 12 h and 24 h after the last drug administration on day 1.

Notes:

[45] - 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[46]	15 ^[47]	2 ^[48]	
Units: Litres				
geometric mean (geometric coefficient of variation)				
6 to <12 years (N=5, 8, 0)	129 (± 12.3)	149 (± 29.7)	99999 (± 99999)	
12 to <18 years (N=4, 6, 1)	236 (± 19.4)	251 (± 37.3)	99999 (± 99999)	

Notes:

[46] - Pharmacokinetic Set (PKS)

[47] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

[48] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

Statistical analyses

No statistical analyses for this end point

Primary: Ae 0-12,ss

End point title	Ae 0-12,ss ^[49]
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End point description:

Amount of pramipexole that is eliminated in urine at steady state over a time interval t1 to t2 (0-12h), (Ae 0-12,ss).

Patients were stratified into two age groups for analysis: 6 to < 12 years and 12 to < 18 years
For arm MIRAPEX® 0.5mg (6 to < 12 years): No patients were recruited for this category and for (12 to < 18 years): No subjects were analysed as the data were not evaluable.

End point type	Primary
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End point timeframe:

12 hours after last study drug administration on day 1

Notes:

[49] - 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[50]	15 ^[51]	2 ^[52]	
Units: ng				
geometric mean (geometric coefficient of variation)				
6 to <12 years (N=4, 6, 0)	50600 (± 14.6)	123000 (± 50.7)	99999 (± 99999)	
12 to <18 years (N=3, 6, 0)	55200 (± 41.5)	82300 (± 52.7)	99999 (± 99999)	

Notes:

[50] - Pharmacokinetic Set (PKS)

2 subjects were not analysed as their data were not evaluable.

[51] - Pharmacokinetic Set (PKS)

3 subjects were not analysed as their data were not evaluable.

[52] - No subjects were analysed as the data were not evaluable.

Statistical analyses

No statistical analyses for this end point

Primary: fe 0-12,ss

End point title fe 0-12,ss^[53]

End point description:

Fraction of administered drug excreted unchanged in urine at steady state over a time interval t1 to t2 (0-12h), (fe 0-12,ss).

Patients were stratified into two age groups for analysis: 6 to < 12 years and 12 to < 18 years

For arm MIRAPEX® 0.5mg (6 to <12 years): No patients were recruited for this category and for (12 to <18 years): No subjects were analysed as the data were not evaluable.

99999 (PPX (MIRAPEX®, 0.125 mg), 12 to <18 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the gMean and gCV are not calculated according to internal rules.

99999 (PPX (MIRAPEX®, 0.25 mg), 6 to <12 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the gMean and gCV are not calculated according to internal rules.

End point type Primary

End point timeframe:

12 hours after last study drug administration on day 1.

Notes:

[53] - 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[54]	15 ^[55]	2 ^[56]	
Units: % of pramipexole excreted				
geometric mean (geometric coefficient of variation)				
6 to <12 years (N=4, 2, 0)	58 (± 14.6)	99999 (± 99999)	99999 (± 99999)	
12 to <18 years (N=2, 5, 0)	99999 (± 99999)	42 (± 48.1)	99999 (± 99999)	

Notes:

[54] - Pharmacokinetic Set (PKS)

3 subjects were not analysed as their data were not evaluable.

[55] - Pharmacokinetic Set (PKS)

8 subjects were not analysed as their data were not evaluable.

[56] - No subjects were analysed as the data were not evaluable.

Statistical analyses

No statistical analyses for this end point

Primary: CLR 0-12,ss

End point title	CLR 0-12,ss ^[57]
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End point description:

Renal clearance of the pramipexole at steady state (CLR 0-12,ss).

Patients were stratified into two age groups for analysis: 6 to < 12 years and 12 to < 18 years

For arm PPX (MIRAPEX®, 0.5mg) , 6 to < 12 years): No patients were recruited for this category and for (12 to < 18 years): No subjects were analysed as the data were not evaluable.

99999 (PPX (MIRAPEX®, 0.125 mg), 12 to < 18 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the gMean and gCV are not calculated according to internal rules.

99999 (MIRAPEX® (0.25 mg), 6 to < 12 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the gMean and gCV are not calculated according to internal rules.

End point type	Primary
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End point timeframe:

12h after last study drug administration on day 1

Notes:

[57] - 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[58]	15 ^[59]	2 ^[60]	
Units: mL/min				
geometric mean (geometric coefficient of variation)				
6 to <12 years (N=4, 2, 0)	201 (± 34.1)	99999 (± 99999)	99999 (± 99999)	
12 to <18 years (N=2, 5, 0)	99999 (± 99999)	253 (± 34.1)	99999 (± 99999)	

Notes:

[58] - Pharmacokinetic Set (PKS)

3 subjects were not analysed as their data were not evaluable.

[59] - Pharmacokinetic Set (PKS)

8 subjects were not analysed as their data were not evaluable.

[60] - No subjects were analysed as the data were not evaluable.

Statistical analyses

No statistical analyses for this end point

Primary: PTF

End point title	PTF ^[61]
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End point description:

Peak-trough fluctuation (PTF) is defined as the difference between C_{max} and C_{min} divided by C_{avg} and multiplied with 100% at steady-state.

Patients were stratified into two age groups for analysis: 6 to < 12 years and 12 to < 18 years

99999 (PPX (MIRAPEX®, 0.5 mg), 6 to < 12 years): No patients were recruited for this category.

99999 (PPX (MIRAPEX®, 0.5 mg), 12 to < 18 years): The reliable estimation can only be performed when at least 2/3 of the data are available and thus the gMean and gCV are not calculated according to internal rules.

End point type	Primary
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End point timeframe:

0.25h before the drug administration on day 1 and 0.5 h, 1 h, 2 h, 3 h, 5 h, 7 h, 12 h and 24 h after the last drug administration on day 1.

Notes:

[61] - 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[62]	15 ^[63]	2 ^[64]	
Units: % of PTF				
geometric mean (geometric coefficient of variation)				
6 to <12 years (N=5, 8, 0)	250 (± 10.1)	209 (± 31.8)	99999 (± 99999)	
12 to <18 years (N=4, 6, 1)	216 (± 24)	168 (± 34.2)	99999 (± 99999)	

Notes:

[62] - Pharmacokinetic Set (PKS)

[63] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

[64] - Pharmacokinetic Set (PKS)

1 subject was not analysed as its data was not evaluable.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with drug related adverse events

End point title	Number of patients with drug related adverse events
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End point description:

Number of patients with adverse events due to study drug.

Safety Set: The safety population comprised all patients who provided informed consent and received at least one dose of study drug.

End point type	Secondary
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End point timeframe:

From first drug administration until 24 hours after last study drug administration, upto 48 days

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	15	2	
Units: Participants	1	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Vital Signs (Systolic and Diastolic Blood Pressure)

End point title	Vital Signs (Systolic and Diastolic Blood Pressure)
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End point description:

Vital signs (systolic and diastolic blood pressure (both supine and after standing for 1 minute)).

99999 (PPX (MIRAPEX®, 0.5 mg)): The data of only one patient is available and thus standard deviation is not calculable.

End point type	Secondary
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End point timeframe:

-0:15h (hours) pre-dose, and 0:30h, 1:00h, 2:00h, 3:00h, 5:00h, 7:00h, 12:00h, 24:00h post-dose

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[65]	15 ^[66]	2 ^[67]	
Units: mmHg				
arithmetic mean (standard deviation)				
Systolic blood pressure–supine(N= 9,15,2): -0:15h	109.33 (± 6.76)	109.2 (± 10.8)	117 (± 4.24)	
Systolic blood pressure–supine(N= 9,15,2): 0:30h	112.89 (± 13.9)	110.33 (± 14.07)	116 (± 4.24)	
Systolic blood pressure–supine(N= 9,15,2): 1:00h	113 (± 11.07)	108.07 (± 12.92)	105.5 (± 0.71)	
Systolic blood pressure-supine(N= 9,15,2): 2:00h	111 (± 7.43)	111.93 (± 13.79)	113 (± 9.9)	
Systolic blood pressure-supine(N= 9,15,1): 3:00h	106.89 (± 10.4)	110.53 (± 11.34)	113 (± 99999)	
Systolic blood pressure-supine(N= 9,15,1): 5:00h	105.11 (± 12.71)	108.8 (± 14.89)	104 (± 99999)	
Systolic blood pressure-supine(N= 9,14,1): 7:00h	108.44 (± 12.27)	109.86 (± 14.11)	108 (± 99999)	
Systolic blood pressure-supine(N= 9,14,1): 12:00h	107.56 (± 16.38)	106.93 (± 16.28)	109 (± 99999)	
Systolic blood pressure-supine(N= 9,14,1): 24:00h	109.22 (± 11.38)	112.21 (± 13.76)	120 (± 99999)	
Diastolic blood pressure-supine(N= 9,15,2): -0:15	66.67 (± 7.35)	65.73 (± 10.19)	76 (± 0)	
Diastolic blood pressure-supine(N= 9,15,2): 0:30	68.67 (± 8.93)	65.8 (± 12.62)	73 (± 2.83)	
Diastolic blood pressure-supine(N= 9,15,2): 1:00	69.33 (± 6.52)	65.73 (± 7.8)	64 (± 12.73)	
Diastolic blood pressure-supine(N= 9,15,2): 2:00	66 (± 8.23)	65.8 (± 8.76)	75 (± 8.49)	
Diastolic blood pressure-supine(N= 9,15,1): 3:00	66.78 (± 9.36)	65.4 (± 9.96)	75 (± 99999)	
Diastolic blood pressure-supine(N= 9,15,1): 5:00	64.22 (± 9.83)	63.87 (± 9.78)	70 (± 99999)	
Diastolic blood pressure-supine(N= 9,14,1): 7:00	67.56 (± 13.47)	62.43 (± 8.08)	67 (± 99999)	

Diastolic blood pressure-supine(N=9,14,1): 12:00	70 (± 12.03)	61 (± 9.12)	66 (± 99999)
Diastolic blood pressure-supine(N=9,14,1): 24:00	66.56 (± 6)	65.71 (± 7.61)	78 (± 99999)
Systolic blood pressure-standing(N=9,15,2): -0:15	109.89 (± 8.57)	113.93 (± 9.97)	122 (± 9.9)
Systolic blood pressure-standing(N=9,15,2): 0:30h	113.56 (± 13.62)	113.67 (± 13.69)	115.5 (± 6.36)
Systolic blood pressure-standing(N=9,15,2): 1:00h	110.11 (± 13.81)	110.07 (± 14.26)	125.5 (± 23.33)
Systolic blood pressure-standing(N=9,15,2): 2:00h	110.33 (± 8.76)	112.27 (± 12.26)	115 (± 2.83)
Systolic blood pressure-standing(N=9,15,1): 3:00h	110.11 (± 16.5)	113.07 (± 16.15)	108 (± 99999)
Systolic blood pressure-standing(N=9,14,1): 5:00h	110.22 (± 11.88)	111.93 (± 14.91)	115 (± 99999)
Systolic blood pressure-standing(N=9,13,1): 7:00h	109.11 (± 11.76)	103.85 (± 17.56)	65 (± 99999)
Systolic blood pressure-standing(N=9,14,1): 12:00h	108.22 (± 9.59)	107.14 (± 15.83)	100 (± 99999)
Systolic blood pressure-standing(N=9,14,1): 24:00h	113.89 (± 11.25)	115.5 (± 14.43)	102 (± 99999)
Diastolic blood pressure-standing(N=9,15,2): -0:15	68.11 (± 11.87)	71.2 (± 8.09)	86 (± 0)
Diastolic blood pressure-standing(N=9,15,2): 0:30h	70.11 (± 7.44)	69.2 (± 12.11)	80 (± 1.41)
Diastolic blood pressure-standing(N=9,15,2): 1:00h	69.22 (± 6.36)	72 (± 9.54)	91 (± 7.07)
Diastolic blood pressure-standing(N=9,15,2): 2:00h	71.11 (± 8.82)	73.13 (± 9.36)	86.5 (± 3.54)
Diastolic blood pressure-standing(N=9,15,1): 3:00h	72.67 (± 5.94)	71.47 (± 8.98)	79 (± 99999)
Diastolic blood pressure-standing(N=9,14,1): 5:00h	74 (± 10.82)	70.57 (± 9.2)	98 (± 99999)
Diastolic blood pressure-standing(N=9,13,1): 7:00h	72 (± 13.01)	66.69 (± 10.9)	48 (± 99999)
Diastolic blood pressure-standing(N=9,14,1):12:00h	74.33 (± 11.19)	70.07 (± 10.51)	62 (± 99999)
Diastolic blood pressure-standing(N=9,14,1):24:00h	73.11 (± 8.13)	73.57 (± 9.62)	84 (± 99999)

Notes:

[65] - Safety Set

[66] - Safety Set

[67] - Safety Set

Statistical analyses

No statistical analyses for this end point

Secondary: Vital Signs (Pulse Rate)

End point title	Vital Signs (Pulse Rate)
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End point description:

Vital signs (Pulse rate (both supine and after standing for 1 minute)).

99999 (PPX (MIRAPEX®, 0.5 mg)): The data of only one patient is available and thus standard deviation is not calculable.

End point type	Secondary
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End point timeframe:

-0:15h(hours) pre-dose, and 0:30h, 1:00h, 2:00h, 3:00h, 5:00h, 7:00h, 12:00h, 24:00h

End point values	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.25 mg)	PPX (MIRAPEX®, 0.5 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[68]	15 ^[69]	2 ^[70]	
Units: bpm				
arithmetic mean (standard deviation)				
Pulse rate–supine(N= 9,15,2): –0:15h	82.4 (± 18.6)	73.3 (± 6.8)	75.5 (± 24.7)	
Pulse rate–supine(N= 9,15,2): 0:30h	76.7 (± 17.5)	78 (± 11.7)	92 (± 32.5)	
Pulse rate–supine(N= 9,15,2): 1:00h	82.7 (± 22.2)	75.2 (± 6.8)	87 (± 36.8)	
Pulse rate–supine(N= 9,15,2): 2:00h	85.4 (± 19.6)	77.9 (± 8)	94.5 (± 26.2)	
Pulse rate–supine(N= 9,15,1): 3:00h	89.3 (± 19.1)	79.9 (± 13.6)	72 (± 99999)	
Pulse rate–supine(N= 9,15,1): 5:00h	82.7 (± 16)	75.9 (± 6.9)	77 (± 99999)	
Pulse rate–supine(N= 9,14,1): 7:00h	88.1 (± 18.1)	72 (± 9)	78 (± 99999)	
Pulse rate–supine(N= 9,14,1): 12:00h	77.8 (± 15.2)	68.6 (± 6.2)	69 (± 99999)	
Pulse rate–supine(N= 9,14,1): 24:00h	77.9 (± 13.6)	77.6 (± 8.5)	77 (± 99999)	
Pulse rate– standing(N=9,15,2): –0:15h	90.8 (± 18.3)	79.4 (± 8.7)	99 (± 22.6)	
Pulse rate– standing(N=9,15,2): 0:30h	84.7 (± 15.5)	81.5 (± 12.2)	103 (± 27.6)	
Pulse rate– standing(N=9,15,2): 1:00h	94.8 (± 20.3)	85.4 (± 10.9)	123 (± 43.1)	
Pulse rate– standing(N=9,15,2): 2:00h	92.8 (± 17)	89.3 (± 11.2)	121 (± 1.4)	
Pulse rate– standing(N=9,15,1): 3:00h	99 (± 18.2)	92.7 (± 12.9)	109 (± 99999)	
Pulse rate– standing(N=9,14,1): 5:00h	99.3 (± 27)	87.1 (± 11.4)	76 (± 99999)	
Pulse rate– standing(N=9,13,1): 7:00h	100 (± 17)	82.1 (± 14.4)	72 (± 99999)	
Pulse rate– standing(N=9,14,1): 12:00h	97.8 (± 12.4)	81.2 (± 12.3)	86 (± 99999)	
Pulse rate– standing(N=9,14,1): 24:00h	90 (± 18.8)	85.8 (± 6.7)	86 (± 99999)	

Notes:

[68] - Safety Set

[69] - Safety Set

[70] - Safety Set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first drug administration until 24 hours after last study drug administration, upto 48 days

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	10.1
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Reporting groups

Reporting group title	PPX (MIRAPEX®, 0.125 mg)
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Reporting group description:

Orally administered single daily maintenance dose of MIRAPEX® (0.125 mg) tablet per day in evening with 240 mL of water in a fasting state.

Reporting group title	PPX (MIRAPEX®, 0.5 mg)
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Reporting group description:

Orally administered single daily maintenance dose of MIRAPEX® (0.5 mg) tablet per day in evening with 240 mL of water in a fasting state.

Reporting group title	PPX (MIRAPEX®, 0.25 mg)
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Reporting group description:

Orally administered single daily maintenance dose of MIRAPEX® (0.25 mg) tablet per day in evening with 240 mL of water in a fasting state.

Serious adverse events	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.5 mg)	PPX (MIRAPEX®, 0.25 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	0 / 15 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	PPX (MIRAPEX®, 0.125 mg)	PPX (MIRAPEX®, 0.5 mg)	PPX (MIRAPEX®, 0.25 mg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 9 (22.22%)	1 / 2 (50.00%)	3 / 15 (20.00%)
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Infusion site erythema			

subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 2 (0.00%) 0	1 / 15 (6.67%) 1
Infusion site irritation subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 2 (0.00%) 0	1 / 15 (6.67%) 1
Infusion site pain subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 2 (0.00%) 0	1 / 15 (6.67%) 1
Vessel puncture site erythema subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 2 (0.00%) 0	1 / 15 (6.67%) 1
Vessel puncture site pain subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 2 (0.00%) 0	1 / 15 (6.67%) 1
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 2 (50.00%) 1	0 / 15 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 2 (50.00%) 1	1 / 15 (6.67%) 1
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 2 (0.00%) 0	0 / 15 (0.00%) 0

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

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

A "Missing" category is unavailable for the country wise and age group breakdown of enrolled patients. Hence, 3 subjects with a missing age group have been added to "Children (2-11 years)".

Notes: