Clinical trial results:
A Multicentre, Open-label, Single Ascending Dose Phase 1 Study to Evaluate the Pharmacokinetics, Safety and Tolerability of Mirabegron OCAS Tablets in Pediatric Subjects from 5 to Less than 18 Years of Age with Neurogenic Detrusor Overactivity (NDO) or Overactive Bladder (OAB)

Summary

EudraCT number	2014-000340-15
Trial protocol	DE BE NO DK
Global end of trial date	21 September 2015

Results information

Result version number	v1 (current)
This version publication date	30 March 2016
First version publication date	30 March 2016

Trial information

Trial identification

Sponsor protocol code	178-CL-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02211846
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Astellas Pharma Europe B.V.
Sponsor organisation address	Sylviusweg 62, Leiden, Netherlands, 2333 BE
Public contact	Clinical Trial Disclosure, Astellas Pharma Global Development, Inc., astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Trial Disclosure, Astellas Pharma Global Development, Inc., astellas.resultsdisclosure@astellas.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000597-PIP10-04, EMEA-000597-PIP15-01
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	21 September 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 September 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the pharmacokinetics of mirabegron Oral Controlled Absorption System (OCAS) tablets after single-dose administration at different dose levels in children and adolescents with NDO or OAB.

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki. Astellas ensures that the use and disclosure of protected health information (PHI) obtained during a research study complies with the federal, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 September 2014
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	Belgium: 1
Country: Number of subjects enrolled	Denmark: 11
Country: Number of subjects enrolled	Norway: 8
Country: Number of subjects enrolled	Poland: 14
Worldwide total number of subjects	34
EEA total number of subjects	34

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)	19

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: -

Pre-assignment

Screening details:

Children and adolescents with NDO or OAB, who consented to enter this study and fulfilled all the eligibility criteria were enrolled. A wash-out of prohibited medication for 5 half-lives was performed if a participant was using prohibited medication.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Adolescents Low Dose (Fed)

Arm description:

Adolescents aged 12 to less than 18 years received a single, weight-based dose of mirabegron after a light breakfast on day 1. Participants weighing 20.0 to < 55.0 kg received 25 mg mirabegron; participants ≥ 55.0 kg received 50 mg (both referred to as low dose, predicted to achieve the low exposure target).

Arm type	Experimental
Investigational medicinal product name	Mirabegron
Investigational medicinal product code	YM178
Other name	Myrbetriq®, Betmiga™
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received a single dose of mirabegron prolonged-release tablet/s (with strengths of 25 mg or 50 mg), with a glass of water on day 1.

Arm title	Children Low Dose (Fed)

Arm description:

Children aged 5 to less than 12 years received a single, weight-based dose of mirabegron after a light breakfast on day 1. Participants weighing 20.0 to < 55.0 kg received 25 mg mirabegron; participants ≥ 55.0 kg received 50 mg (both referred to as low dose, predicted to achieve the low exposure target).

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Participants received a single dose of mirabegron prolonged-release tablet/s (with strengths of 25 mg or 50 mg), with a glass of water on day 1.

Arm title	Adolescents High Dose (Fed)

Arm description:

Adolescents aged 12 to less than 18 years received a single, weight-based dose of mirabegron after a light breakfast on day 1. Participants weighing 20.0 to < 40.0 kg received 50 mg mirabegron; participants ≥ 40.0 kg received 75 mg (50 mg tablet + 25 mg tablet) (both referred to as high dose, predicted to achieve the high exposure target).

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Arm description:

Children aged 5 to less than 12 years received a single, weight-based dose of mirabegron after a light breakfast on day 1. Participants weighing 20.0 to < 40.0 kg received 50 mg mirabegron; participants ≥ 40.0 kg received 75 mg (50 mg tablet + 25 mg tablet) (both referred to as high dose, predicted to achieve the high exposure target).

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Dosage and administration details:

Participants received a single dose of mirabegron prolonged-release tablet/s (with strengths of 25 mg or 50 mg), with a glass of water on day 1.

Arm title	Children High Dose (Fasted)

Arm description:

Children aged 5 to less than 12 years received a single, weight-based dose of mirabegron under fasted conditions (fasted from at least midnight the day before before until 4 hours after dosing). Participants weighing 20.0 to < 40.0 kg received 50 mg mirabegron; participants ≥ 40.0 kg received 75 mg (50 mg tablet + 25 mg tablet) (both referred to as high dose, predicted to achieve the high exposure target).

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Routes of administration	Oral use

Dosage and administration details:

Participants received a single dose of mirabegron prolonged-release tablet/s (with strengths of 25 mg or 50 mg), with a glass of water on day 1.

Number of subjects in period 1	Adolescents Low Dose (Fed)	Children Low Dose (Fed)	Adolescents High Dose (Fed)
Started	7	7	8
Safety Analysis Set (SAF)	7	7	8
Pharmacokinetic Analysis Set (PKAS)	7	7	8
Completed	7	7	8

Number of subjects in period 1	Children High Dose (Fed)	Children High Dose (Fasted)
Started	6	6

Safety Analysis Set (SAF)	6	6
Pharmacokinetic Analysis Set (PKAS)	6	6
Completed	6	6

Baseline characteristics

Reporting groups	
Reporting group title	Adolescents Low Dose (Fed)
Reporting group description:	
Adolescents aged 12 to less than 18 years received a single, weight-based dose of mirabegron after a light breakfast on day 1. Participants weighing 20.0 to < 55.0 kg received 25 mg mirabegron; participants ≥ 55.0 kg received 50 mg (both referred to as low dose, predicted to achieve the low exposure target).	
Reporting group title	Children Low Dose (Fed)
Reporting group description:	
Children aged 5 to less than 12 years received a single, weight-based dose of mirabegron after a light breakfast on day 1. Participants weighing 20.0 to < 55.0 kg received 25 mg mirabegron; participants ≥ 55.0 kg received 50 mg (both referred to as low dose, predicted to achieve the low exposure target).	
Reporting group title	Adolescents High Dose (Fed)
Reporting group description:	
Adolescents aged 12 to less than 18 years received a single, weight-based dose of mirabegron after a light breakfast on day 1. Participants weighing 20.0 to < 40.0 kg received 50 mg mirabegron; participants ≥ 40.0 kg received 75 mg (50 mg tablet + 25 mg tablet) (both referred to as high dose, predicted to achieve the high exposure target).	
Reporting group title	Children High Dose (Fed)
Reporting group description:	
Children aged 5 to less than 12 years received a single, weight-based dose of mirabegron after a light breakfast on day 1. Participants weighing 20.0 to < 40.0 kg received 50 mg mirabegron; participants ≥ 40.0 kg received 75 mg (50 mg tablet + 25 mg tablet) (both referred to as high dose, predicted to achieve the high exposure target).	
Reporting group title	Children High Dose (Fasted)
Reporting group description:	
Children aged 5 to less than 12 years received a single, weight-based dose of mirabegron under fasted conditions (fasted from at least midnight the day before before until 4 hours after dosing). Participants weighing 20.0 to < 40.0 kg received 50 mg mirabegron; participants ≥ 40.0 kg received 75 mg (50 mg tablet + 25 mg tablet) (both referred to as high dose, predicted to achieve the high exposure target).	

Reporting group values	Adolescents Low Dose (Fed)	Children Low Dose (Fed)	Adolescents High Dose (Fed)
Number of subjects	7	7	8
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	14.9	8.1	14.1
standard deviation	± 1.6	± 0.9	± 1.6
Gender categorical Units:			
Male	2	2	2
Female	5	5	6
Diagnosis at Screening Units: Subjects			
NDO	2	2	3
OAB	5	5	5

Reporting group values	Children High Dose (Fed)	Children High Dose (Fasted)	Total

Number of subjects	6	6	34
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	8.2	9.3	
standard deviation	± 0.8	± 0.8	-
Gender categorical Units:			
Male	2	3	11
Female	4	3	23
Diagnosis at Screening Units: Subjects			
NDO	2	2	11
OAB	4	4	23

End points

End points reporting groups

Reporting group title	Adolescents Low Dose (Fed)
Reporting group description:	
Adolescents aged 12 to less than 18 years received a single, weight-based dose of mirabegron after a light breakfast on day 1. Participants weighing 20.0 to < 55.0 kg received 25 mg mirabegron; participants ≥ 55.0 kg received 50 mg (both referred to as low dose, predicted to achieve the low exposure target).	
Reporting group title	Children Low Dose (Fed)
Reporting group description:	
Children aged 5 to less than 12 years received a single, weight-based dose of mirabegron after a light breakfast on day 1. Participants weighing 20.0 to < 55.0 kg received 25 mg mirabegron; participants ≥ 55.0 kg received 50 mg (both referred to as low dose, predicted to achieve the low exposure target).	
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Reporting group description:	
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Reporting group title	Children High Dose (Fed)
Reporting group description:	
Children aged 5 to less than 12 years received a single, weight-based dose of mirabegron after a light breakfast on day 1. Participants weighing 20.0 to < 40.0 kg received 50 mg mirabegron; participants ≥ 40.0 kg received 75 mg (50 mg tablet + 25 mg tablet) (both referred to as high dose, predicted to achieve the high exposure target).	
Reporting group title	Children High Dose (Fasted)
Reporting group description:	
Children aged 5 to less than 12 years received a single, weight-based dose of mirabegron under fasted conditions (fasted from at least midnight the day before before until 4 hours after dosing). Participants weighing 20.0 to < 40.0 kg received 50 mg mirabegron; participants ≥ 40.0 kg received 75 mg (50 mg tablet + 25 mg tablet) (both referred to as high dose, predicted to achieve the high exposure target).	

Primary: Area Under the Concentration-Time Curve to Infinity (AUCinf) for Mirabegron

End point title	Area Under the Concentration-Time Curve to Infinity (AUCinf) for Mirabegron[1]
End point description:	
The analysis population was the pharmacokinetic analysis set (PKAS), which consisted of all participants who received the dose of study drug and who had concentration values for a sufficient number of timepoints to reliably calculate at least 1 pharmacokinetic parameter.	
End point type	Primary
End point timeframe:	
Days 1-7:Adolescents [5 samples on day 1&2]: 0.5-2, 3-4, 5-6, 7-8, 24-32 h postdose; Children [4 samples on day 1&2]: 0.5-2, 3-5, 6-8, 24-32 h post dose; All [2 samples from days 3-7]: 48-56, 72-80, or 96-104 h postdose/72-80,120-128 or 144–152 h postdose	

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 study was written with no planned statistical analyses (inferential) to be performed for any end points due to the simple design and purpose of the study.

End point values	Adolescents Low Dose (Fed)	Children Low Dose (Fed)	Adolescents High Dose (Fed)	Children High Dose (Fed)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[2]	7	8	5[3]
Units: ng*h/mL				
arithmetic mean (standard deviation)	90.83 (± 25.56)	128.8 (± 65.48)	394.9 (± 205.5)	596.5 (± 385.5)

Notes:

[2] - Participants with available data.

[3] - Participants with available data.

End point values	Children High Dose (Fasted)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ng*h/mL				
arithmetic mean (standard deviation)	830.4 (± 384.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Concentration (Cmax) of Mirabegron

End point title	Maximum Concentration (Cmax) of Mirabegron[4]

End point description:

The analysis population was the PKAS.

End point type	Primary

End point timeframe:

Days 1-7:Adolescents [5 samples on day 1&2]: 0.5-2, 3-4, 5-6, 7-8, 24-32 h postdose; Children [4 samples on day 1&2]: 0.5-2, 3-5, 6-8, 24-32 h post dose; All [2 samples from days 3-7]: 48-56, 72-80, or 96-104 h postdose/72-80,120-128 or 144–152 h postdose

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: This study was written with no planned statistical analyses (inferential) to be performed for any end points due to the simple design and purpose of the study.

End point values	Adolescents Low Dose (Fed)	Children Low Dose (Fed)	Adolescents High Dose (Fed)	Children High Dose (Fed)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	7	8	6
Units: ng/mL				
arithmetic mean (standard deviation)	4.73 (± 2.717)	6.909 (± 4.67)	31.98 (± 26.1)	43.99 (± 31.93)

End point values	Children High Dose (Fasted)			

Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ng/mL				
arithmetic mean (standard deviation)	56.42 (± 17.73)			

Statistical analyses

No statistical analyses for this end point

Primary: Time at Which Cmax Occurred (tmax) for Mirabegron

End point title	Time at Which Cmax Occurred (tmax) for Mirabegron[5]

End point description:

The analysis population was the PKAS.

End point type	Primary

End point timeframe:

Days 1-7:Adolescents [5 samples on day 1&2]: 0.5-2, 3-4, 5-6, 7-8, 24-32 h postdose; Children [4 samples on day 1&2]: 0.5-2, 3-5, 6-8, 24-32 h post dose; All [2 samples from days 3-7]: 48-56, 72-80, or 96-104 h postdose/72-80,120-128 or 144–152 h postdose

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 study was written with no planned statistical analyses (inferential) to be performed for any end points due to the simple design and purpose of the study.

End point values	Adolescents Low Dose (Fed)	Children Low Dose (Fed)	Adolescents High Dose (Fed)	Children High Dose (Fed)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	7	8	6
Units: hours				
median (full range (min-max))	5.03 (3.95 to 5.75)	4.17 (2.55 to 6.37)	4.475 (3.08 to 7.08)	4.28 (3.88 to 4.42)

End point values	Children High Dose (Fasted)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hours				
median (full range (min-max))	3.95 (3.47 to 4.27)			

Statistical analyses

No statistical analyses for this end point

Primary: Elimination Half Life (t1/2) of Mirabegron

End point title	Elimination Half Life (t1/2) of Mirabegron[6]

End point description:

The analysis population was the PKAS.

End point type	Primary

End point timeframe:

Days 1-7:Adolescents [5 samples on day 1&2]: 0.5-2, 3-4, 5-6, 7-8, 24-32 h postdose; Children [4 samples on day 1&2]: 0.5-2, 3-5, 6-8, 24-32 h post dose; All [2 samples from days 3-7]: 48-56, 72-80, or 96-104 h postdose/72-80,120-128 or 144–152 h postdose

Notes:

[6] - 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 study was written with no planned statistical analyses (inferential) to be performed for any end points due to the simple design and purpose of the study.

End point values	Adolescents Low Dose (Fed)	Children Low Dose (Fed)	Adolescents High Dose (Fed)	Children High Dose (Fed)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[7]	7	8	5[8]
Units: hours				
arithmetic mean (standard deviation)	27.16 (± 6.664)	30.76 (± 8.119)	29.2 (± 4.51)	28.97 (± 6.076)

Notes:

[7] - Participants with available data.

[8] - Participants with available data.

End point values	Children High Dose (Fasted)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hours				
arithmetic mean (standard deviation)	26.16 (± 2.931)			

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Oral Clearance (CL/F) for Mirabegron

End point title	Apparent Oral Clearance (CL/F) for Mirabegron[9]

End point description:

The analysis population was the PKAS.

End point type	Primary

End point timeframe:

Days 1-7:Adolescents [5 samples on day 1&2]: 0.5-2, 3-4, 5-6, 7-8, 24-32 h postdose; Children [4 samples on day 1&2]: 0.5-2, 3-5, 6-8, 24-32 h post dose; All [2 samples from days 3-7]: 48-56, 72-80, or 96-104 h postdose/72-80,120-128 or 144–152 h postdose

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 study was written with no planned statistical analyses (inferential) to be performed for any end points due to the simple design and purpose of the study.

End point values	Adolescents Low Dose (Fed)	Children Low Dose (Fed)	Adolescents High Dose (Fed)	Children High Dose (Fed)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[10]	7	8	5[11]
Units: L/h				
arithmetic mean (standard deviation)	339.1 (± 97.54)	248.7 (± 132.5)	230.1 (± 137.4)	113 (± 62.89)

Notes:

[10] - Participants with available data.

[11] - Participants with available data.

End point values	Children High Dose (Fasted)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: L/h				
arithmetic mean (standard deviation)	79.08 (± 45.64)			

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Volume of Distribution (Vz/F) of Mirabegron

End point title	Apparent Volume of Distribution (Vz/F) of Mirabegron[12]

End point description:

The analysis population was the PKAS.

End point type	Primary

End point timeframe:

Days 1-7:Adolescents [5 samples on day 1&2]: 0.5-2, 3-4, 5-6, 7-8, 24-32 h postdose; Children [4 samples on day 1&2]: 0.5-2, 3-5, 6-8, 24-32 h post dose; All [2 samples from days 3-7]: 48-56, 72-80, or 96-104 h postdose/72-80,120-128 or 144–152 h postdose

Notes:

[12] - 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 study was written with no planned statistical analyses (inferential) to be performed for any end points due to the simple design and purpose of the study.

End point values	Adolescents Low Dose (Fed)	Children Low Dose (Fed)	Adolescents High Dose (Fed)	Children High Dose (Fed)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[13]	7	8	5[14]
Units: liters				
arithmetic mean (standard deviation)	13063 (± 4569)	9959 (± 3639)	9918 (± 6702)	4895 (± 2921)

Notes:

[13] - Participants with available data.

[14] - Participants with available data.

End point values	Children High Dose (Fasted)			

Subject group type	Reporting group			
Number of subjects analysed	6			
Units: liters				
arithmetic mean (standard deviation)	2866 (± 1438)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Concentration-Time Curve to 24 Hours (AUC24) for Mirabegron

End point title	Area Under the Concentration-Time Curve to 24 Hours (AUC24) for Mirabegron[15]

End point description:

The analysis population was the PKAS.

End point type	Primary

End point timeframe:

Time Frame: Days 1-2: Adolescents [5 samples on day 1&2]: 0.5-2, 3-4, 5-6, 7-8, 24-32 h postdose; Children [4 samples on day 1&2]: 0.5-2, 3-5, 6-8, 24-32 h post dose

Notes:

[15] - 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 study was written with no planned statistical analyses (inferential) to be performed for any end points due to the simple design and purpose of the study.

End point values	Adolescents Low Dose (Fed)	Children Low Dose (Fed)	Adolescents High Dose (Fed)	Children High Dose (Fed)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	7	8	6
Units: ng*h/mL				
arithmetic mean (standard deviation)	47.9 (± 14.24)	66.33 (± 31.66)	230.7 (± 132.5)	336 (± 225.4)

End point values	Children High Dose (Fasted)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ng*h/mL				
arithmetic mean (standard deviation)	508.6 (± 190.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs)

End point description:

Safety was assessed by collecting AEs, which included abnormalities identified during a medical test (e.g. laboratory tests, vital sign, electrocardiogram, etc.) if the abnormality induced clinical signs or symptoms, needed active intervention, interruption or discontinuation of study medication or was clinically significant. A serious AE (SAE) was an event resulting in death, persistent or significant disability/incapacity or congenital anomaly or birth defect, was life-threatening, required or prolonged hospitalization or was considered medically important. A treatment-emergent adverse event (TEAE) was defined as an AE that occurred after administration of the first dose of study drug until 7 days after the last dose of study drug. A related SAE or TEAE was possible or probable, as assessed by the Investigator, or records where relationship is missing. The analysis population was the Safety Analysis Set (SAF) which consisted of all participants who took the dose of study drug.

End point type	Secondary

End point timeframe:

From dosing up to 7 days postdose

End point values	Adolescents Low Dose (Fed)	Children Low Dose (Fed)	Adolescents High Dose (Fed)	Children High Dose (Fed)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	7	8	6
Units: participants				
TEAE	1	1	1	0
Related TEAE	0	0	1	0
Death	0	0	0	0
SAE	0	0	0	0
Drug-related SAE	0	0	0	0

End point values	Children High Dose (Fasted)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: participants				
TEAE	1			
Related TEAE	0			
Death	0			
SAE	0			
Drug-related SAE	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From dosing up to 7 days postdose	
Adverse event reporting additional description:	
SAF	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	Adolescents Low Dose (Fed)
Reporting group description:	
Male and female adolescents aged 12 to less than 18 years) who received a low dose of mirabegron under fed conditons.	
Reporting group title	Children Low Dose (Fed)
Reporting group description:	
Male and female children aged 5 to less than 12 years who received a low dose of mirabegron under fed conditons.	
Reporting group title	Adolescents High Dose (Fed)
Reporting group description:	
Male and female adolescents aged 12 to less than 18 years) who received a high dose of mirabegron under fed conditons.	
Reporting group title	Children High Dose (Fed)
Reporting group description:	
Male and female children aged 5 to less than 12 years who received a high dose of mirabegron under fed conditons.	
Reporting group title	Children High Dose (Fasted)
Reporting group description:	
Male and female children aged 5 to less than 12 years who received a high dose of mirabegron under fasted conditons (fasted from at least midnight the day before before until 4 hours after dosing).	

Serious adverse events	Adolescents Low Dose (Fed)	Children Low Dose (Fed)	Adolescents High Dose (Fed)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Children High Dose (Fed)	Children High Dose (Fasted)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Adolescents Low Dose (Fed)	Children Low Dose (Fed)	Adolescents High Dose (Fed)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)	1 / 7 (14.29%)	1 / 8 (12.50%)
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Children High Dose (Fed)	Children High Dose (Fasted)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 September 2014	In this global amendment, changes include: (1) The United States was added as a study location; (2) The method for estimated glomerular filtration rate calculation was amended from the modification of diet in renal disease (MDRD) study equation method to the revised Schwartz method; (3) Cystatin C was added as a biochemistry parameter.
06 February 2015	In this global amendment, changes include: (1)The Investigator's Brochure was listed as a source for contraindications or precautions to exclusion criterion 12; (2) The required wash-out period for mirabegron before the planned reference day (day -4 to day -1) was amended from 24 days to 12 days; (3) Current, untreated constipation (or fecal impaction for NDO participants) were added as an exclusion criterion at screening; (4) Use of botox within 4 months prior to screening was added as an exclusion criterion at screening; (5) Symptomatic Urinary tract infection (UTI) was added as a day 1 exclusion criterion; (6) Several sections were updated to allow preselected study visits to take place outside the clinic; (7) The pharmacokinetic-specific restrictions for dosing on Friday and weekend samplings were removed; (8) Assessments of palatability (taste) and acceptability (ease of swallowing) were included in the protocol as exploratory endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported