Clinical trial results:
A Phase 3, Open-label, Baseline-controlled, Multi-center, Sequential Dose-titration Study to Assess the Pharmacokinetics, Long-term Efficacy and Safety of Solifenacin Succinate Suspension in Children from 6 Months to less than 5 Years of Age with Neurogenic Detrusor Overactivity

Summary

EudraCT number	2012-003178-22
Trial protocol	GB NL BE DK
Global end of trial date	18 December 2015

Results information

Result version number	v2
This version publication date	05 April 2017
First version publication date	29 June 2016
Version creation reason	• New data added to full data set • Correction of full data set Non-Serious Adverse Events section updated to include 2 new adverse events in updated clinical study report.

Trial information

Trial identification

Sponsor protocol code	905-CL-074

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01981954
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-000573-PIP02-13
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	18 December 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term efficacy, safety and pharmacokinetics (PK) of solifenacin succinate suspension after multiple-dose administration.

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 (especially ICH E11), 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	25 September 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Philippines: 6
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 1
Country: Number of subjects enrolled	Belgium: 1
Worldwide total number of subjects	23
EEA total number of subjects	11

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)	4
Children (2-11 years)	19
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Children aged 6 months to <5 years old with Neurogenic Detrusor Overactivity (NDO) were enrolled from Belgium (1 site), United Kingdom (1 site), Poland (2 sites), United States (1 site), the Philippines (1 site) and South Korea (2 sites).

Pre-assignment

Screening details:

Children who met the eligibility criteria were treated with sequential doses of solifenacin up to 12 weeks to determine each participant's optimal dose, after which a fixed dose of solifenacin was given for at least 40 weeks. A washout period was required between screening and baseline if the children were being treated with antimuscarinic agents.

Period 1

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

Arms

Arm title	Solifenacin succinate

Arm description:

Children aged 6 months to <5 years who received solifenacin once daily, with sequential titrated doses for 12 weeks during the Titration period.

Arm type	Experimental
Investigational medicinal product name	Solifenacin succinate
Investigational medicinal product code	YM905
Other name	solifenacin, solifenacin succinate suspension
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

An initial dose of solifenacin (1 mg/mL) was administered on the baseline visit for children aged 6 months to <2 years and the day after the baseline visit for children aged 2 years to <5 years, then once daily for a 12-week Titration period, to determine the participant's optimal dose. Doses were calculated per weight determined at the baseline visit of this study and based on a physiologically-based pharmacokinetic (PK) model, targeting to have equivalent doses of 2.5, 5, 7.5 and 10 mg doses of solifenacin once daily in adults (referred to as PED2.5, PED5, PED7.5 and PED10). During the 12-week Titration period, the dose of solifenacin was down-titrated, up-titrated or maintained depending on the study’s titration criteria, which were based on a combination of diary endpoints, urodynamic assessments and adverse event (AE) criteria.

Number of subjects in period 1	Solifenacin succinate
Started	23
Treated	23
Completed	22
Not completed	1
Protocol Violation	1

Period 2

Period 2 title	Fixed-Dose Assessment Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Solifenacin succinate

Arm description:

Children aged 6 months to <5 years who received solifenacin once daily, with a fixed dose of solifenacin once daily for 40 weeks in the Fixed-dose assessment period.

Arm type	Experimental
Investigational medicinal product name	Solifenacin succinate
Investigational medicinal product code	YM905
Other name	solifenacin, solifenacin succinate suspension
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

When a fixed and optimal dose of solifenacin was confirmed by Week 12, a participant continued on to receive solifenacin orally once daily until end of the study (Week 52).

Number of subjects in period 2	Solifenacin succinate
Started	22
Treated	22
Completed	21
Not completed	1
Lack of efficacy	1

Baseline characteristics

Reporting groups	
Reporting group title	Solifenacin succinate
Reporting group description:	
Children aged 6 months to <5 years who received solifenacin once daily, with sequential titrated doses for 12 weeks during the Titration period.	

Reporting group values	Solifenacin succinate	Total	
Number of subjects	23	23	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	4	4	
Children (2-11 years)	19	19	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: months			
arithmetic mean	35.3		
standard deviation	± 12.7	-	
Gender categorical			
Units:			
Male	9	9	
Female	14	14	
Weight			
Units: kg			
arithmetic mean	13.2		
standard deviation	± 2.87	-	
Duration of NDO Disease			
Units: years			
median	1.99		
full range (min-max)	0.13 to 4.51	-	

End points

End points reporting groups

Reporting group title	Solifenacin succinate
Reporting group description:	
Children aged 6 months to <5 years who received solifenacin once daily, with sequential titrated doses for 12 weeks during the Titration period.	
Reporting group title	Solifenacin succinate
Reporting group description:	
Children aged 6 months to <5 years who received solifenacin once daily, with a fixed dose of solifenacin once daily for 40 weeks in the Fixed-dose assessment period.	

Primary: Change from Baseline to Week 24 in Maximum Cystometric Capacity (MCC)

End point title	Change from Baseline to Week 24 in Maximum Cystometric Capacity (MCC)[1]
End point description:	
MCC was the volume instilled into the bladder prior to leakage or end of bladder-filling (whichever was reached first), as assessed by urodynamics (procedure: the bladder was to be filled until voiding/leakage began, or until it was stopped because either the participant experienced pain or discomfort or 135% of expected bladder capacity [EBC] was reached for participants ≥ 2 years or of maximum catheterized volume [MCV] for participants aged 6 months to <2 years; the participants' bladder was emptied via catheterization). The analysis population was the Full Analysis Set (FAS), which consisted of all participants who took at least one dose of study drug and provided both valid baseline and at least one post-baseline value for the primary efficacy endpoint. Change from baseline to week 24 with and without last observation carried forward (LOCF) imputation are reported. "N" indicates the number of participants included in each analysis.	
End point type	Primary
End point timeframe:	
Baseline and Week 24	

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: As this is a one treatment arm study, showing statistical analysis is not possible due to system limitations.

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: mL				
arithmetic mean (standard deviation)				
Change at Week 24 [N=21]	37 (± 35.9)			
Change at Week 24 LOCF [N=22]	35.2 (± 36.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 3, 6, 9, 12 and 52 in MCC

End point title	Change from Baseline to Weeks 3, 6, 9, 12 and 52 in MCC

End point description:

MCC was the volume instilled into the bladder prior to leakage or end of bladder-filling (whichever was reached first), as assessed by urodynamics (procedure: the bladder was to be filled until voiding/leakage began, or until it was stopped because either the participant experienced pain or discomfort or 135% of EBC was reached for participants ≥ 2 years or of MCV for participants aged 6 months to <2 years. The participants' bladder was emptied via catheterization). The analysis population was the Full Analysis Set (FAS), which consisted of all participants who took at least one dose of study drug and provided both valid baseline and at least one post-baseline value for the primary efficacy endpoint. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 3, 6, 9, 12, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: mL				
arithmetic mean (standard deviation)				
Week 3 [N=11]	45.2 (± 44.8)			
Week 6 [N=11]	36.5 (± 36.6)			
Week 9 [N=9]	20.8 (± 54.7)			
Week 12 [N=16]	40.2 (± 37.9)			
Week 52 [N=14]	58.6 (± 34.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Bladder Compliance

End point title	Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Bladder Compliance

End point description:

Bladder compliance was calculated by dividing the volume change by the change in detrusor pressure during that change in bladder volume using urodynamic assessments. The values for bladder volume and detrusor pressure at the beginning and end of filling were taken and used. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 3, 6, 9, 12, 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: mL/cmH2O				
arithmetic mean (standard deviation)				
Week 3 [N=11]	4.55 (± 4.3)			
Week 6 [N=11]	5.45 (± 8.45)			
Week 9 [N=9]	8.92 (± 15.69)			
Week 12 [N=16]	4.14 (± 4.2)			
Week 24 [N=21]	5.1 (± 6.82)			
Week 52 [N=14]	5.94 (± 4.24)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Detrusor Pressure at End of Bladder-Filling

End point title	Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Detrusor Pressure at End of Bladder-Filling

End point description:

Detrusor pressure was expressed as bladder pressure minus intra-abdominal pressure as assessed by urodynamics. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 3, 6, 9, 12, 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: cmH2O				
arithmetic mean (standard deviation)				
Week 3 [N=11]	-5.2 (± 12.9)			
Week 6 [N=11]	-8.3 (± 14.8)			
Week 9 [N=9]	-8.9 (± 17.5)			
Week 12 [N=16]	-0.6 (± 23.4)			
Week 24 [N=21]	-1 (± 13.9)			
Week 52 [N=14]	-9.8 (± 19.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Detrusor Pressure 5 Minutes After End of Bladder-Filling

End point title	Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Detrusor Pressure 5 Minutes After End of Bladder-Filling

End point description:

Detrusor pressure was expressed as bladder pressure minus intra-abdominal pressure as assessed by urodynamics. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 3, 6, 9, 12, 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: cmH2O				
arithmetic mean (standard deviation)				
Week 3 [N=11]	0.9 (± 8.4)			
Week 6 [N=11]	1.3 (± 10.4)			
Week 9 [N=9]	0.7 (± 11.1)			
Week 12 [N=16]	-4.1 (± 10.9)			
Week 24 [N=21]	-2 (± 9.4)			
Week 52 [N=14]	-2.3 (± 14.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Catheterized Volume 5 Minutes After End of Bladder-Filling

End point title	Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Catheterized Volume 5 Minutes After End of Bladder-Filling

End point description:

Catheterized volume was measured when the bladder was emptied via catheterization 5 minutes after the end of bladder-filling. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 3, 6, 9, 12, 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: mL				
arithmetic mean (standard deviation)				
Week 3 [N=5]	38.6 (± 52.6)			
Week 6 [N=6]	41.8 (± 25.5)			
Week 9 [N=4]	50.5 (± 40.5)			
Week 12 [N=10]	50.5 (± 46.6)			
Week 24 [N=13]	44 (± 29.5)			
Week 52 [N=8]	59.8 (± 27)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Bladder Volume Until First Detrusor Contraction >15 cmH2O

End point title	Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Bladder Volume Until First Detrusor Contraction >15 cmH2O

End point description:

Bladder volume as assessed by urodynamics. The analysis population was FAS. "N" indicates the number of participants with available data at each time point and excluding participants who did not have a detrusor contraction.

End point type	Secondary

End point timeframe:

Baseline and Weeks 3, 6, 9, 12, 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: mL				
arithmetic mean (standard deviation)				
Week 3 [N=4]	47 (± 31.3)			
Week 6 [N=2]	87.4 (± 57.4)			
Week 9 [N=5]	60.8 (± 82.9)			
Week 12 [N=5]	18.7 (± 37.5)			
Week 24 [N=11]	22.9 (± 52.3)			
Week 52 [N=4]	89.2 (± 58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Bladder Volume at 10 cmH20 Detrusor Pressure

End point title	Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Bladder Volume at 10 cmH20 Detrusor Pressure

End point description:

Bladder volume as assessed by urodynamics. The analysis population was FAS. "N" indicates the number of participants with available data at each time point and whose pressure reached 10 cmH2O.

End point type	Secondary

End point timeframe:

Baseline and Weeks 3, 6, 9, 12, 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: mL				
arithmetic mean (standard deviation)				
Week 3 [N=8]	31.9 (± 47.3)			
Week 6 [N=8]	47.8 (± 55.9)			
Week 9 [N=6]	31.5 (± 54.1)			
Week 12 [N=14]	30.1 (± 37.9)			
Week 24 [N=17]	28.7 (± 47.9)			
Week 52 [N=10]	49.4 (± 40.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Bladder Volume at 20 cmH20 Detrusor Pressure

End point title	Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Bladder Volume at 20 cmH20 Detrusor Pressure

End point description:

Bladder volume as assessed by urodynamics. The analysis population was FAS. "N" indicates the number of participants with available data at each time point and participants whose pressure reached 20 cmH2O.

End point type	Secondary

End point timeframe:

Baseline and Weeks 3, 6, 9, 12, 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: mL				
arithmetic mean (standard deviation)				
Week 3 [N=6]	52.4 (± 59.4)			
Week 6 [N=4]	65.5 (± 54.9)			
Week 9 [N=3]	52 (± 58)			
Week 12 [N=6]	53.9 (± 67.6)			
Week 24 [N=10]	40.1 (± 56.2)			
Week 52 [N=3]	75.4 (± 71.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Bladder Volume at 30 cmH20 Detrusor Pressure

End point title	Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Bladder Volume at 30 cmH20 Detrusor Pressure

End point description:

Bladder volume as assessed by urodynamics. The analysis population was FAS. "N" indicates the number of participants with available data at each time point and participants whose pressure reached 30 cmH2O. Due to low number of participants whose pressure did not reach 30 cmH20, no data has been calculated and is denoted as "99999."

End point type	Secondary

End point timeframe:

Baseline and Weeks 3, 6, 9, 12, 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: nL				
arithmetic mean (standard deviation)				
Week 3 [N=2]	101.9 (± 0.2)			
Week 6 [N=1]	-2.3 (± 99999)			
Week 9 [N=2]	76 (± 120.2)			
Week 12 [N=2]	74.7 (± 54.9)			
Week 24 [N=2]	67.5 (± 118.1)			
Week 52 [N=1]	93.6 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Number of Overactive Detrusor Contractions (> 15 cmH2O) until Leakage or End of Bladder-Filling

End point title	Change from Baseline to Weeks 3, 6, 9, 12, 24 and 52 in Number of Overactive Detrusor Contractions (> 15 cmH2O) until Leakage or End of Bladder-Filling

End point description:

The analysis population was FAS. "N" indicates the number of participants with available data at each time point and excluding participants who did not have a detrusor contraction.

End point type	Secondary

End point timeframe:

Baseline and Weeks 3, 6, 9, 12, 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: contractions				
arithmetic mean (standard deviation)				
Week 3 [N=11]	-3.4 (± 3.9)			
Week 6 [N=11]	-4.2 (± 5.3)			
Week 9 [N=9]	-6 (± 6.2)			
Week 12 [N=16]	-6.8 (± 8.9)			
Week 24 [N=21]	-7 (± 8.6)			
Week 52 [N=14]	-7.2 (± 10.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 3, 6, 9, 12, 24, 36 and 52 in Average Catheterized Volume per Catheterization

End point title	Change from Baseline to Weeks 3, 6, 9, 12, 24, 36 and 52 in Average Catheterized Volume per Catheterization

End point description:

The average catheterized volume per catheterization was calculated using all available (non-zero) catheterized volumes recorded over both of the 2 measuring days in the diary, whether or not these 2 days were concurrent. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 3, 6, 9, 12, 24, 36, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: mL				
arithmetic mean (standard deviation)				
Week 3 [N=19]	20.7 (± 25.7)			
Week 6 [N=18]	23.34 (± 23.23)			
Week 9 [N=19]	24.82 (± 24.25)			
Week 12 [N=19]	37.34 (± 21.84)			
Week 24 [N=19]	33.73 (± 32.23)			
Week 36 [N=18]	44.35 (± 33.19)			
Week 52 [N=17]	41.88 (± 31.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 3, 6, 9, 12, 24, 36 and 52 in Maximum Catheterized Volume (MCV)

End point title	Change from Baseline to Weeks 3, 6, 9, 12, 24, 36 and 52 in Maximum Catheterized Volume (MCV)

End point description:

The maximum catheterized volume per day was calculated using all available (non-zero) catheterized volumes recorded for the 2 measuring days in the diary, whether or not these 2 days were concurrent. The maximum value was calculated separately for each measuring day and the mean of these two values was used. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 3, 6, 9, 12, 24, 36, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: mL				
arithmetic mean (standard deviation)				
Week 3 [N=19]	29.13 (± 31.38)			
Week 6 [N=18]	30.47 (± 33.43)			
Week 9 [N=19]	28.71 (± 32.98)			
Week 12 [N=19]	42.29 (± 25.11)			

Week 24 [N=19]	40.26 (± 50.02)			
Week 36 [N=18]	61.03 (± 48.1)			
Week 52 [N=17]	44.09 (± 46.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 3, 6, 9, 12, 24, 36 and 52 in Average First Morning Catheterized Volume

End point title	Change from Baseline to Weeks 3, 6, 9, 12, 24, 36 and 52 in Average First Morning Catheterized Volume

End point description:

The first morning catheterized volume was the volume associated with the first morning catheterization. The average first morning catheterized volume was calculated as the average of the available first morning catheterized volumes recorded for the 2 measuring days in the diary, whether or not these 2 days are concurrent. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 3, 6, 9, 12, 24, 36, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: mL				
arithmetic mean (standard deviation)				
Week 3 [N=19]	18.34 (± 34.12)			
Week 6 [N=18]	23.14 (± 34.76)			
Week 9 [N=19]	22.76 (± 35.49)			
Week 12 [N=19]	31.53 (± 35.25)			
Week 24 [N=19]	39.37 (± 41.05)			
Week 36 [N=18]	42.5 (± 43.56)			
Week 52 [N=17]	41.15 (± 34.21)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 3, 6, 9, 12, 24, 36 and 52 in Mean

Number of Periods Between the Clean Intermittent Catheterizations (CICs) with Incontinence per 24 Hours

End point title	Change from Baseline to Weeks 3, 6, 9, 12, 24, 36 and 52 in Mean Number of Periods Between the Clean Intermittent Catheterizations (CICs) with Incontinence per 24 Hours

End point description:

Participants were required to have 4-6 CICs per day on a schedule fixed for the duration of the study. To calculate the number of periods between CICs with incontinence in a diary day, the diary day was divided into periods between CICs (i.e. inter-CIC periods). The hour period, rather than the exact time, of each CIC and incontinence episode was recorded in the diary. When an incontinence episode and a CIC were marked in the same hour period, the incontinence episode was counted as occurring prior to the CIC (when the bladder had not yet emptied), rather than after it (when the bladder had recently been emptied), i.e. the inter-CIC period ended with the hour in which the CIC was recorded. The mean number of periods between CICs with incontinence per 24 hours was the number of periods between CICs when incontinence occurred, divided by the total number of valid diary days. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 3, 6, 9, 12, 24, 36, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: periods				
arithmetic mean (standard deviation)				
Week 3 [N=18]	-1.07 (± 1.44)			
Week 6 [N=16]	-1.29 (± 1.22)			
Week 9 [N=16]	-1.37 (± 1.2)			
Week 12 [N=17]	-1.22 (± 1.29)			
Week 24 [N=18]	-1.31 (± 1.35)			
Week 36 [N=17]	-1.02 (± 1.23)			
Week 52 [N=15]	-1.22 (± 1.39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Catheterizations for Each Hour of 24 Hour day at Baseline

End point title	Incidence of Catheterizations for Each Hour of 24 Hour day at Baseline

End point description:

For each one hour period of the 24 hour day, the incidence of catheterization was assessed as the number of days with catheterization occurring within the one hour period divided by the number of valid diary days over all participants. Each participant contributed to up to three days of valid diary data for each visit. The analysis population was FAS.

End point type	Secondary

End point timeframe:

3 days prior to Baseline visit

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of days with catheterization				
number (not applicable)				
06:00-07:00	49.1			
07:00-08:00	28.1			
08:00-09:00	17.5			
09:00-10:00	26.3			
10:00-11:00	15.8			
11:00-12:00	26.3			
12:00-13:00	42.1			
13:00-14:00	19.3			
14:00-15:00	19.3			
15:00-16:00	28.1			
16:00-17:00	26.3			
17:00-18:00	14			
18:00-19:00	38.6			
19:00-20:00	33.3			
20:00-21:00	14			
21:00-22:00	36.8			
22:00-23:00	14			
23:00-00:00	12.3			
00:00-01:00	28.1			
01:00-02:00	8.8			
02:00-03:00	1.8			
03:00-04:00	3.5			
04:00-05:00	0			
05:00-06:00	12.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Catheterizations for Each Hour of 24 Hour day During Week 3

End point title	Incidence of Catheterizations for Each Hour of 24 Hour day During Week 3

End point description:

For each one hour period of the 24 hour day, the incidence of catheterization was assessed as the number of days with catheterization occurring within the one hour period divided by the number of valid diary days over all participants. Each participant contributed to up to three days of valid diary data for each visit. The analysis population was FAS.

End point type	Secondary

End point timeframe:

3 days prior to Week 3 visit

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of days with catheterization				
number (not applicable)				
06:00-07:00	37.9			
07:00-08:00	28.8			
08:00-09:00	19.7			
09:00-10:00	25.8			
10:00-11:00	21.2			
11:00-12:00	21.2			
12:00-13:00	34.8			
13:00-14:00	33.3			
14:00-15:00	16.7			
15:00-16:00	25.8			
16:00-17:00	19.7			
17:00-18:00	27.3			
18:00-19:00	34.8			
19:00-20:00	27.3			
20:00-21:00	21.2			
21:00-22:00	34.8			
22:00-23:00	16.7			
23:00-00:00	10.6			
00:00-01:00	25.8			
01:00-02:00	13.6			
02:00-03:00	3			
03:00-04:00	0			
04:00-05:00	0			
05:00-06:00	12.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Catheterizations for Each Hour of 24 Hour day During Week 6

End point title	Incidence of Catheterizations for Each Hour of 24 Hour day During Week 6

End point description:

For each one hour period of the 24 hour day, the incidence of catheterization was assessed as the number of days with catheterization occurring within the one hour period divided by the number of valid diary days over all participants. Each participant contributed to up to three days of valid diary data for each visit. The analysis population was FAS.

End point type	Secondary

End point timeframe:

3 days prior to Week 6 visit

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of days with catheterization				
number (not applicable)				
06:00-07:00	36.5			
07:00-08:00	28.6			
08:00-09:00	19			
09:00-10:00	34.9			
10:00-11:00	15.9			
11:00-12:00	14.3			
12:00-13:00	41.3			
13:00-14:00	31.7			
14:00-15:00	17.5			
15:00-16:00	30.2			
16:00-17:00	23.8			
17:00-18:00	19			
18:00-19:00	34.9			
19:00-20:00	30.2			
20:00-21:00	11.1			
21:00-22:00	38.1			
22:00-23:00	17.5			
23:00-00:00	15.9			
00:00-01:00	22.2			
01:00-02:00	0			
02:00-03:00	4.8			
03:00-04:00	3.2			
04:00-05:00	0			
05:00-06:00	7.9			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Catheterizations for Each Hour of 24 Hour day During Week 9

End point title	Incidence of Catheterizations for Each Hour of 24 Hour day During Week 9

End point description:

For each one hour period of the 24 hour day, the incidence of catheterization was assessed as the number of days with catheterization occurring within the one hour period divided by the number of valid diary days over all participants. Each participant contributed to up to three days of valid diary data for

each visit. The analysis population was FAS.

End point type	Secondary

End point timeframe:

3 days prior to Week 9 visit

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of days with catheterization				
number (not applicable)				
06:00-07:00	37.9			
07:00-08:00	34.8			
08:00-09:00	18.2			
09:00-10:00	22.7			
10:00-11:00	18.2			
11:00-12:00	21.2			
12:00-13:00	40.9			
13:00-14:00	25.8			
14:00-15:00	21.2			
15:00-16:00	30.3			
16:00-17:00	15.2			
17:00-18:00	22.7			
18:00-19:00	36.4			
19:00-20:00	30.3			
20:00-21:00	16.7			
21:00-22:00	36.4			
22:00-23:00	12.1			
23:00-00:00	18.2			
00:00-01:00	21.2			
01:00-02:00	6.1			
02:00-03:00	1.5			
03:00-04:00	1.5			
04:00-05:00	1.5			
05:00-06:00	9.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Catheterizations for Each Hour of 24 Hour day During Week 12

End point title	Incidence of Catheterizations for Each Hour of 24 Hour day During Week 12

End point description:

For each one hour period of the 24 hour day, the incidence of catheterization was assessed as the number of days with catheterization occurring within the one hour period divided by the number of valid

diary days over all participants. Each participant contributed to up to three days of valid diary data for each visit. The analysis population was FAS.

End point type	Secondary

End point timeframe:

3 days prior to Week 12 visit

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of days with catheterization				
number (not applicable)				
06:00-07:00	44.9			
07:00-08:00	29			
08:00-09:00	18.8			
09:00-10:00	24.6			
10:00-11:00	20.3			
11:00-12:00	20.3			
12:00-13:00	55.1			
13:00-14:00	17.4			
14:00-15:00	11.6			
15:00-16:00	29			
16:00-17:00	29			
17:00-18:00	14.5			
18:00-19:00	37.7			
19:00-20:00	29			
20:00-21:00	24.6			
21:00-22:00	34.8			
22:00-23:00	10.1			
23:00-00:00	13			
00:00-01:00	36.2			
01:00-02:00	1.4			
02:00-03:00	2.9			
03:00-04:00	2.9			
04:00-05:00	0			
05:00-06:00	5.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Catheterizations for Each Hour of 24 Hour day During Week 24

End point title	Incidence of Catheterizations for Each Hour of 24 Hour day During Week 24

End point description:

For each one hour period of the 24 hour day, the incidence of catheterization was assessed as the

number of days with catheterization occurring within the one hour period divided by the number of valid diary days over all participants. Each participant contributed to up to three days of valid diary data for each visit. The analysis population was FAS.

End point type	Secondary

End point timeframe:

3 days prior to Week 24 visit

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of days with catheterization				
number (not applicable)				
06:00-07:00	36.4			
07:00-08:00	31.8			
08:00-09:00	21.2			
09:00-10:00	15.2			
10:00-11:00	27.3			
11:00-12:00	18.2			
12:00-13:00	42.4			
13:00-14:00	31.8			
14:00-15:00	9.1			
15:00-16:00	27.3			
16:00-17:00	25.8			
17:00-18:00	25.8			
18:00-19:00	33.3			
19:00-20:00	33.3			
20:00-21:00	19.7			
21:00-22:00	36.4			
22:00-23:00	6.1			
23:00-00:00	16.7			
00:00-01:00	28.8			
01:00-02:00	3			
02:00-03:00	3			
03:00-04:00	0			
04:00-05:00	0			
05:00-06:00	6.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Catheterizations for Each Hour of 24 Hour day During Week 36

End point title	Incidence of Catheterizations for Each Hour of 24 Hour day During Week 36

End point description:

For each one hour period of the 24 hour day, the incidence of catheterization was assessed as the number of days with catheterization occurring within the one hour period divided by the number of valid diary days over all participants. Each participant contributed to up to three days of valid diary data for each visit. The analysis population was FAS.

End point type	Secondary

End point timeframe:

3 days prior to Week 36 visit

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of days with catheterization				
number (not applicable)				
06:00-07:00	39.7			
07:00-08:00	33.3			
08:00-09:00	25.4			
09:00-10:00	19			
10:00-11:00	20.6			
11:00-12:00	15.9			
12:00-13:00	50.8			
13:00-14:00	28.6			
14:00-15:00	11.1			
15:00-16:00	25.4			
16:00-17:00	25.4			
17:00-18:00	22.2			
18:00-19:00	41.3			
19:00-20:00	25.4			
20:00-21:00	22.2			
21:00-22:00	36.5			
22:00-23:00	4.8			
23:00-00:00	14.3			
00:00-01:00	28.6			
01:00-02:00	4.8			
02:00-03:00	1.6			
03:00-04:00	0			
04:00-05:00	1.6			
05:00-06:00	1.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Catheterizations for Each Hour of 24 Hour day During Week 52

End point title	Incidence of Catheterizations for Each Hour of 24 Hour day

	During Week 52

End point description:

For each one hour period of the 24 hour day, the incidence of catheterization was assessed as the number of days with catheterization occurring within the one hour period divided by the number of valid diary days over all subjects. Each participant contributed to up to three days of valid diary data for each visit. The analysis population was FAS.

End point type	Secondary

End point timeframe:

3 days prior to Week 52 visit

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of days with catheterization				
number (not applicable)				
06:00-07:00	36.7			
07:00-08:00	33.3			
08:00-09:00	26.7			
09:00-10:00	21.7			
10:00-11:00	16.7			
11:00-12:00	20			
12:00-13:00	48.3			
13:00-14:00	25			
14:00-15:00	10			
15:00-16:00	31.7			
16:00-17:00	18.3			
17:00-18:00	23.3			
18:00-19:00	45			
19:00-20:00	26.7			
20:00-21:00	20			
21:00-22:00	35			
22:00-23:00	15			
23:00-00:00	20			
00:00-01:00	16.7			
01:00-02:00	0			
02:00-03:00	0			
03:00-04:00	0			
04:00-05:00	0			
05:00-06:00	3.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Incontinence for Each Hour of 24 Hour day at Baseline

End point title	Incidence of Incontinence for Each Hour of 24 Hour day at

	Baseline

End point description:

Incontinence was defined as leakage where a diaper is not used, or dampness where a diaper is used. For each one hour period of the 24 hour day, the incidence of incontinence was assessed as the number of days with incontinence occurring within the one hour period divided by the number of valid diary days over all participants. Each participant contributed to up to three days of valid diary data for each visit.The analysis population was FAS.

End point type	Secondary

End point timeframe:

3 days prior to Baseline visit

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of days with incontinence				
number (not applicable)				
06:00-07:00	31.6			
07:00-08:00	26.3			
08:00-09:00	15.8			
09:00-10:00	35.1			
10:00-11:00	24.6			
11:00-12:00	26.3			
12:00-13:00	33.3			
13:00-14:00	31.6			
14:00-15:00	24.6			
15:00-16:00	35.1			
16:00-17:00	35.1			
17:00-18:00	22.8			
18:00-19:00	22.8			
19:00-20:00	33.3			
20:00-21:00	15.8			
21:00-22:00	33.3			
22:00-23:00	14			
23:00-00:00	8.8			
00:00-01:00	12.3			
01:00-02:00	5.3			
02:00-03:00	1.8			
03:00-04:00	1.8			
04:00-05:00	1.8			
05:00-06:00	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Incontinence for Each Hour of 24 Hour day During Week 3

End point title	Incidence of Incontinence for Each Hour of 24 Hour day During Week 3

End point description:

Incontinence was defined as leakage where a diaper is not used, or dampness where a diaper is used. For each one hour period of the 24 hour day, the incidence of incontinence was assessed as the number of days with incontinence occurring within the one hour period divided by the number of valid diary days over all participants. Each participant contributed to up to three days of valid diary data for each visit.The analysis population was FAS.

End point type	Secondary

End point timeframe:

3 days prior to Week 3 visit

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of days with incontinence				
number (not applicable)				
06:00-07:00	19.7			
07:00-08:00	24.2			
08:00-09:00	10.6			
09:00-10:00	21.2			
10:00-11:00	22.7			
11:00-12:00	16.7			
12:00-13:00	15.2			
13:00-14:00	15.2			
14:00-15:00	21.2			
15:00-16:00	22.7			
16:00-17:00	15.2			
17:00-18:00	19.7			
18:00-19:00	13.6			
19:00-20:00	28.8			
20:00-21:00	19.7			
21:00-22:00	18.2			
22:00-23:00	3			
23:00-00:00	9.1			
00:00-01:00	4.5			
01:00-02:00	4.5			
02:00-03:00	1.5			
03:00-04:00	1.5			
04:00-05:00	0			
05:00-06:00	10.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Incontinence for Each Hour of 24 Hour day During Week 6

End point title	Incidence of Incontinence for Each Hour of 24 Hour day During Week 6

End point description:

Incontinence was defined as leakage where a diaper is not used, or dampness where a diaper is used. For each one hour period of the 24 hour day, the incidence of incontinence was assessed as the number of days with incontinence occurring within the one hour period divided by the number of valid diary days over all participants. Each participant contributed to up to three days of valid diary data for each visit.The analysis population was FAS.

End point type	Secondary

End point timeframe:

3 days prior Week 6 visit

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of days with incontinence				
number (not applicable)				
06:00-07:00	27			
07:00-08:00	17.5			
08:00-09:00	11.1			
09:00-10:00	11.1			
10:00-11:00	20.6			
11:00-12:00	22.2			
12:00-13:00	12.7			
13:00-14:00	6.3			
14:00-15:00	14.3			
15:00-16:00	27			
16:00-17:00	20.6			
17:00-18:00	22.2			
18:00-19:00	15.9			
19:00-20:00	27			
20:00-21:00	9.5			
21:00-22:00	22.2			
22:00-23:00	4.8			
23:00-00:00	4.8			
00:00-01:00	1.6			
01:00-02:00	0			
02:00-03:00	3.2			
03:00-04:00	1.6			
04:00-05:00	3.2			
05:00-06:00	4.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Incontinence for Each Hour of 24 Hour day During Week 9

End point title	Incidence of Incontinence for Each Hour of 24 Hour day During Week 9

End point description:

Incontinence was defined as leakage where a diaper is not used, or dampness where a diaper is used. For each one hour period of the 24 hour day, the incidence of incontinence was assessed as the number of days with incontinence occurring within the one hour period divided by the number of valid diary days over all participants. Each participant contributed to up to three days of valid diary data for each visit.The analysis population was FAS.

End point type	Secondary

End point timeframe:

3 days prior to Week 9 visit

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of days with incontinence				
number (not applicable)				
06:00-07:00	18.2			
07:00-08:00	19.7			
08:00-09:00	9.1			
09:00-10:00	9.1			
10:00-11:00	25.8			
11:00-12:00	24.2			
12:00-13:00	10.6			
13:00-14:00	10.6			
14:00-15:00	15.2			
15:00-16:00	21.2			
16:00-17:00	19.7			
17:00-18:00	19.7			
18:00-19:00	10.6			
19:00-20:00	19.7			
20:00-21:00	13.6			
21:00-22:00	10.6			
22:00-23:00	6.1			
23:00-00:00	4.5			
00:00-01:00	3			
01:00-02:00	3			
02:00-03:00	1.5			
03:00-04:00	3			
04:00-05:00	1.5			
05:00-06:00	9.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Incontinence for Each Hour of 24 Hour day During Week 12

End point title	Incidence of Incontinence for Each Hour of 24 Hour day During Week 12

End point description:

Incontinence was defined as leakage where a diaper is not used, or dampness where a diaper is used. For each one hour period of the 24 hour day, the incidence of incontinence was assessed as the number of days with incontinence occurring within the one hour period divided by the number of valid diary days over all participants. Each participant contributed to up to three days of valid diary data for each visit.The analysis population was FAS.

End point type	Secondary

End point timeframe:

3 days prior to Week 12 visit

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of days with incontinence				
number (not applicable)				
06:00-07:00	23.2			
07:00-08:00	10.1			
08:00-09:00	8.7			
09:00-10:00	26.1			
10:00-11:00	20.3			
11:00-12:00	23.2			
12:00-13:00	23.2			
13:00-14:00	4.3			
14:00-15:00	8.7			
15:00-16:00	31.9			
16:00-17:00	11.6			
17:00-18:00	15.9			
18:00-19:00	15.9			
19:00-20:00	23.2			
20:00-21:00	11.6			
21:00-22:00	10.1			
22:00-23:00	8.7			
23:00-00:00	5.8			
00:00-01:00	7.2			
01:00-02:00	1.4			
02:00-03:00	1.4			
03:00-04:00	1.4			
04:00-05:00	0			
05:00-06:00	7.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Incontinence for Each Hour of 24 Hour day During Week 24

End point title	Incidence of Incontinence for Each Hour of 24 Hour day During Week 24

End point description:

Incontinence was defined as leakage where a diaper is not used, or dampness where a diaper is used. For each one hour period of the 24 hour day, the incidence of incontinence was assessed as the number of days with incontinence occurring within the one hour period divided by the number of valid diary days over all participants. Each participant contributed to up to three days of valid diary data for each visit.The analysis population was FAS.

End point type	Secondary

End point timeframe:

3 days prior to Week 24 visit

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of days with incontinence				
number (not applicable)				
06:00-07:00	27.3			
07:00-08:00	13.6			
08:00-09:00	7.6			
09:00-10:00	15.2			
10:00-11:00	31.8			
11:00-12:00	22.7			
12:00-13:00	10.6			
13:00-14:00	10.6			
14:00-15:00	9.1			
15:00-16:00	25.8			
16:00-17:00	13.6			
17:00-18:00	28.8			
18:00-19:00	16.7			
19:00-20:00	22.7			
20:00-21:00	15.2			
21:00-22:00	7.6			
22:00-23:00	7.6			
23:00-00:00	6.1			
00:00-01:00	4.5			
01:00-02:00	3			

02:00-03:00	1.5			
03:00-04:00	0			
04:00-05:00	0			
05:00-06:00	4.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Incontinence for Each Hour of 24 Hour day During Week 36

End point title	Incidence of Incontinence for Each Hour of 24 Hour day During Week 36

End point description:

Incontinence was defined as leakage where a diaper is not used, or dampness where a diaper is used. For each one hour period of the 24 hour day, the incidence of incontinence was assessed as the number of days with incontinence occurring within the one hour period divided by the number of valid diary days over all participants. Each participant contributed to up to three days of valid diary data for each visit.The analysis population was FAS.

End point type	Secondary

End point timeframe:

3 days prior to Week 36 visit

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of days with incontinence				
number (not applicable)				
06:00-07:00	28.6			
07:00-08:00	12.7			
08:00-09:00	11.1			
09:00-10:00	17.5			
10:00-11:00	22.2			
11:00-12:00	19			
12:00-13:00	20.6			
13:00-14:00	12.7			
14:00-15:00	12.7			
15:00-16:00	31.7			
16:00-17:00	11.1			
17:00-18:00	15.9			
18:00-19:00	11.1			
19:00-20:00	33.3			
20:00-21:00	20.6			
21:00-22:00	17.5			
22:00-23:00	4.8			
23:00-00:00	11.1			
00:00-01:00	7.9			

01:00-02:00	3.2			
02:00-03:00	0			
03:00-04:00	1.6			
04:00-05:00	1.6			
05:00-06:00	4.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Incontinence for Each Hour of 24 Hour day During Week 52

End point title	Incidence of Incontinence for Each Hour of 24 Hour day During Week 52

End point description:

Incontinence was defined as leakage where a diaper is not used, or dampness where a diaper is used. For each one hour period of the 24 hour day, the incidence of incontinence was assessed as the number of days with incontinence occurring within the one hour period divided by the number of valid diary days over all participants. Each participant contributed to up to three days of valid diary data for each visit.The analysis population was FAS.

End point type	Secondary

End point timeframe:

3 days prior to Week 52 visit

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of days with incontinence				
number (not applicable)				
06:00-07:00	18.3			
07:00-08:00	20			
08:00-09:00	16.7			
09:00-10:00	13.3			
10:00-11:00	25			
11:00-12:00	35			
12:00-13:00	16.7			
13:00-14:00	8.3			
14:00-15:00	11.7			
15:00-16:00	33.3			
16:00-17:00	16.7			
17:00-18:00	21.7			
18:00-19:00	18.3			
19:00-20:00	23.3			
20:00-21:00	16.7			
21:00-22:00	20			
22:00-23:00	1.7			
23:00-00:00	3.3			

00:00-01:00	6.7			
01:00-02:00	3.3			
02:00-03:00	3.3			
03:00-04:00	1.7			
04:00-05:00	5			
05:00-06:00	3.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 and 52 in Infant and Toddler Quality of Life Short Form-47 questionnaire (ITQoL SF-47) - Overall Health Score

End point title	Change from Baseline to Week 24 and 52 in Infant and Toddler Quality of Life Short Form-47 questionnaire (ITQoL SF-47) - Overall Health Score

End point description:

The ITQoL SF-47 consisted of 47 individual items and was filled in by the child's parent. The individual items are based on Likert scales with either 5 responses (coded as 1 through to 5) or 4 responses (coded as 1 through to 4). Before calculating a scale, the value of each item is coded so that it ranges from 0 (worst possible) to 100 (best possible). From subsets of these coded values, 11 scales are derived: overall health, physical activities, development, discomfort, moods and temperaments, perceptions of current past and future health and perception of changes. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 24 [N=21]	-1.7 (± 18.7)			
Week 52 [N=16]	10.9 (± 18.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 and 52 in ITQoL SF-47 – Physical Abilities Score

End point title	Change from Baseline to Week 24 and 52 in ITQoL SF-47 – Physical Abilities Score

End point description:

The ITQoL SF-47 consisted of 47 individual items and was filled in by the child's parent. The individual

items are based on Likert scales with either 5 responses (coded as 1 through to 5) or 4 responses (coded as 1 through to 4). Before calculating a scale, the value of each item is coded so that it ranges from 0 (worst possible) to 100 (best possible). From subsets of these coded values, 11 scales are derived: overall health, physical activities, development, discomfort, moods and temperaments, perceptions of current past and future health and perception of changes. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 24 [N=21]	2.59 (± 18.33)			
Week 52 [N=16]	9.24 (± 25.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 and 52 in ITQoL SF-47 – Growth and Development Score

End point title	Change from Baseline to Week 24 and 52 in ITQoL SF-47 – Growth and Development Score

End point description:

The ITQoL SF-47 consisted of 47 individual items and was filled in by the child's parent. The individual items are based on Likert scales with either 5 responses (coded as 1 through to 5) or 4 responses (coded as 1 through to 4). Before calculating a scale, the value of each item is coded so that it ranges from 0 (worst possible) to 100 (best possible). From subsets of these coded values, 11 scales are derived: overall health, physical activities, development, discomfort, moods and temperaments, perceptions of current past and future health and perception of changes. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 24 [N=21]	-0.48 (± 12.03)			
Week 52 [N=16]	3.44 (± 13.51)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 and 52 in ITQoL SF-47 – Pain Score

End point title	Change from Baseline to Week 24 and 52 in ITQoL SF-47 – Pain Score

End point description:

The ITQoL SF-47 consisted of 47 individual items and was filled in by the child's parent. The individual items are based on Likert scales with either 5 responses (coded as 1 through to 5) or 4 responses (coded as 1 through to 4). Before calculating a scale, the value of each item is coded so that it ranges from 0 (worst possible) to 100 (best possible). From subsets of these coded values, 11 scales are derived: overall health, physical activities, development, discomfort, moods and temperaments, perceptions of current past and future health and perception of changes. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 24 [N=19]	-5.26 (± 32.63)			
Week 52 [N=16]	-0.78 (± 20.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 and 52 in ITQoL SF-47 – Temperament and Moods Score

End point title	Change from Baseline to Week 24 and 52 in ITQoL SF-47 – Temperament and Moods Score

End point description:

The ITQoL SF-47 consisted of 47 individual items and was filled in by the child's parent. The individual items are based on Likert scales with either 5 responses (coded as 1 through to 5) or 4 responses (coded as 1 through to 4). Before calculating a scale, the value of each item is coded so that it ranges from 0 (worst possible) to 100 (best possible). From subsets of these coded values, 11 scales are derived: overall health, physical activities, development, discomfort, moods and temperaments, perceptions of current past and future health and perception of changes. The analysis population was

FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 24 [N=19]	-2.41 (± 15.79)			
Week 52 [N=16]	-1.56 (± 15.58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 and 52 in ITQoL SF-47 – Behaviour Score

End point title	Change from Baseline to Week 24 and 52 in ITQoL SF-47 – Behaviour Score

End point description:

The ITQoL SF-47 consisted of 47 individual items and was filled in by the child's parent. The individual items are based on Likert scales with either 5 responses (coded as 1 through to 5) or 4 responses (coded as 1 through to 4). Before calculating a scale, the value of each item is coded so that it ranges from 0 (worst possible) to 100 (best possible). From subsets of these coded values, 11 scales are derived: overall health, physical activities, development, discomfort, moods and temperaments, perceptions of current past and future health and perception of changes. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 24 [N=18]	-1.6 (± 8.01)			
Week 52 [N=14]	-0.35 (± 6.68)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 and 52 in ITQoL SF-47 – General Health Score

End point title	Change from Baseline to Week 24 and 52 in ITQoL SF-47 – General Health Score

End point description:

The ITQoL SF-47 consisted of 47 individual items and was filled in by the child's parent. The individual items are based on Likert scales with either 5 responses (coded as 1 through to 5) or 4 responses (coded as 1 through to 4). Before calculating a scale, the value of each item is coded so that it ranges from 0 (worst possible) to 100 (best possible). From subsets of these coded values, 11 scales are derived: overall health, physical activities, development, discomfort, moods and temperaments, perceptions of current past and future health and perception of changes. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 24 [N=18]	-0.32 (± 20.75)			
Week 52 [N=14]	3.57 (± 16.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 and 52 in ITQoL SF-47 – Change in Health Score

End point title	Change from Baseline to Week 24 and 52 in ITQoL SF-47 – Change in Health Score

End point description:

The ITQoL SF-47 consisted of 47 individual items and was filled in by the child's parent. The individual items are based on Likert scales with either 5 responses (coded as 1 through to 5) or 4 responses (coded as 1 through to 4). Before calculating a scale, the value of each item is coded so that it ranges from 0 (worst possible) to 100 (best possible). From subsets of these coded values, 11 scales are derived: overall health, physical activities, development, discomfort, moods and temperaments,

perceptions of current past and future health and perception of changes. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 24 [N=18]	1.39 (± 23.44)			
Week 52 [N=14]	7.14 (± 20.64)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 and 52 in ITQoL SF-47 – Parent-Emotional Impact Score

End point title	Change from Baseline to Week 24 and 52 in ITQoL SF-47 – Parent-Emotional Impact Score

End point description:

The ITQoL SF-47 consisted of 47 individual items and was filled in by the child's parent. The individual items are based on Likert scales with either 5 responses (coded as 1 through to 5) or 4 responses (coded as 1 through to 4). Before calculating a scale, the value of each item is coded so that it ranges from 0 (worst possible) to 100 (best possible). From subsets of these coded values, 11 scales are derived: overall health, physical activities, development, discomfort, moods and temperaments, perceptions of current past and future health and perception of changes. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 24 [N=18]	-1.74 (± 24.04)			
Week 52 [N=14]	5.36 (± 27.17)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 and 52 in ITQoL SF-47 – Parent-Time Impact Score

End point title	Change from Baseline to Week 24 and 52 in ITQoL SF-47 – Parent-Time Impact Score

End point description:

The ITQoL SF-47 consisted of 47 individual items and was filled in by the child's parent. The individual items are based on Likert scales with either 5 responses (coded as 1 through to 5) or 4 responses (coded as 1 through to 4). Before calculating a scale, the value of each item is coded so that it ranges from 0 (worst possible) to 100 (best possible). From subsets of these coded values, 11 scales are derived: overall health, physical activities, development, discomfort, moods and temperaments, perceptions of current past and future health and perception of changes. The analysis population was FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 24 [N=17]	15.2 (± 26.6)			
Week 52 [N=14]	6.5 (± 23.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 24 and 52 in ITQoL SF-47 – Family Cohesion Impact Score

End point title	Change from baseline to Week 24 and 52 in ITQoL SF-47 – Family Cohesion Impact Score

End point description:

The ITQoL SF-47 consisted of 47 individual items and was filled in by the child's parent. The individual items are based on Likert scales with either 5 responses (coded as 1 through to 5) or 4 responses (coded as 1 through to 4). Before calculating a scale, the value of each item is coded so that it ranges from 0 (worst possible) to 100 (best possible). From subsets of these coded values, 11 scales are derived: overall health, physical activities, development, discomfort, moods and temperaments, perceptions of current past and future health and perception of changes. The analysis population was

FAS. "N" indicates the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 24, 52

End point values	Solifenacin succinate			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 24 [N=17]	1.5 (± 16.7)			
Week 52 {N=14]	-5 (± 17.2)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug to last dose of study drug (up to 54 weeks)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	Solifenacin succinate
Reporting group description:	
Children aged 6 months to less than 5 years who received solifenacin once daily for 52 weeks.	

Serious adverse events	Solifenacin succinate		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 23 (13.04%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Teratoma			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pharyngitis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			

subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Solifenacin succinate		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 23 (47.83%)		
Investigations			
Bacterial test positive			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Burns second degree			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Joint dislocation			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Dry mouth			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Diarrhoea			

subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Enteritis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Escherichia urinary tract infection			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	4		
Otitis media			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Respiratory tract infection			

subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Urinary tract infection			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Urinary tract infection bacterial			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Urinary tract infection enterococcal			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 June 2014	Changes summarized: • Change in the planned study period: the duration of the study was increased from 4Q2014 to 3Q2015. Recruitment timeframe was extended to include children under the age of 2 years. • Change in the dosing rationale: the model used to select the drug dose was updated to a PBPK model to account for age-related physiological changes in clearance and distribution processes. • Adjustment in the automated dose volume: the volume of medication was adjusted at visit 7 and 8 if any change in weight placed the patient in a new category. The dose volume was adjusted to ensure that patients were being treated effectively as weight in young infants could have increased substantially during the study. • Added optional unscheduled urodynamic evaluation: new unscheduled urodynamic assessment was permitted 3 weeks after visit 6 (week 12). This evaluation allowed the investigator to confirm that the balance of efficacy and symptoms of intolerability had been established for patients who have had their dose adjusted at visit 6. • Revised calculation of baseline mean QT interval corrected for heart rate by Bazett's formula (QTcB): new calculations included the averages of the QTcB mean from visit 1 and 2. Previous calculations used only the QTcB mean from visit 2. This revision was done as statistical analysis of the intra-patient variation in baseline QTcB between visit 1 and visit 2 showed that a more precise estimate of QTcB could be obtained using the measurements from both visits. • Addition of medical assessment of safety profile of children: New assessment used descriptive statistics rather than formal statistics comparisons given that only a small number of patients under the age of 2 years enrolled. • Change in the lower age range of patients: the lower age limit was decreased from 2 years to 6 months. The inclusion of children from 6 months of age aligns the study with the approved PIP for solifenacin (EMEA-000573-PIP01-09).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported