Clinical trial results:
A Randomized, Double-blind, Parallel-group, Active-controlled, Multicenter Study to Evaluate the Long-term Safety and Efficacy of Combination of Solifenacin Succinate with Mirabegron Compared to Solifenacin Succinate and Mirabegron Monotherapy in Patients with Overactive Bladder

Summary

EudraCT number	2012-005736-29
Trial protocol	NL BE HU IT FI GB EE SE SK CZ LV DK SI PL ES LT BG GR
Global end of trial date	08 September 2016

Results information

Result version number	v2 (current)
This version publication date	19 July 2018
First version publication date	17 August 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	178-CL-102

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02045862
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 Europe B.V., astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Trial Disclosure, Astellas Pharma Europe B.V., astellas.resultsdisclosure@astellas.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 September 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the safety and tolerability of long-term combination treatment with solifenacin (5 mg) and mirabegron (50 mg) compared to solifenacin and mirabegron monotherapy. The study comprised a single-blind, 2-week placebo run-in period followed by a randomized, double-blind, active-controlled, 12-month treatment period and then by a 2-week follow-up period.

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	17 March 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	Canada: 71
Country: Number of subjects enrolled	United States: 311
Country: Number of subjects enrolled	Mexico: 8
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	Finland: 1
Country: Number of subjects enrolled	Germany: 94
Country: Number of subjects enrolled	Italy: 29
Country: Number of subjects enrolled	Norway: 32
Country: Number of subjects enrolled	Spain: 27
Country: Number of subjects enrolled	Sweden: 13
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Netherlands: 14
Country: Number of subjects enrolled	Bulgaria: 61
Country: Number of subjects enrolled	Czech Republic: 142

Country: Number of subjects enrolled	Estonia: 6
Country: Number of subjects enrolled	Hungary: 75
Country: Number of subjects enrolled	Latvia: 24
Country: Number of subjects enrolled	Lithuania: 39
Country: Number of subjects enrolled	Poland: 278
Country: Number of subjects enrolled	Romania: 32
Country: Number of subjects enrolled	Russian Federation: 86
Country: Number of subjects enrolled	Slovakia: 108
Country: Number of subjects enrolled	Slovenia: 2
Country: Number of subjects enrolled	Ukraine: 154
Country: Number of subjects enrolled	Malaysia: 3
Country: Number of subjects enrolled	Singapore: 8
Country: Number of subjects enrolled	Korea, Republic of: 122
Country: Number of subjects enrolled	Thailand: 4
Country: Number of subjects enrolled	Australia: 30
Country: Number of subjects enrolled	New Zealand: 12
Country: Number of subjects enrolled	South Africa: 26
Worldwide total number of subjects	1829
EEA total number of subjects	994

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	1201
From 65 to 84 years	622
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

Participants who had symptoms of "wet" overactive bladder (OAB) (urgency, urinary frequency and urgency incontinence) for ≥ 3 months were enrolled in 251 centers globally. A majority of the participants were recruited from participants who enrolled and completed studies 178-CL-101 or 905-EC-012.

Pre-assignment

Screening details:

A total of 2084 participants were screened, 2063 participants received placebo run-in treatment and 1829 participants were randomized into 1 of 3 treatment arms in a 1:1:4 ratio in the 52-week double-blind treatment period. Randomization was stratified by sex, age group (< 65 years, ≥ 65 years) and geographic region.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Mirabegron 50 mg

Arm description:

Participants received mirabegron 50 mg once a day for 52 weeks.

Arm type	Active comparator
Investigational medicinal product name	Mirabegron
Investigational medicinal product code	YM178
Other name	Myrbetriq, Myrbetric, Betanis, Betmiga
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received mirabegron 50 mg orally once a day at the same time each day.

Investigational medicinal product name	Placebo to solifenacin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received placebo to match solifenacin 5 mg orally once a day at the same time each day. This intervention was given to maintain the blind during the study.

Arm title	Solifenacin 5 mg

Arm description:

Participants received solifenacin 5 mg once a day for 52 weeks.

Arm type	Active comparator
Investigational medicinal product name	Solifenacin succinate
Investigational medicinal product code	YM905
Other name	Solifenacin, Vesicare, Vesikur, Vesitrim
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: Participants received solifenacin 5 mg orally once a day at the same time each day.	
Investigational medicinal product name	Placebo to mirabegron
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Participants received placebo to match mirabegron 50 mg orally once a day at the same time each day. This intervention was given to maintain the blind during the study.	
Arm title	Solifenacin 5 mg + mirabegron 50 mg
Arm description: Participants received solifenacin 5 mg and mirabegron 50 mg once a day for 52 weeks.	
Arm type	Experimental
Investigational medicinal product name	Mirabegron
Investigational medicinal product code	YM178
Other name	Myrbetriq, Myrbetric, Betanis, Betmiga
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Participants received mirabegron 50 mg orally once a day at the same time each day.	
Investigational medicinal product name	Solifenacin succinate
Investigational medicinal product code	YM905
Other name	Solifenacin, Vesicare, Vesikur, Vesitrim
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Participants received solifenacin 5 mg orally once a day at the same time each day.	

Number of subjects in period 1	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg
Started	306	305	1218
Treated	306	303	1210
Safety Analysis Set (SAF)	305	303	1206
Full Analysis Set (FAS)	302	299	1193
Completed	267	265	1092
Not completed	39	40	126
Lack of Efficacy	8	4	13
Adverse Event	7	5	27
Randomized but not received study drug	-	2	8
Lost to Follow-up	1	2	6
Death	-	-	1
Miscellaneous	5	-	8
Protocol Violation	-	-	6
Withdrawal by patient	18	27	57

Baseline characteristics

Reporting groups	
Reporting group title	Mirabegron 50 mg
Reporting group description:	
Participants received mirabegron 50 mg once a day for 52 weeks.	
Reporting group title	Solifenacin 5 mg
Reporting group description:	
Participants received solifenacin 5 mg once a day for 52 weeks.	
Reporting group title	Solifenacin 5 mg + mirabegron 50 mg
Reporting group description:	
Participants received solifenacin 5 mg and mirabegron 50 mg once a day for 52 weeks.	

Reporting group values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg
Number of subjects	306	305	1218
Age categorical Units: Subjects			
Age continuous			
Randomized analysis set (RAS), comprised of all randomized participants.			
Units: years			
arithmetic mean	58.8	59.0	58.3
standard deviation	± 12.7	± 13.3	± 13.0
Gender categorical			
RAS			
Units:			
Male	63	60	245
Female	243	245	973
Mean Number of Incontinence Episodes per 24 Hours			
RAS; data only available for 1818 participants [306, 303, 1209].			
Units: incontinence episodes			
arithmetic mean	3.17	3.08	3.03
standard deviation	± 3.58	± 3.56	± 3.16
Mean Number of Micturitions per 24 Hours			
RAS; data only available for 1818 participants [306, 303, 1209].			
Units: micturitions			
arithmetic mean	10.51	10.74	10.56
standard deviation	± 2.4	± 2.82	± 2.73
Mean Volume Voided per Micturition			
RAS; data only available for 1815 participants [306, 303, 1206].			
Units: mL			
arithmetic mean	161.37	159.98	158.74
standard deviation	± 59.92	± 58.58	± 58.41
Number of Incontinence Episodes per Week			
RAS; data only available for 1818 participants [306, 303, 1209].			
Units: incontinence episodes/week			

arithmetic mean	21.96	21.45	20.88
standard deviation	± 24.91	± 24.91	± 21.82
Mean Number of Urgency Incontinence Episodes per 24 Hours			
RAS; data only available for 1809 participants [306, 301, 1202]. Only participants with ≥ 1 urgency incontinence episode at baseline were included. An urgency incontinence episode is defined as the involuntary leakage of urine accompanied by or immediately proceeded by urgency.			
Units: urgency incontinence episodes			
arithmetic mean	2.88	2.89	2.74
standard deviation	± 3.32	± 3.47	± 2.78
Number of Urgency Incontinence Episodes per Week			
RAS; data only available for 1809 participants [306, 301, 1202]. Only participants with ≥ 1 urgency incontinence episode at baseline were included.			
Units: urgency incontinence episodes/week			
arithmetic mean	19.92	20.13	18.87
standard deviation	± 23.04	± 24.33	± 19.07
Mean Number of Urgency Episodes (Grade 3 or 4) per 24 Hours			
RAS; data only available for 1818 participants [306, 303, 1209]. Only participants with ≥ 1 urgency episode at baseline were included. An urgency episode is a complaint of a sudden, compelling desire to pass urine, which is difficult to defer; it is recorded when a micturition or incontinence episode is recorded and the severity of urinary urgency recorded is 3 (severe urgency) or 4 (urgency incontinence) according to the Patient Perception of Intensity of Urgency Scale (PPIUS).			
Units: urgency episodes			
arithmetic mean	6.38	6.62	6.55
standard deviation	± 4.15	± 4.07	± 3.69
Mean Number of Nocturia Episodes per 24 Hours			
RAS; data only available for 1563 participants [265, 256, 1042]. Only participants with ≥ 1 nocturia episode at baseline were included. A nocturia episode is defined as waking at night 1 or more times to void (i.e., any voiding associated with sleep disturbance between the time the participant goes to bed with the intention to sleep until the time the participant gets up in the morning with the intention to stay awake).			
Units: nocturia episodes			
arithmetic mean	1.49	1.57	1.5
standard deviation	± 0.95	± 0.94	± 0.94
Number of Nocturia Episodes per Week			
RAS; data only available for 1563 participants [265, 256, 1042]. Only participants with ≥ 1 nocturia episode at baseline were included.			
Units: nocturia episodes/week			
arithmetic mean	10.38	10.93	10.36
standard deviation	± 6.68	± 6.58	± 6.48
Mean Number of Pads Used per 24 Hours			
RAS; data only available for 1187 participants [204, 197, 786]. Only participants with ≥ 1 pad used at baseline were included.			
Units: pads			
arithmetic mean	2.49	2.75	2.57
standard deviation	± 3.74	± 3.12	± 2.58
Number of Pads Used per Week			
RAS; data only available for 1187 participants [204, 197, 786]. Only participants with ≥ 1 pad used at baseline were included.			
Units: pads/week			
arithmetic mean	17.13	19.06	17.66
standard deviation	± 25.93	± 21.84	± 17.53

Reporting group values	Total		
Number of subjects	1829		
Age categorical Units: Subjects			

Age continuous			
Randomized analysis set (RAS), comprised of all randomized participants.			
Units: years arithmetic mean standard deviation	- 		
Gender categorical			
RAS			
Units:			
Male	368		
Female	1461		
Mean Number of Incontinence Episodes per 24 Hours			
RAS; data only available for 1818 participants [306, 303, 1209].			
Units: incontinence episodes arithmetic mean standard deviation	- 		
Mean Number of Micturitions per 24 Hours			
RAS; data only available for 1818 participants [306, 303, 1209].			
Units: micturitions arithmetic mean standard deviation	- 		
Mean Volume Voided per Micturition			
RAS; data only available for 1815 participants [306, 303, 1206].			
Units: mL arithmetic mean standard deviation	- 		
Number of Incontinence Episodes per Week			
RAS; data only available for 1818 participants [306, 303, 1209].			
Units: incontinence episodes/week arithmetic mean standard deviation	- 		
Mean Number of Urgency Incontinence Episodes per 24 Hours			
RAS; data only available for 1809 participants [306, 301, 1202]. Only participants with ≥ 1 urgency incontinence episode at baseline were included. An urgency incontinence episode is defined as the involuntary leakage of urine accompanied by or immediately proceeded by urgency.			
Units: urgency incontinence episodes arithmetic mean standard deviation	- 		
Number of Urgency Incontinence Episodes per Week			
RAS; data only available for 1809 participants [306, 301, 1202]. Only participants with ≥ 1 urgency incontinence episode at baseline were included.			
Units: urgency incontinence episodes/week arithmetic mean standard deviation	- 		

Mean Number of Urgency Episodes (Grade 3 or 4) per 24 Hours			
RAS; data only available for 1818 participants [306, 303, 1209]. Only participants with ≥ 1 urgency episode at baseline were included. An urgency episode is a complaint of a sudden, compelling desire to pass urine, which is difficult to defer; it is recorded when a micturition or incontinence episode is recorded and the severity of urinary urgency recorded is 3 (severe urgency) or 4 (urgency incontinence) according to the Patient Perception of Intensity of Urgency Scale (PPIUS).			
Units: urgency episodes arithmetic mean standard deviation	- -		
Mean Number of Nocturia Episodes per 24 Hours			
RAS; data only available for 1563 participants [265, 256, 1042]. Only participants with ≥ 1 nocturia episode at baseline were included. A nocturia episode is defined as waking at night 1 or more times to void (i.e., any voiding associated with sleep disturbance between the time the participant goes to bed with the intention to sleep until the time the participant gets up in the morning with the intention to stay awake).			
Units: nocturia episodes arithmetic mean standard deviation	- -		
Number of Nocturia Episodes per Week			
RAS; data only available for 1563 participants [265, 256, 1042]. Only participants with ≥ 1 nocturia episode at baseline were included.			
Units: nocturia episodes/week arithmetic mean standard deviation	- -		
Mean Number of Pads Used per 24 Hours			
RAS; data only available for 1187 participants [204, 197, 786]. Only participants with ≥ 1 pad used at baseline were included.			
Units: pads arithmetic mean standard deviation	- -		
Number of Pads Used per Week			
RAS; data only available for 1187 participants [204, 197, 786]. Only participants with ≥ 1 pad used at baseline were included.			
Units: pads/week arithmetic mean standard deviation	- -		

End points

End points reporting groups

Reporting group title	Mirabegron 50 mg
Reporting group description:	
Participants received mirabegron 50 mg once a day for 52 weeks.	
Reporting group title	Solifenacin 5 mg
Reporting group description:	
Participants received solifenacin 5 mg once a day for 52 weeks.	
Reporting group title	Solifenacin 5 mg + mirabegron 50 mg
Reporting group description:	
Participants received solifenacin 5 mg and mirabegron 50 mg once a day for 52 weeks.	

Primary: Number of Participants with Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Participants with Treatment-Emergent Adverse Events (TEAEs)[1]

End point description:

A TEAE is defined as an adverse event (AE) observed after taking the first dose of double-blind treatment until 14 days after taking the last dose of double-blind treatment for non-serious AEs and until 30 days after taking the last dose of double-blind treatment for serious adverse events (SAEs). This includes abnormal laboratory tests, vital signs or electrocardiogram data that were defined as AEs if the abnormality induced clinical signs or symptoms, required active intervention, interruption or discontinuation of study drug or was clinically significant in the investigator's opinion. The severity of an AE was measured by: Mild (No disruption of normal daily activities); Moderate (Affected normal daily activities) and Severe (Inability to perform daily activities). The analysis population was the Safety Analysis Set (SAF), which consisted of all participants who received ≥ 1 dose of double-blind study drug and excluded participants from one site due to protocol noncompliance.

End point type	Primary

End point timeframe:

From first dose of double-blind study drug up to 30 days after last dose of double-blind study drug (up to 56 weeks)

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: There were no pre-determined hypothesis or comparative statistical analyses performed on the primary safety endpoint. However, hypothesis testing was performed for the primary and secondary efficacy endpoints.

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	305	303	1206	
Units: participants				
Any TEAEs	126	134	596	
Mild TEAEs	61	69	306	
Moderate TEAEs	52	58	238	
Severe TEAEs	13	7	52	
Drug-related TEAEs	35	42	200	
Serious TEAEs	8	8	51	
Drug-related serious TEAEs	1	0	0	
TEAEs leading to discontiuation of study drug	7	5	25	

Drug-related TEAEs leading to discont. of drug	4	4	17	
TEAEs leading to death	0	0	1	

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline to End of Treatment (EoT) in Mean Number of Incontinence Episodes per 24 Hours

End point title	Change from Baseline to End of Treatment (EoT) in Mean Number of Incontinence Episodes per 24 Hours

End point description:

An incontinence episode is defined as the complaint of any involuntary leakage of urine. The mean number of incontinence episodes per 24 hours was calculated from data recorded by the participant in a micturition diary for 7 days prior to the baseline and week 52 clinic visits. The analysis population was the Full Analysis Set (FAS), which was comprised of all randomized participants who took ≥ 1 dose of double-blind treatment, reported ≥ 1 micturition in the baseline diary and ≥ 1 micturition postbaseline, reported ≥ 1 incontinence episode in the baseline diary and excluded participants from 2 sites due to protocol noncompliance and data integrity issues. Last observation carried forward (LOCF) was used for EoT.

End point type	Primary

End point timeframe:

Baseline and Week 52

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	301	297	1184	
Units: incontinence episodes				
least squares mean (standard error)	-1.58 (± 0.11)	-1.90 (± 0.11)	-2.03 (± 0.05)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg

Statistical analysis description:

Difference of the adjusted mean (i.e., least squares mean) was calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg + mirabegron 50 mg v Mirabegron 50 mg

Number of subjects included in analysis	1485
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [2]
Method	Stratified rank ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	-0.21
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[2] - The 2-sided P value was for pairwise comparisons between the combination therapy group and the corresponding monotherapy group from the stratified rank ANCOVA.

Statistical analysis title	Difference vs. Solifenacin 5 mg

Statistical analysis description:

Difference of the adjusted mean (i.e., least squares mean) was calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1481
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [3]
Method	Stratified rank ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.37
upper limit	0.11
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[3] - The 2-sided P value was for pairwise comparisons between the combination therapy group and the corresponding monotherapy group from the stratified rank ANCOVA.

Primary: Change from Baseline to EoT in Mean Number of Micturitions per 24 Hours

End point title	Change from Baseline to EoT in Mean Number of Micturitions per 24 Hours

End point description:

A micturition is defined as any voluntary micturition (excluding incontinence only episodes). The mean number of micturitions per 24 hours was calculated from data recorded by the participant in a micturition diary for 7-days before the baseline and week 52 clinic visits. The analysis population was the FAS. LOCF was used for EoT.

End point type	Primary

End point timeframe:

Baseline and Week 52

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	301	297	1184	
Units: micturitions				
least squares mean (standard error)	-2.10 (± 0.13)	-2.16 (± 0.13)	-2.58 (± 0.07)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg

Statistical analysis description:

Difference of the adjusted mean (i.e., least squares mean) was calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1485
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [4]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.77
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[4] - The 2-sided P value was for pairwise comparisons between the combination therapy group and the corresponding monotherapy group from the ANCOVA model.

Statistical analysis title	Difference vs. Solifenacin 5 mg

Statistical analysis description:

Difference of the adjusted mean (i.e., least squares mean) was calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg

Number of subjects included in analysis	1481
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [5]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	-0.13
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[5] - The 2-sided P value was for pairwise comparisons between the combination therapy group and the corresponding monotherapy group from the ANCOVA model.

Secondary: Change from Baseline to EoT in Mean Volume Voided per Micturition

End point title	Change from Baseline to EoT in Mean Volume Voided per Micturition

End point description:

The mean volume voided per micturition was calculated from the data recorded by the participant during 3 consecutive days with volume measurements during the 7-day micturition diary period. The analysis population was the FAS, with baseline and at least one post-baseline measurement. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	289	293	1162	
Units: mL				
least squares mean (standard error)	21.83 (± 3.12)	24.90 (± 3.10)	37.67 (± 1.55)	

Statistical analyses

Statistical analysis title	Difference vs. Solifenacin 5 mg

Statistical analysis description:

Difference of the adjusted mean (i.e., least squares mean) was calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg

Number of subjects included in analysis	1455
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	12.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.98
upper limit	19.57
Variability estimate	Standard error of the mean
Dispersion value	3.47

Statistical analysis title	Difference vs. Mirabegron 50 mg

Statistical analysis description:

Difference of the adjusted mean (i.e., least squares mean) was calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1451
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	15.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.99
upper limit	22.69
Variability estimate	Standard error of the mean
Dispersion value	3.49

Secondary: Change from Baseline to EoT in OAB Questionnaire (OAB-q) Symptom Bother Score

End point title	Change from Baseline to EoT in OAB Questionnaire (OAB-q) Symptom Bother Score

End point description:

The OAB-q is a self-reported questionnaire with items relating to symptom bother and health-related quality of life (HRQoL). The symptom bother portion consists of 8 items, rated on a 6-point Likert scale (1 through 6). The total symptom bother score was calculated from the 8 answers and then transformed to range from 0 (least severity) to 100 (worst severity). A negative change from baseline indicates an improvement. The analysis population was the FAS, with baseline and at least one post-baseline measurement. LOCF was used for EoT.

End point type	Secondary
End point timeframe:	
Baseline and Week 52	

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	290	294	1163	
Units: units on a scale				
least squares mean (standard error)	-21.96 (± 1.14)	-24.91 (± 1.13)	-29.51 (± 0.57)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg

Statistical analysis description:

Difference of the adjusted mean (i.e., least squares mean) was calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1453
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-7.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.05
upper limit	-5.05
Variability estimate	Standard error of the mean
Dispersion value	1.27

Statistical analysis title	Difference vs. Solifenacin 5 mg

Statistical analysis description:

Difference of the adjusted mean (i.e., least squares mean) was calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg

Number of subjects included in analysis	1457
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.09
upper limit	-2.12
Variability estimate	Standard error of the mean
Dispersion value	1.27

Secondary: Change from Baseline to EoT in the Patient's Assessment of Treatment Satisfaction-Visual Analogue Scale (TS-VAS)

End point title	Change from Baseline to EoT in the Patient's Assessment of Treatment Satisfaction-Visual Analogue Scale (TS-VAS)

End point description:

The TS-VAS is a visual analogue scale which asks participants to rate their satisfaction with the treatment by placing a vertical mark on a line that runs from 0 (No, not at all) on the left to 10 (Yes, completely) on the right. A positive change from baseline indicated improvement. The analysis population was the FAS, with baseline and at least one post-baseline measurement. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	289	294	1163	
Units: units on a scale				
least squares mean (standard error)	2.19 (± 0.12)	2.15 (± 0.12)	2.73 (± 0.06)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg

Statistical analysis description:

Difference of the adjusted mean (i.e., least squares mean) was calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1452
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	0.82
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Difference vs. Solifenacin 5 mg

Statistical analysis description:

Difference of the adjusted mean (i.e., least squares mean) was calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1457
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	0.86
Variability estimate	Standard error of the mean
Dispersion value	0.14

Secondary: Change from Baseline to Months 1, 3, 6, 9 and 12 in Mean Number of Incontinence Episodes per 24 Hours

End point title	Change from Baseline to Months 1, 3, 6, 9 and 12 in Mean Number of Incontinence Episodes per 24 Hours

End point description:

An incontinence episode was defined as the complaint of any involuntary leakage of urine. The mean number of incontinence episodes per 24 hours was calculated from data recorded by the participant in a micturition diary for 7 days prior to the baseline and prior to each visit. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: incontinence episodes				
least squares mean (standard error)				
Month 1 [N=291, 288, 1158]	-0.97 (± 0.10)	-1.29 (± 0.11)	-1.45 (± 0.05)	
Month 3 [N=282, 288, 1137]	-1.31 (± 0.11)	-1.71 (± 0.11)	-1.78 (± 0.05)	
Month 6 [N=266, 273, 1107]	-1.42 (± 0.11)	-1.78 (± 0.11)	-1.93 (± 0.05)	
Month 9 [N=264, 261, 1070]	-1.53 (± 0.11)	-1.90 (± 0.11)	-2.00 (± 0.06)	
Month 12 [N=258, 256, 1048]	-1.67 (± 0.11)	-1.92 (± 0.11)	-2.06 (± 0.06)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Incontinence Episodes Reported During the 7-Day Micturition Diary Period Prior to Each Visit (at Months 1, 3, 6, 9, 12 and EoT)

End point title	Number of Incontinence Episodes Reported During the 7-Day Micturition Diary Period Prior to Each Visit (at Months 1, 3, 6, 9, 12 and EoT)

End point description:

An incontinence episode was defined as the complaint of any involuntary leakage of urine. The number of incontinence episodes was the total number of times a participant recorded an incontinence episode during the 7-day micturition diary period prior to each visit. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: incontinence episodes				
arithmetic mean (standard error)				
Month 1 [N=291, 288, 1158]	14.88 (± 1.52)	12.41 (± 1.22)	10.80 (± 0.58)	
Month 3 [N=282, 288, 1137]	12.23 (± 1.12)	9.23 (± 1.02)	8.33 (± 0.52)	
Month 6 [N=266, 273, 1107]	10.62 (± 1.08)	8.18 (± 1.01)	7.28 (± 0.48)	
Month 9 [N=264, 261, 1070]	10.53 (± 1.19)	7.28 (± 0.91)	6.74 (± 0.45)	

Month 12 [N=258, 266, 1048]	9.09 (± 1.10)	7.06 (± 0.94)	6.10 (± 0.46)	
EoT [N=301, 297, 1184]	10.32 (± 1.08)	8.09 (± 0.94)	6.85 (± 0.47)	

Statistical analyses

Statistical analysis title	Rate ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Rate ratio of number of incontinence episodes during the EoT 7-day diary between the combination therapy group and the mirabegron monotherapy group is calculated from a negative binomial regression model incl. treatment group, sex, age group (< 65, ≥ 65 years), geographic region and previous study history as factors, log(number of incontinence episodes divided by number of valid diary days) at baseline included as a covariate and number of valid diary day at EoT as the offset variable.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed Effects Poisson-negative binomial
Parameter estimate	Rate ratio
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	0.84
Variability estimate	Standard error of the mean
Dispersion value	0.12

Statistical analysis title	Rate ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Rate ratio of number of incontinence episodes during the EoT 7-day diary between the combination therapy group and the solifenacin monotherapy group is calculated from a negative binomial regression model incl. treatment group, sex, age group (< 65, ≥ 65 years), geographic region and previous study history as factors, log(number of incontinence episodes divided by number of valid diary days) at baseline included as a covariate and number of valid diary day at EoT as the offset variable.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029
Method	Mixed Effects Poisson-negative binomial
Parameter estimate	Rate ratio
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	0.97

Variability estimate	Standard error of the mean
Dispersion value	0.12

Secondary: Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Number of Incontinence Episodes Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point title	Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Number of Incontinence Episodes Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point description:

An incontinence episode was defined as the complaint of any involuntary leakage of urine. The number of incontinence episodes was the total number of times a participant recorded an incontinence episode during the 7-day micturition diary period prior to each visit. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: incontinence episodes				
least squares mean (standard error)				
Month 1 [N=291, 288, 1158]	-6.77 (± 0.73)	-9.17 (± 0.73)	-10.31 (± 0.36)	
Month 3 [N=282, 288, 1137]	-9.21 (± 0.76)	-12.05 (± 0.75)	-12.55 (± 0.38)	
Month 6 [N=266, 273, 1107]	-10.36 (± 0.76)	-12.50 (± 0.75)	-13.49 (± 0.37)	
Month 9 [N=264, 261, 1070]	-10.62 (± 0.76)	-13.51 (± 0.77)	-14.06 (± 0.38)	
Month 12 [N=258, 256, 1048]	-11.84 (± 0.77)	-13.47 (± 0.77)	-14.43 (± 0.38)	
EoT [N=301, 297, 1184]	-11.17 (± 0.75)	-13.37 (± 0.75)	-14.29 (± 0.37)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg

Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Stratified rank ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-3.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.76
upper limit	-1.49
Variability estimate	Standard error of the mean
Dispersion value	0.83

Statistical analysis title	Difference vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Stratified rank ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.57
upper limit	0.72
Variability estimate	Standard error of the mean
Dispersion value	0.84

Secondary: Number of Incontinence-Free Days Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point title	Number of Incontinence-Free Days Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point description:

The number of incontinence-free days was the number of valid diary days during the 7-day micturition diary period with no incontinence episodes recorded. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: incontinence-free days				
arithmetic mean (standard error)				
Month 1 [N=291, 288, 1158]	2.73 (± 0.15)	3.35 (± 0.17)	3.46 (± 0.08)	
Month 3 [N=282, 288, 1137]	3.30 (± 0.17)	3.98 (± 0.17)	4.17 (± 0.08)	
Month 6 [N=266, 273, 1107]	3.64 (± 0.17)	4.08 (± 0.17)	4.44 (± 0.08)	
Month 9 [N=264, 261, 1070]	3.97 (± 0.18)	4.33 (± 0.17)	4.56 (± 0.08)	
Month 12 [N=258, 256, 1048]	4.23 (± 0.18)	4.50 (± 0.18)	4.81 (± 0.08)	
EoT [N=301, 297, 1184]	3.98 (± 0.17)	4.29 (± 0.16)	4.64 (± 0.08)	

Statistical analyses

Statistical analysis title	Odds ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Odds ratio is from a overdispersed binomial regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and log transformed baseline mean number of incontinence episodes per 24 hours as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Overdispersed binomial regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.26
upper limit	2.01

Statistical analysis title	Odds ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Odds ratio is from a overdispersed binomial regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and log transformed baseline mean number of incontinence episodes per 24 hours as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg

Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	Overdispersed binomial regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	1.75

Secondary: Number of Incontinence-Free Days with < 8 Micturitions per Day Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point title	Number of Incontinence-Free Days with < 8 Micturitions per Day Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point description:

The number of incontinence-free days with < 8 micturitions per day was the number of valid diary days during the 7-day micturition diary period with no incontinence episodes recorded and with < 8 micturitions per day. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: days				
arithmetic mean (standard error)				
Month 1 [N=291, 288, 1158]	1.03 (± 0.11)	1.01 (± 0.10)	1.33 (± 0.06)	
Month 3 [N=282, 288, 1137]	1.24 (± 0.12)	1.48 (± 0.13)	1.91 (± 0.07)	
Month 6 [N=266, 273, 1107]	1.56 (± 0.14)	1.66 (± 0.14)	2.13 (± 0.08)	
Month 9 [N=264, 261, 1070]	1.56 (± 0.14)	1.64 (± 0.14)	2.20 (± 0.08)	
Month 12 [N=258, 256, 1048]	1.87 (± 0.15)	1.92 (± 0.15)	2.54 (± 0.08)	
EoT [N=301, 297, 1184]	1.75 (± 0.14)	1.90 (± 0.14)	2.43 (± 0.07)	

Statistical analyses

Statistical analysis title	Odds ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Odds ratio is from a overdispersed binomial regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and log transformed baseline mean number of incontinence episodes per 24 hours and baseline mean number of micturitions per 24 hours as a covariates.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Overdispersed binomial regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.14
upper limit	1.85

Statistical analysis title	Odds ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Odds ratio is from a overdispersed binomial regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and log transformed baseline mean number of incontinence episodes per 24 hours and baseline mean number of micturitions per 24 hours as a covariates.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Overdispersed binomial regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.26
upper limit	2.05

Secondary: Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Mean Number of Urgency Incontinence Episodes per 24 Hours

End point title	Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Mean Number of Urgency Incontinence Episodes per 24 Hours

End point description:

An urgency incontinence episode was defined as the involuntary leakage of urine accompanied by or immediately preceded by urgency. The mean number of urgency incontinence episodes was calculated from data recorded by the participant in a micturition diary for 7 days prior to each visit. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. Only participants with ≥ 1 urgency incontinence episode at baseline were included in the analysis. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	297	1187	
Units: urgency incontinence episodes				
least squares mean (standard error)				
Month 1 [N=291, 286, 1152]	-0.93 (± 0.10)	-1.25 (± 0.10)	-1.43 (± 0.05)	
Month 3 [N=282, 286, 1132]	-1.30 (± 0.10)	-1.64 (± 0.10)	-1.71 (± 0.05)	
Month 6 [N=266, 271, 1101]	-1.40 (± 0.10)	-1.67 (± 0.10)	-1.86 (± 0.05)	
Month 9 [N=264, 259, 1066]	-1.60 (± 0.11)	-1.78 (± 0.11)	-1.92 (± 0.05)	
Month 12 [N=258, 254, 1043]	-1.60 (± 0.10)	-1.82 (± 0.10)	-1.98 (± 0.05)	
EoT [N=301, 295, 1178]	-1.51 (± 0.10)	-1.81 (± 0.10)	-1.94 (± 0.05)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [6]
Method	Stratified rank ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	-0.21
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[6] - The two-sided p-value is for pairwise comparisons between the combination therapy group and the solifenacin monotherapy group from stratified rank ANCOVA.

Statistical analysis title	Difference vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin

monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1484
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009 [7]
Method	Stratified rank ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[7] - The two-sided p-value is for pairwise comparisons between the combination therapy group and the solifenacin monotherapy group from stratified rank ANCOVA.

Secondary: Number of Urgency Incontinence Episodes Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point title	Number of Urgency Incontinence Episodes Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point description:

An urgency incontinence episode was defined as the involuntary leakage of urine accompanied by or immediately preceded by urgency. The number of urgency incontinence episodes was the total number of urgency incontinence episodes recorded by the participant during the 7-day micturition diary period prior to each visit. The analysis population was the FAS. Only participants with ≥ 1 urgency incontinence episode at baseline were included in the analysis. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	297	1187	
Units: urgency incontinence episodes				
arithmetic mean (standard error)				
Month 1 [N=291, 286, 1152]	13.14 (± 1.42)	11.21 (± 1.19)	8.99 (± 0.47)	
Month 3 [N=282, 286, 1132]	10.37 (± 1.00)	8.12 (± 0.98)	6.95 (± 0.44)	
Month 6 [N=266, 271, 1101]	8.97 (± 0.95)	7.31 (± 0.96)	5.88 (± 0.41)	
Month 9 [N=264, 259, 1066]	8.08 (± 1.01)	6.51 (± 0.89)	5.47 (± 0.40)	
Month 12 [N=258, 254, 1043]	7.73 (± 1.00)	6.06 (± 0.85)	4.88 (± 0.38)	
EoT [N=301, 295, 1178]	8.86 (± 0.98)	7.04 (± 0.86)	5.57 (± 0.40)	

Statistical analyses

Statistical analysis title	Rate ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Rate ratio of number of incontinence episodes during the EoT 7-day diary between the combination therapy group and the mirabegron monotherapy group is calculated from a negative binomial regression model incl. treatment group, sex, age group (< 65, ≥65 years), geographic region and previous study history as factors, log(number of urgency incontinence episodes divided by number of valid diary days) included as a covariate and post baseline number of valid diary days at EoT as the offset variable.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Negative binomial regression
Parameter estimate	Rate ratio
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	0.79
Variability estimate	Standard error of the mean
Dispersion value	0.13

Statistical analysis title	Rate ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Rate ratio of number of incontinence episodes during the EoT 7-day diary between the combination therapy group and the solifenacin monotherapy group is calculated from a negative binomial regression model incl. treatment group, sex, age group (< 65, ≥ 65 years), geographic region and previous study history as factors, log(number of urgency incontinence episodes divided by number of valid diary days) included as a covariate and post baseline number of valid diary day at EoT as the offset variable

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1484
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.023
Method	Negative binomial regression
Parameter estimate	Rate ratio
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	0.96

Variability estimate	Standard error of the mean
Dispersion value	0.13

Secondary: Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Number of Urgency Incontinence Episodes Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point title	Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Number of Urgency Incontinence Episodes Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point description:

An urgency incontinence episode was defined as the involuntary leakage of urine accompanied by or immediately preceded by urgency. The number of urgency incontinence episodes was the total number of urgency incontinence episodes recorded by the participant during the 7-day micturition diary period prior to each visit. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. Only participants with ≥ 1 urgency incontinence episode at baseline were included in the analysis. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: urgency incontinence episodes				
least squares mean (standard error)				
Month 1 [N=291, 286, 1152]	-6.45 (± 0.69)	-8.77 (± 0.69)	-10.10 (± 0.34)	
Month 3 [N=282, 286, 1132]	-9.06 (± 0.72)	-11.48 (± 0.71)	-11.99 (± 0.36)	
Month 6 [N=266, 271, 1101]	-10.09 (± 0.72)	-11.71 (± 0.71)	-13.00 (± 0.35)	
Month 9 [N=264, 259, 1066]	-11.10 (± 0.72)	-12.60 (± 0.73)	-13.44 (± 0.36)	
Month 12 [N=258, 254, 1043]	-11.27 (± 0.71)	-12.80 (± 0.71)	-13.80 (± 0.35)	
EoT [N=301, 295, 1178]	-10.61 (± 0.70)	-12.66 (± 0.70)	-13.59 (± 0.35)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg

Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [8]
Method	Stratified rank ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-2.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.51
upper limit	-1.46
Variability estimate	Standard error of the mean
Dispersion value	0.78

Notes:

[8] - The 2-sided P value was for pairwise comparisons between the combination therapy group and the corresponding monotherapy group from the stratified rank ANCOVA.

Statistical analysis title	Difference vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006 [9]
Method	Stratified rank ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.47
upper limit	0.61
Variability estimate	Standard error of the mean
Dispersion value	0.78

Notes:

[9] - The 2-sided P value was for pairwise comparisons between the combination therapy group and the corresponding monotherapy group from the stratified rank ANCOVA.

Secondary: Change from Baseline to Months 1, 3, 6, 9 and 12 in Mean Number of Micturitions per 24 Hours

End point title	Change from Baseline to Months 1, 3, 6, 9 and 12 in Mean Number of Micturitions per 24 Hours

End point description:

A micturition was defined as any voluntary urination (excluding incontinence only episodes). The mean number of micturitions per 24 hours was calculated from data recorded by the participant in a micturition diary for 7-days before the baseline and prior to each visit. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: micturitions				
least squares mean (standard error)				
Month 1 [N=291, 288, 1158]	-1.09 (± 0.12)	-1.36 (± 0.12)	-1.64 (± 0.06)	
Month 3 [N=282, 288, 1137]	-1.63 (± 0.13)	-1.87 (± 0.12)	-2.16 (± 0.06)	
Month 6 [N=266, 273, 1107]	-1.85 (± 0.13)	-2.04 (± 0.13)	-2.39 (± 0.06)	
Month 9 [N=264, 261, 1070]	-2.03 (± 0.13)	-2.03 (± 0.13)	-2.42 (± 0.06)	
Month 12 [N=258, 256, 1048]	-2.20 (± 0.13)	-2.13 (± 0.14)	-2.64 (± 0.07)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Days with < 8 Micturitions per Day Reported During the 7-Day Micturition Diary Period Prior to Each Visit (at Months 1, 3, 6, 9, 12 and EoT)

End point title	Number of Days with < 8 Micturitions per Day Reported During the 7-Day Micturition Diary Period Prior to Each Visit (at Months 1, 3, 6, 9, 12 and EoT)

End point description:

The number of days with < 8 micturitions was the number of valid diary days during the 7-day micturition diary period with with less than 8 micturitions per day. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: days				
arithmetic mean (standard error)				
Month 1 [N=291, 288, 1158]	1.90 (± 0.13)	1.60 (± 0.12)	2.08 (± 0.07)	
Month 3 [N=282, 288, 1137]	2.07 (± 0.14)	2.14 (± 0.14)	2.66 (± 0.08)	
Month 6 [N=266, 273, 1107]	2.35 (± 0.15)	2.34 (± 0.15)	2.87 (± 0.08)	
Month 9 [N=264, 261, 1070]	2.38 (± 0.16)	2.33 (± 0.15)	2.93 (± 0.08)	
Month 12 [N=258, 256, 1048]	2.61 (± 0.16)	2.58 (± 0.16)	3.17 (± 0.08)	
EoT [N=301, 297, 1184]	2.52 (± 0.15)	2.58 (± 0.15)	3.10 (± 0.08)	

Statistical analyses

Statistical analysis title	Odds ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Odds ratio is from a overdispersed binomial regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of micturitions per 24 hours as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	Overdispersed binomial regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.09
upper limit	1.73

Statistical analysis title	Odds ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Odds ratio is from a overdispersed binomial regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of micturitions per 24 hours as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Overdispersed binomial regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.14
upper limit	1.8

Secondary: Change from Baseline to EoT in Corrected Micturition Frequency

End point title	Change from Baseline to EoT in Corrected Micturition Frequency

End point description:

Corrected micturition frequency was defined as the mean number of micturitions per 24 hours that participants had at end of treatment if their fluid intake had remained unchanged since baseline. Corrected micturition frequency was calculated as the baseline mean volume voided per micturition multiplied by the baseline mean number of micturitions per 24 hours divided by the mean volume voided per micturition at EoT. The analysis population was the FAS. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Month 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	301	297	1184	
Units: micturitions				
least squares mean (standard error)	-0.72 (± 0.17)	-1.11 (± 0.17)	-1.51 (± 0.08)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline mean number of micturitions per 24 hours as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1485
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.16
upper limit	-0.41
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Difference vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline mean number of micturitions per 24 hours as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1481
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.037
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.77
upper limit	-0.02
Variability estimate	Standard error of the mean
Dispersion value	0.19

Secondary: Change from Baseline to Months 3, 6 and 12 in Mean Volume Voided per Micturition

End point title	Change from Baseline to Months 3, 6 and 12 in Mean Volume Voided per Micturition

End point description:

The mean volume voided per micturition was calculated from the data recorded by the participant during 3 consecutive days with volume measurements during the 7-day micturition diary period prior to each visit. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point.

End point type	Secondary

End point timeframe:

Baseline and Months 3, 6, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: mL				
least squares mean (standard error)				
Month 3 [N=274, 280, 1125]	15.34 (± 2.96)	23.71 (± 2.92)	34.89 (± 1.45)	
Month 6 [N=265, 268, 1102]	20.87 (± 3.21)	27.08 (± 3.19)	38.56 (± 1.57)	
Month 12 [N=248, 254, 1028]	21.85 (± 3.42)	24.05 (± 3.37)	38.72 (± 1.67)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Mean Number of Urgency Episodes (Grade 3 or 4) per 24 Hours

End point title	Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Mean Number of Urgency Episodes (Grade 3 or 4) per 24 Hours

End point description:

Urgency was defined as a complaint of a sudden, compelling desire to pass urine, which is difficult to defer. An urgency episode was defined as any micturition or incontinence episode recorded by the participant in the micturition diary for 7 days prior to each visit as 3 or 4 on the Patient Perception of Intensity of Urgency Scale (PPIUS), where 0 = No urgency; 1 = Mild urgency; 2 = Moderate urgency, could delay voiding a short while; 3 = Severe urgency, could not delay voiding; 4 = Urge incontinence, leaked before arriving to the toilet. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. Only participants with ≥ 1 urgency episode at baseline were included in the analysis. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: urgency episodes				
least squares mean (standard error)				
Month 1 [N=291, 288, 1158]	-1.93 (± 0.17)	-2.31 (± 0.17)	-2.68 (± 0.09)	
Month 3 [N=282, 288, 1137]	-2.68 (± 0.17)	-3.02 (± 0.17)	-3.36 (± 0.08)	
Month 6 [N=266, 273, 1107]	-2.93 (± 0.17)	-3.17 (± 0.17)	-3.72 (± 0.08)	
Month 9 [N=264, 261, 1070]	-3.40 (± 0.18)	-3.55 (± 0.18)	-3.87 (± 0.09)	
Month 12 [N=258, 256, 1048]	-3.40 (± 0.17)	-3.56 (± 0.17)	-3.95 (± 0.09)	
EoT [N=301, 297, 1184]	-3.11 (± 0.17)	-3.45 (± 0.17)	-3.84 (± 0.08)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg

Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.37
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Difference vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	-0.03
Variability estimate	Standard error of the mean
Dispersion value	0.19

Secondary: Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Mean Number of Nocturia Episodes per 24 Hours

End point title	Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Mean Number of Nocturia Episodes per 24 Hours

End point description:

A nocturia episode was defined as waking at night 1 or more times to void (i.e., any voiding associated with sleep disturbance between the time the participant goes to bed with the intention to sleep until the time the participant gets up in the morning with the intention to stay awake). The mean number of nocturia episodes was calculated from data recorded by the participant in the micturition diary for 7 days prior to each visit. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. Only participants with ≥ 1 nocturia episode at baseline were included in the analysis. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	262	252	1027	
Units: nocturia episodes				
least squares mean (standard error)				
Month 1 [N=253, 244, 1000]	-0.20 (± 0.04)	-0.22 (± 0.04)	-0.34 (± 0.02)	
Month 3 [N=247, 244, 985]	-0.34 (± 0.04)	-0.38 (± 0.04)	-0.46 (± 0.02)	
Month 6 [N=231, 231, 958]	-0.41 (± 0.05)	-0.39 (± 0.05)	-0.49 (± 0.02)	
Month 9 [N=229, 221, 927]	-0.42 (± 0.05)	-0.44 (± 0.05)	-0.50 (± 0.02)	
Month 12 [N=225, 217, 906]	-0.46 (± 0.05)	-0.44 (± 0.05)	-0.56 (± 0.02)	
EoT [N=262, 251, 1023]	-0.45 (± 0.04)	-0.45 (± 0.04)	-0.55 (± 0.02)	

Statistical analyses

Statistical analysis title	Difference vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1279
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.068
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Difference vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron

monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1289
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.059
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.05

Secondary: Number of Nocturia Episodes Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point title	Number of Nocturia Episodes Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point description:

A nocturia episode was defined as waking at night 1 or more times to void (i.e., any voiding associated with sleep disturbance between the time the participant goes to bed with the intention to sleep until the time the participant gets up in the morning with the intention to stay awake). The number of nocturia episodes was the number of times a participant recorded a nocturia episode during the 7-day micturition diary period prior to each visit. The analysis population was the FAS. Only participants with ≥ 1 nocturia episode at baseline were included in the analysis. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	262	252	1027	
Units: nocturia episodes				
arithmetic mean (standard error)				
Month 1 [N=253, 244, 1000]	8.76 (± 0.41)	9.23 (± 0.44)	8.00 (± 0.20)	
Month 3 [N=247, 244, 985]	7.93 (± 0.39)	7.92 (± 0.40)	7.17 (± 0.19)	
Month 6 [N=231, 231, 958]	7.12 (± 0.35)	7.86 (± 0.43)	6.96 (± 0.20)	
Month 9 [N=229, 221, 927]	7.40 (± 0.38)	7.48 (± 0.41)	6.84 (± 0.20)	
Month 12 [N=225, 217, 906]	6.88 (± 0.38)	7.39 (± 0.44)	6.33 (± 0.19)	
EoT [N=262, 251, 1023]	7.13 (± 0.37)	7.47 (± 0.42)	6.51 (± 0.19)	

Statistical analyses

Statistical analysis title	Rate ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Rate ratio of number of nocturia episodes during the EoT 7-day diary between the combination therapy group and the mirabegron monotherapy group is calculated from a negative binomial regression model incl. treatment group, sex, age group (< 65, ≥ 65 years), geographic region and previous study history as factors, log(number of nocturia episodes divided by number of valid diary days) included as a covariate and post baseline number of valid diary days as the offset variable.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1289
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.067
Method	Negative binomial regression
Parameter estimate	Rate ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.01
Variability estimate	Standard error of the mean
Dispersion value	0.06

Statistical analysis title	Rate ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Rate ratio of number of nocturia episodes during the EoT 7-day diary between the combination therapy group and the solifenacin monotherapy group is calculated from a negative binomial regression model incl. treatment group, sex, age group (< 65, ≥ 65 years), geographic region and previous study history as factors, log(number of nocturia episodes divided by number of valid diary days) included as a covariate and post baseline number of valid diary day as the offset variable.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1279
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.131
Method	Negative binomial regression
Parameter estimate	Rate ratio
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.03

Variability estimate	Standard error of the mean
Dispersion value	0.06

Secondary: Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Number of Nocturia Episodes Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point title	Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Number of Nocturia Episodes Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point description:

A nocturia episode was defined as waking at night 1 or more times to void (i.e., any voiding associated with sleep disturbance between the time the participant goes to bed with the intention to sleep until the time the participant gets up in the morning with the intention to stay awake). The number of nocturia episodes was the number of times a participant recorded a nocturia episode during the 7-day micturition diary period prior to each visit. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. Only participants with ≥ 1 nocturia episode at baseline were included in the analysis. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	262	252	1027	
Units: nocturia episodes				
least squares mean (standard error)				
Month 1 [N=253, 244, 1000]	-1.56 (± 0.29)	-1.58 (± 0.29)	-2.39 (± 0.15)	
Month 3 [N=247, 244, 985]	-2.45 (± 0.29)	-2.78 (± 0.30)	-3.26 (± 0.15)	
Month 6 [N=231, 231, 958]	-3.08 (± 0.33)	-2.81 (± 0.33)	-3.44 (± 0.16)	
Month 9 [N=229, 221, 927]	-2.91 (± 0.32)	-3.13 (± 0.32)	-3.55 (± 0.16)	
Month 12 [N=225, 217, 906]	-3.29 (± 0.32)	-3.08 (± 0.33)	-3.97 (± 0.16)	
EoT [N=262, 251, 1023]	-3.24 (± 0.31)	-3.20 (± 0.32)	-3.90 (± 0.16)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg

Number of subjects included in analysis	1289
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.055
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.34
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.35

Statistical analysis title	Difference vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1279
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.048
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.39
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.35

Secondary: Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Mean Number of Pads Used per 24 Hours

End point title	Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Mean Number of Pads Used per 24 Hours

End point description:

The mean number of pads used per 24 hours was calculated from data recorded by the participant in the micturition diary for 7 days prior to each visit. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. Only participants with ≥ 1 pads used at baseline were included in the analysis. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	201	193	771	
Units: pads				
least squares mean (standard error)				
Month 1 [N=193, 185, 741]	-0.67 (± 0.10)	-0.96 (± 0.11)	-1.25 (± 0.05)	
Month 3 [N=188, 184, 734]	-1.12 (± 0.11)	-1.30 (± 0.11)	-1.49 (± 0.06)	
Month 6 [N=174, 173, 712]	-1.30 (± 0.12)	-1.24 (± 0.12)	-1.59 (± 0.06)	
Month 9 [N=173, 166, 689]	-1.38 (± 0.12)	-1.31 (± 0.13)	-1.65 (± 0.06)	
Month 12 [N=170, 162, 678]	-1.35 (± 0.12)	-1.37 (± 0.13)	-1.67 (± 0.06)	
EoT [N=200, 191, 762]	-1.23 (± 0.12)	-1.38 (± 0.12)	-1.66 (± 0.06)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	972
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	-0.16
Variability estimate	Standard error of the mean
Dispersion value	0.13

Statistical analysis title	Difference vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.039
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.14

Secondary: Number of Pads Used Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point title	Number of Pads Used Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point description:

The number of pads used was the number of times a participant recorded a new pad used during the 7-day micturition diary period prior to each visit. The analysis population was the FAS. Only participants with ≥ 1 pad used at baseline were included in the analysis. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	201	193	771	
Units: pads				
arithmetic mean (standard error)				
Month 1 [N=193, 185, 741]	12.67 (± 1.98)	12.55 (± 1.59)	8.75 (± 0.50)	
Month 3 [N=188, 184, 734]	9.61 (± 1.12)	9.47 (± 1.28)	7.23 (± 0.50)	
Month 6 [N=174, 173, 712]	7.99 (± 1.03)	9.16 (± 1.28)	6.51 (± 0.47)	
Month 9 [N=173, 166, 689]	7.65 (± 1.08)	8.91 (± 1.28)	6.18 (± 0.46)	
Month 12 [N=170, 162, 678]	7.60 (± 1.05)	8.09 (± 1.23)	5.70 (± 0.44)	
EoT [N=200, 191, 762]	9.09 (± 1.07)	8.54 (± 1.10)	6.33 (± 0.45)	

Statistical analyses

Statistical analysis title	Rate ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Rate ratio of number of pads during the EoT 7-day diary between the combination therapy group and the mirabegron monotherapy group is calculated from a negative binomial regression model incl. treatment group, sex, age group (< 65, ≥ 65 years), geographic region and previous study history as factors, log(number of pads divided by number of valid diary days) included as a covariate and post baseline number of valid diary days as the offset variable.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	972
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Negative binomial regression
Parameter estimate	Rate ratio
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	0.76
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Rate ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Rate ratio of number of pads during the EoT 7-day diary between the combination therapy group and the solifenacin monotherapy group is calculated from a negative binomial regression model incl. treatment group, sex, age group (< 65, ≥ 65 years), geographic region and previous study history as factors, log(number of pads divided by number of valid diary days) included as a covariate and post baseline number of valid diary days as the offset variable.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044
Method	Negative binomial regression
Parameter estimate	Rate ratio
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	0.99
Variability estimate	Standard error of the mean
Dispersion value	0.14

Secondary: Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Number of Pads Used Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point title	Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Number of Pads Used Reported During the 7-Day Micturition Diary Period Prior to Each Visit

End point description:

The number of pads used was the number of times a participant recorded a new pad used during the 7-day micturition diary period prior to each visit. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. Only participants with ≥ 1 pad used at baseline were included in the analysis. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	201	193	771	
Units: pads				
least squares mean (standard error)				
Month 1 [N=193, 185, 741]	-4.74 (± 0.71)	-6.72 (± 0.72)	-8.89 (± 0.36)	
Month 3 [N=188, 184, 734]	-7.83 (± 0.77)	-9.21 (± 0.78)	-10.47 (± 0.39)	
Month 6 [N=174, 173, 712]	-9.09 (± 0.85)	-8.86 (± 0.85)	-11.12 (± 0.42)	
Month 9 [N=173, 166, 689]	-9.59 (± 0.87)	-9.33 (± 0.89)	-11.44 (± 0.43)	
Month 12 [N=170, 162, 678]	-9.39 (± 0.85)	-9.92 (± 0.87)	-11.66 (± 0.42)	
EoT [N=200, 191, 762]	-8.59 (± 0.82)	-9.89 (± 0.84)	-11.58 (± 0.42)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	972
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-2.98

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.78
upper limit	-1.18
Variability estimate	Standard error of the mean
Dispersion value	0.92

Statistical analysis title	Difference vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.072
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-1.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.52
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.93

Secondary: Change from Baseline to Months 1, 3, 6, 9 and 12 in the OAB-q Symptom Bother Score

End point title	Change from Baseline to Months 1, 3, 6, 9 and 12 in the OAB-q Symptom Bother Score

End point description:

The OAB-q is a self-reported questionnaire with items relating to symptom bother and health-related quality of life (HRQoL). The symptom bother portion consists of 8 items, rated on a 6-point Likert scale (1 through 6). The total symptom bother score was calculated from the 8 answers and then transformed to range from 0 (least severity) to 100 (worst severity). A negative change from baseline indicated an improvement. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: units on a scale				
least squares mean (standard error)				
Month 1 [N=281, 286, 1132]	-16.37 (± 1.08)	-20.82 (± 1.07)	-22.86 (± 0.54)	
Month 3 [N=278, 286, 1137]	-19.69 (± 1.08)	-23.13 (± 1.07)	-26.88 (± 0.53)	
Month 6 [N=260, 272, 1108]	-20.97 (± 1.14)	-24.27 (± 1.12)	-27.73 (± 0.55)	
Month 9 [N=261, 264, 1077]	-21.41 (± 1.15)	-25.82 (± 1.14)	-28.45 (± 0.56)	
Month 12 [N=250, 255, 1049]	-23.41 (± 1.19)	-25.38 (± 1.18)	-30.18 (± 0.58)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Health-Related Quality of Life Questionnaire (HRQL): Total score

End point title	Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Health-Related Quality of Life Questionnaire (HRQL): Total score

End point description:

The OAB-q is a self-reported questionnaire with items relating to symptom bother and HRQoL. The HRQoL portion consists of 25 HRQoL items comprising 4 HRQoL subscales (Coping, Concern, Sleep, and Social Interaction), each item was scored 1-6. The total score was calculated by adding the 4 HRQoL subscale scores and transforming to a scale from 0 to 100, with higher scores indicating better quality of life. A positive change from baseline indicated an improvement. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: units on a scale				
least squares mean (standard error)				
Month 1 [N=281, 286, 1132]	11.67 (± 0.92)	14.01 (± 0.91)	15.69 (± 0.45)	
Month 3 [N=278, 286, 1137]	15.25 (± 0.95)	16.41 (± 0.94)	19.26 (± 0.47)	
Month 6 [N=260, 272, 1108]	16.63 (± 1.02)	17.96 (± 1.00)	20.03 (± 0.49)	
Month 9 [N=261, 264, 1077]	16.69 (± 1.02)	18.53 (± 1.01)	20.75 (± 0.50)	
Month 12 [N=250, 255, 1049]	17.33 (± 1.04)	18.80 (± 1.03)	21.82 (± 0.51)	

EoT [N=290, 294, 1163]	16.57 (± 1.00)	18.47 (± 0.99)	21.33 (± 0.50)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	4.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.56
upper limit	6.96
Variability estimate	Standard error of the mean
Dispersion value	1.12

Statistical analysis title	Difference vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	2.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	5.04

Variability estimate	Standard error of the mean
Dispersion value	1.11

Secondary: Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Health-Related Quality of Life (HRQL) Subscale Score: Coping

End point title	Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Health-Related Quality of Life (HRQL) Subscale Score: Coping

End point description:

The OAB-q is a self-reported questionnaire with items relating to symptom bother and HRQoL. The HRQoL portion consists of 25 HRQoL items comprising 4 HRQoL subscales (Coping, Concern, Sleep, and Social Interaction), each item was scored 1-6. HRQoL subscales (coping, concern, sleep and social) and total score were transformed to range from 0 (worst quality of life) to 100 (best quality of life), with higher scores indicating better quality of life. A positive change from baseline indicated an improvement. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: units on a scale				
least squares mean (standard error)				
Month 1 [N=281, 286, 1132]	13.05 (± 1.09)	15.40 (± 1.08)	17.58 (± 0.54)	
Month 3 [N=278, 286, 1137]	17.57 (± 1.14)	18.38 (± 1.13)	21.64 (± 0.56)	
Month 6 [N=260, 272, 1108]	19.68 (± 1.22)	20.53 (± 1.19)	22.73 (± 0.59)	
Month 9 [N=261, 264, 1077]	19.54 (± 1.21)	21.21 (± 1.20)	23.58 (± 0.59)	
Month 12 [N=250, 255, 1049]	19.47 (± 1.25)	21.90 (± 1.23)	24.86 (± 0.61)	
EoT [N=290, 294, 1163]	18.54 (± 1.19)	21.13 (± 1.18)	24.14 (± 0.59)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg

Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.99
upper limit	8.2
Variability estimate	Standard error of the mean
Dispersion value	1.33

Statistical analysis title	Difference vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	3.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	5.6
Variability estimate	Standard error of the mean
Dispersion value	1.32

Secondary: Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Health-Related Quality of Life (HRQL) Subscale Score: Concern

End point title	Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Health-Related Quality of Life (HRQL) Subscale Score: Concern

End point description:

The OAB-q is a self-reported questionnaire with items relating to symptom bother and HRQoL. The HRQoL portion consists of 25 HRQoL items comprising 4 HRQoL subscales (Coping, Concern, Sleep, and Social Interaction), each item was scored 1-6. HRQoL subscales (coping, concern, sleep and social) and total score were transformed to range from 0 (worst quality of life) to 100 (best quality of life), with higher scores indicating better quality of life. A positive change from baseline indicated an improvement. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: units on a scale				
least squares mean (standard error)				
Month 1 [N=281, 286, 1132]	13.24 (± 1.03)	15.49 (± 1.02)	17.60 (± 0.51)	
Month 3 [N=278, 286, 1137]	16.37 (± 1.05)	17.64 (± 1.04)	21.23 (± 0.52)	
Month 6 [N=260, 272, 1108]	17.77 (± 1.10)	19.05 (± 1.07)	21.73 (± 0.53)	
Month 9 [N=261, 264, 1077]	18.15 (± 1.11)	19.74 (± 1.10)	22.30 (± 0.54)	
Month 12 [N=250, 255, 1049]	19.10 (± 1.12)	19.40 (± 1.10)	23.30 (± 0.54)	
EoT [N=290, 294, 1163]	17.98 (± 1.08)	19.22 (± 1.07)	23.00 (± 0.54)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	5.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.65
upper limit	7.38
Variability estimate	Standard error of the mean
Dispersion value	1.21

Statistical analysis title	Difference vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin

monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	3.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.43
upper limit	6.13
Variability estimate	Standard error of the mean
Dispersion value	1.2

Secondary: Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Health-Related Quality of Life (HRQL) Subscale Score: Sleep

End point title	Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Health-Related Quality of Life (HRQL) Subscale Score: Sleep

End point description:

The OAB-q is a self-reported questionnaire with items relating to symptom bother and HRQoL. The HRQoL portion consisted of 25 HRQoL items comprising 4 HRQoL subscales (Coping, Concern, Sleep, and Social Interaction), each time was scored 1-6. HRQoL subscales (coping, concern, sleep and social) and total score were transformed to range from 0 (worst quality of life) to 100 (best quality of life), with higher scores indicating better quality of life. A positive change from baseline indicated an improvement. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: units on a scale				
least squares mean (standard error)				
Month 1 [N=281, 286, 1132]	10.96 (± 1.08)	14.24 (± 1.07)	15.82 (± 0.54)	
Month 3 [N=278, 286, 1137]	14.09 (± 1.12)	16.71 (± 1.10)	19.75 (± 0.55)	
Month 6 [N=260, 272, 1108]	14.84 (± 1.22)	17.70 (± 1.19)	20.09 (± 0.59)	
Month 9 [N=261, 264, 1077]	14.86 (± 1.22)	17.73 (± 1.21)	21.15 (± 0.60)	
Month 12 [N=250, 255, 1049]	16.53 (± 1.29)	18.28 (± 1.27)	22.17 (± 0.63)	
EoT [N=290, 294, 1163]	16.44 (± 1.22)	18.32 (± 1.21)	21.59 (± 0.61)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	5.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.47
upper limit	7.83
Variability estimate	Standard error of the mean
Dispersion value	1.36

Statistical analysis title	Difference vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.016
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	3.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	5.93

Variability estimate	Standard error of the mean
Dispersion value	1.35

Secondary: Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Health-Related Quality of Life (HRQL) Subscale Score: Social

End point title	Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Health-Related Quality of Life (HRQL) Subscale Score: Social

End point description:

The OAB-q is a self-reported questionnaire with items relating to symptom bother and HRQoL. The HRQoL portion consists of 25 HRQoL items comprising 4 HRQoL subscales (Coping, Concern, Sleep, and Social Interaction), each item was scored 1-6. HRQoL subscales (coping, concern, sleep and social) and total score were transformed to range from 0 (worst quality of life) to 100 (best quality of life), with higher scores indicating better quality of life. A positive change from baseline indicated an improvement. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: units on a scale				
least squares mean (standard error)				
Month 1 [N=281, 286, 1132]	7.99 (± 0.84)	9.41 (± 0.83)	9.89 (± 0.42)	
Month 3 [N=278, 286, 1137]	11.14 (± 0.85)	11.19 (± 0.84)	12.22 (± 0.42)	
Month 6 [N=260, 272, 1108]	11.89 (± 0.89)	12.54 (± 0.87)	13.30 (± 0.43)	
Month 9 [N=261, 264, 1077]	11.92 (± 0.90)	13.33 (± 0.89)	13.64 (± 0.44)	
Month 12 [N=250, 255, 1049]	12.25 (± 0.90)	13.47 (± 0.89)	14.52 (± 0.44)	
EoT [N=290, 294, 1163]	11.57 (± 0.87)	13.22 (± 0.87)	14.25 (± 0.43)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg

Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	2.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	4.59
Variability estimate	Standard error of the mean
Dispersion value	0.98

Statistical analysis title	Difference vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.287
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.87
upper limit	2.93
Variability estimate	Standard error of the mean
Dispersion value	0.97

Secondary: Change from Baseline to Months 1, 3, 6, 9 and 12 in the Patient's Assessment of Treatment Satisfaction-Visual Analogue Scale (TS-VAS)

End point title	Change from Baseline to Months 1, 3, 6, 9 and 12 in the Patient's Assessment of Treatment Satisfaction-Visual Analogue Scale (TS-VAS)

End point description:

The TS-VAS is a visual analogue scale which asks participants to rate their satisfaction with the treatment by placing a vertical mark on a line that runs from 0 (No, not at all) on the left to 10 (Yes, completely) on the right. A positive change from baseline indicated improvement. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: units on a scale				
least squares mean (standard error)				
Month 1 [N=280, 286, 1131]	1.88 (± 0.12)	1.95 (± 0.12)	2.27 (± 0.06)	
Month 3 [N=277, 286, 1136]	2.10 (± 0.11)	2.06 (± 0.11)	2.57 (± 0.06)	
Month 6 [N=260, 272, 1108]	2.22 (± 0.12)	2.25 (± 0.12)	2.72 (± 0.06)	
Month 9 [N=261, 263, 1076]	2.24 (± 0.12)	2.28 (± 0.12)	2.74 (± 0.06)	
Month 12 [N=250, 255, 1049]	2.33 (± 0.12)	2.34 (± 0.12)	2.89 (± 0.06)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Patient Perception of Bladder Condition Questionnaire (PPBC)

End point title	Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Patient Perception of Bladder Condition Questionnaire (PPBC)

End point description:

The PPBC is a validated, global assessment tool using a 6-point Likert scale on which participants rated their subjective impression of their current bladder condition. Participants assessed their bladder condition using this scale: 1. Does not cause me any problems at all; 2. Causes me some very minor problems; 3. Causes me some minor problems; 4. Causes me (some) moderate problems; 5. Causes me severe problems; 6. Causes me many severe problems. The analysis population is FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: units on a scale				
least squares mean (standard error)				
Month 1 [N=281, 287, 1133]	-0.84 (± 0.07)	-0.89 (± 0.07)	-1.05 (± 0.03)	
Month 3 [N=278, 286, 1137]	-1.09 (± 0.07)	-1.08 (± 0.07)	-1.33 (± 0.03)	
Month 6 [N=260, 272, 1108]	-1.11 (± 0.07)	-1.18 (± 0.07)	-1.42 (± 0.04)	

Month 9 [N=261, 264, 1077]	-1.25 (± 0.07)	-1.31 (± 0.07)	-1.48 (± 0.04)	
Month 12 [N=251, 255, 1049]	-1.29 (± 0.08)	-1.36 (± 0.07)	-1.59 (± 0.04)	
EoT [N=290, 294, 1163]	-1.22 (± 0.07)	-1.34 (± 0.07)	-1.54 (± 0.04)	

Statistical analyses

Statistical analysis title	Difference vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	-0.16
Variability estimate	Standard error of the mean
Dispersion value	0.08

Statistical analysis title	Difference vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	-0.05

Variability estimate	Standard error of the mean
Dispersion value	0.08

Secondary: Percentage of Participants in Each Category of Patient's Global Impression of Change (PGIC) Scale: Impression in Bladder Symptoms at Month 12 and EoT

End point title	Percentage of Participants in Each Category of Patient's Global Impression of Change (PGIC) Scale: Impression in Bladder Symptoms at Month 12 and EoT

End point description:

The PGIC is a 2-part questionnaire, assessing both the change in the participant's overall condition and change in bladder condition since the start of the study (from very much worse to very much improved). The analysis population was the FAS. The number of participants analyzed includes participants with data available. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Month 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: percentage of participants				
number (not applicable)				
Month 12: Very much improved	25.5	23.4	33.8	
Month 12: Much improved	30.5	35.8	34.0	
Month 12: Minimally improved	21.9	19.7	16.1	
Month 12: No change	5.0	6.4	4.5	
Month 12: Minimally worse	0.7	0.7	0.4	
Month 12: Much worse	1.0	0.3	0.1	
Month 12: Very much worse	0.3	0.3	0.5	
EoT: Very much improved	25.8	24.4	34.1	
EoT: Much improved	31.5	37.1	34.7	
EoT: Minimally improved	22.2	20.4	16.6	
EoT: No change	6.3	7.0	5.1	
EoT: Minimally worse	0.7	0.7	0.4	
EoT: Much worse	1.3	0.7	0.1	
EoT: Very much worse	0.3	0.3	0.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in Each Category of PGIC Scale: Impression

in General Health at Month 12 and EoT

End point title	Percentage of Participants in Each Category of PGIC Scale: Impression in General Health at Month 12 and EoT

End point description:

The PGIC is a 2-part questionnaire, assessing both the change in the participant's overall condition and change in bladder condition since the start of the study (from very much worse to very much improved). The analysis population was the FAS. The number of participants analyzed includes participants with data available. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Month 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: percentage of participants				
number (not applicable)				
Month 12: Very much improved	12.9	14.7	18.0	
Month 12: Much improved	23.8	26.8	28.7	
Month 12: Minimally improved	18.9	17.1	18.7	
Month 12: No change	24.2	24.7	20.7	
Month 12: Minimally worse	3.6	2.7	2.7	
Month 12: Much worse	0.7	0	0.4	
Month 12: Very much worse	0.7	0.7	0.3	
EoT: Very much improved	13.2	15.1	18.3	
EoT: Much improved	24.5	27.8	28.9	
EoT: Minimally improved	19.2	18.1	19.1	
EoT: No change	25.8	25.8	21.6	
EoT: Minimally worse	3.6	3.0	2.8	
EoT: Much worse	1.0	0.3	0.5	
EoT: Very much worse	0.7	0.7	0.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change from Baseline to EoT in European Quality of Life in 5 Dimensions (EQ-5D) Questionnaire Subscale Score: Mobility

End point title	Number of Participants With Change from Baseline to EoT in European Quality of Life in 5 Dimensions (EQ-5D) Questionnaire Subscale Score: Mobility

End point description:

The EQ-5D questionnaire is an international, standardized, nondisease specific instrument for describing and valuing health status, and has 5 dimensions: Mobility, Self-care, Usual Activities, Pain/Discomfort, and Anxiety/Depression. Each dimension has 5 response levels ranging from level 1 (no problem or none) to level 5 (unable to perform activity). The analysis population was the FAS. LOCF was used for EoT.

End point type	Secondary
End point timeframe:	
Baseline and Month 12	

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: participants				
number (not applicable)				
No problems -> no problems	164	164	675	
No problems -> slight problems	15	15	56	
No problems -> moderate problems	10	4	26	
No problems -> severe problems	1	1	2	
No problems -> unable to walk about	1	0	0	
No problems -> no data	3	0	7	
Slight problems -> no problems	19	24	83	
Slight problems -> slight problems	18	29	87	
Slight problems -> moderate problems	4	6	26	
Slight problems -> severe problems	3	1	2	
Slight problems -> unable to walk about	0	0	0	
Slight problems -> no data	2	1	0	
Moderate problems -> no problems	14	11	38	
Moderate problems -> slight problems	13	17	47	
Moderate problems -> moderate problems	9	5	50	
Moderate problems -> severe problems	2	4	8	
Moderate problems -> unable to walk about	0	0	0	
Moderate problems -> no data	0	0	1	
Severe problems -> no problems	2	4	15	
Severe problems -> slight problems	2	2	13	
Severe problems -> moderate problems	6	4	16	
Severe problems -> severe problems	5	3	15	
Severe problems -> unable to walk about	1	0	2	
Severe problems -> no data	0	0	0	
Unable to walk about -> no problems	0	0	1	
Unable to walk about -> slight problems	0	0	1	
Unable to walk about -> moderate problems	0	0	0	
Unable to walk about -> severe problems	0	0	0	
Unable to walk about -> unable to walk about	0	0	0	
Unable to walk about -> no data	0	0	0	
No data -> no problems	4	3	19	
No data -> slight problems	4	1	3	
No data -> moderate problems	0	0	0	
No data -> severe problems	0	0	0	

No data -> unable to walk about	0	0	0	
No data -> no data	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change from Baseline to EoT in EQ-5D Questionnaire Subscale Score: Self-care

End point title	Number of Participants With Change from Baseline to EoT in EQ-5D Questionnaire Subscale Score: Self-care

End point description:

The EQ-5D questionnaire is an international, standardized, nondisease specific instrument for describing and valuing health status, and has 5 dimensions: Mobility, Self-care, Usual Activities, Pain/Discomfort, and Anxiety/Depression. Each dimension has 5 response levels ranging from level 1 (no problem or none) to level 5 (unable to perform activity). The analysis population was the FAS. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Month 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: participants				
number (not applicable)				
No problems -> no problems	223	232	906	
No problems -> slight problems	12	9	40	
No problems -> moderate problems	8	0	12	
No problems -> severe problems	0	1	2	
No problems -> unable to wash/dress myself	0	0	0	
No problems -> no data	5	1	7	
Slight problems -> no problems	16	18	64	
Slight problems -> slight problems	9	14	44	
Slight problems -> moderate problems	0	4	12	
Slight problems -> severe problems	0	1	1	
Slight problems -> unable to wash/dress myself	0	0	0	
Slight problems -> no data	0	0	1	
Moderate problems -> no problems	5	4	18	
Moderate problems -> slight problems	5	6	20	
Moderate problems -> moderate problems	5	3	21	
Moderate problems -> severe problems	0	0	2	

Moderate problems -> unable to wash/dress myself	0	0	0	
Moderate problems -> no data	0	0	0	
Severe problems -> no problems	0	1	8	
Severe problems -> slight problems	1	0	3	
Severe problems -> moderate problems	3	1	4	
Severe problems -> severe problems	1	0	5	
Severe problems -> unable to wash/dress myself	0	0	0	
Severe problems -> no data	0	0	0	
Unable to wash/dress myself -> no problems	0	0	0	
Unable to wash/dress myself -> slight problems	0	0	1	
Unable to wash/dress myself -> moderate problems	0	0	0	
Unable to wash/dress myself -> severe problems	0	0	0	
Unable to wash/dress myself ->unable to wash/dress	1	0	0	
Unable to wash/dress myself -> no data	0	0	0	
No data -> no problems	6	3	22	
No data -> slight problems	2	1	0	
No data -> moderate problems	0	0	0	
No data -> severe problems	0	0	0	
No data -> unable to wash/dress myself	0	0	0	
No data -> no data	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change from Baseline to EoT in EQ-5D Questionnaire Subscale Score: Usual Activities

End point title	Number of Participants With Change from Baseline to EoT in EQ-5D Questionnaire Subscale Score: Usual Activities

End point description:

The EQ-5D questionnaire is an international, standardized, nondisease specific instrument for describing and valuing health status, and has 5 dimensions: Mobility, Self-care, Usual Activities, Pain/Discomfort, and Anxiety/Depression. Each dimension has 5 response levels ranging from level 1 (no problem or none) to level 5 (unable to perform activity). The analysis population was the FAS. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Month 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: participants				
No problems -> No problems	165	160	672	
No problems -> Slight problems	13	16	65	
No problems -> Moderate problems	8	4	15	
No problems -> Severe problems	1	0	1	
No problems -> unable to do usual activities	0	0	0	
No problems -> no data	4	0	7	
Slight problems -> no problems	27	39	131	
Slight problems -> slight problems	28	33	85	
Slight problems -> moderate problems	5	6	26	
Slight problems -> severe problems	2	1	1	
Slight problems ->unable to do usual activities	0	0	0	
Slight problems -> no data	1	0	0	
Moderate problems -> no problems	12	12	40	
Moderate problems -> slight problems	11	9	44	
Moderate problems -> moderate problems	7	4	43	
Moderate problems -> severe problems	2	0	2	
Moderate problems ->unable to do usual activities	0	0	0	
Moderate problems -> no data	0	1	1	
Severe problems -> no problems	2	1	10	
Severe problems -> slight problems	0	2	9	
Severe problems -> moderate problems	0	6	7	
Severe problems -> severe problems	4	1	6	
Severe problems -> unable to do usual activities	0	0	1	
Severe problems -> no data	0	0	0	
Unable to do usual activities -> no problems	0	0	0	
Unable to do usual activities -> slight problems	0	0	1	
Unable to do usual activities -> moderate problems	1	0	4	
Unable to do usual activities -> severe problems	0	0	0	
Unable to do usual activities -> unable to do	1	0	0	
Unable to do usual activities -> no data	0	0	0	
No data -> no problems	6	2	20	
No data -> slight problems	1	2	2	
No data -> moderate problems	1	0	0	
No data -> severe problems	0	0	0	
No data -> unable to do usual activities	0	0	0	
No data -> no data	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change from Baseline to EoT in EQ-5D Questionnaire Subscale Score: Pain/Discomfort

End point title	Number of Participants With Change from Baseline to EoT in EQ-5D Questionnaire Subscale Score: Pain/Discomfort

End point description:

The EQ-5D questionnaire is an international, standardized, nondisease specific instrument for describing and valuing health status, and has 5 dimensions: Mobility, Self-care, Usual Activities, Pain/Discomfort, and Anxiety/Depression. Each dimension has 5 response levels ranging from level 1 (no problem or none) to level 5 (unable to perform activity). The analysis population was the FAS. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Month 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: participants				
No pain/discomfort -> no pain/discomfort	120	119	495	
No pain/discomfort -> slight pain/discomfort	21	19	70	
No pain/discomfort -> moderate pain/discomfort	7	1	20	
No pain/discomfort -> severe pain/discomfort	1	0	3	
No pain/discomfort -> extreme pain/discomfort	0	0	0	
No pain/discomfort -> no data	2	1	6	
Slight pain/discomfort -> no pain/discomfort	44	37	132	
Slight pain/discomfort -> slight pain/discomfort	24	48	152	
Slight pain/discomfort -> moderate pain/discomfort	11	9	26	
Slight pain/discomfort -> severe pain/discomfort	2	1	5	
Slight pain/discomfort -> extreme pain/discomfort	0	0	1	
Slight pain/discomfort -> no data	0	0	1	

Moderate pain/discomfort -> no pain/discomfort	9	11	49	
Moderate pain/discomfort -> slight pain/discomfort	19	17	78	
Moderate pain/discomfort -> moderate pain/discomf	16	10	65	
Moderate pain/discomfort -> severe pain/discomfort	2	3	8	
Moderate pain/discomfort -> extreme pain/discomf	0	0	1	
Moderate pain/discomfort -> no data	1	0	1	
Severe pain/discomfort -> no pain/discomfort	3	6	15	
Severe pain/discomfort -> slight pain/discomfort	2	3	9	
Severe pain/discomfort -> moderate pain/discomfort	5	5	13	
Severe pain/discomfort -> severe pain/discomfort	2	3	11	
Severe pain/discomfort -> extreme pain/discomfort	0	0	1	
Severe pain/discomfort -> no data	1	0	0	
Extreme pain/discomfort -> no pain/discomfort	0	0	0	
Extreme pain/discomfort -> slight pain/discomfort	0	0	3	
Extreme pain/discomfort -> moderate pain/discomf	1	0	2	
Extreme pain/discomfort -> severe pain/discomfort	0	2	2	
Extreme pain/discomfort -> extreme pain/discomfort	0	0	2	
Extreme pain/discomfort -> no data	1	0	0	
No data -> no pain/discomfort	5	1	11	
No data -> slight pain/discomfort	3	3	11	
No data -> moderate pain/discomfort	0	0	0	
No data -> severe pain/discomfort	0	0	0	
No data -> extreme pain/discomfort	0	0	0	
No data -> no data	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change from Baseline to EoT in EQ-5D Questionnaire Subscale Score: Anxiety/Depression

End point title	Number of Participants With Change from Baseline to EoT in EQ-5D Questionnaire Subscale Score: Anxiety/Depression

End point description:

The EQ-5D questionnaire is an international, standardized, nondisease specific instrument for describing and valuing health status, and has 5 dimensions: Mobility, Self-care, Usual Activities, Pain/Discomfort, and Anxiety/Depression. Each dimension has 5 response levels ranging from level 1 (no problem or none) to level 5 (unable to perform activity). The analysis population was the FAS. LOCF was used for EoT.

End point type	Secondary

End point timeframe:
Baseline and Month 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: participants				
Not anxious -> not anxious	137	142	588	
Not anxious -> slightly anxious	22	18	68	
Not anxious -> moderately anxious	4	1	7	
Not anxious -> severely anxious	1	0	1	
Not anxious -> extremely anxious	0	0	0	
Not anxious -> no data	3	1	5	
Slightly anxious -> not anxious	35	43	177	
Slightly anxious -> slightly anxious	30	33	106	
Slightly anxious -> moderately anxious	4	8	21	
Slightly anxious -> severely anxious	3	1	0	
Slightly anxious -> extremely anxious	0	1	1	
Slightly anxious -> no data	1	0	1	
Moderately anxious -> not anxious	15	11	37	
Moderately anxious -> slightly anxious	11	14	55	
Moderately anxious -> moderately anxious	12	8	35	
Moderately anxious -> severely anxious	1	1	5	
Moderately anxious -> extremely anxious	0	0	0	
Moderately anxious -> no data	0	0	1	
Severely anxious -> not anxious	2	2	10	
Severely anxious -> slightly anxious	3	2	14	
Severely anxious -> moderately anxious	5	3	13	
Severely anxious -> severely anxious	2	1	7	
Severely anxious -> extremely anxious	1	0	1	
Severely anxious -> no data	1	0	1	
Extremely anxious -> not anxious	0	1	4	
Extremely anxious -> slightly anxious	0	2	2	
Extremely anxious -> moderately anxious	1	0	8	
Extremely anxious -> severely anxious	0	2	2	
Extremely anxious -> extremely anxious	0	0	1	
Extremely anxious -> no data	0	0	0	
No data -> not anxious	6	3	14	
No data -> slightly anxious	1	1	7	
No data -> moderately anxious	1	0	0	
No data -> severely anxious	0	0	0	
No data -> extremely anxious	0	0	1	
No data -> no data	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Months 6, 12 and EoT in Work Productivity and Activity Impairment: Specific Health Problem Questionnaire (WPAI:SHP) Score: Percent Work Time Missed

End point title	Change from Baseline to Months 6, 12 and EoT in Work Productivity and Activity Impairment: Specific Health Problem Questionnaire (WPAI:SHP) Score: Percent Work Time Missed

End point description:

The WPAI:SHP is a self-administered questionnaire with 6 questions (Q1=Employment status; Q2=Hours absent from work due to the bladder condition; Q3=Hours absent from work due to other reasons; Q4=Hours actually worked; Q5=Impact of the bladder condition on productivity while working; Q6=Impact of the bladder condition on productivity while doing regular daily activities other than work) and a 1-week recall period. WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity, i.e., worse outcomes. A negative change from baseline indicates improvement. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. Only participants with both baseline and post-baseline values are included in the analysis. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 6,12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	136	468	
Units: percentage of work time missed				
arithmetic mean (standard deviation)				
Month 6 [N=86, 112, 379]	-0.49 (± 17.12)	-0.59 (± 15.67)	-3.11 (± 20.68)	
Month 12 [N=83, 110, 359]	0.39 (± 15.55)	-1.95 (± 18.51)	-3.74 (± 23.83)	
EoT [N=96, 124, 421]	-0.45 (± 18.51)	-1.30 (± 18.04)	-3.26 (± 22.88)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Months 6, 12 and EoT in WPAI:SHP Score: Percent Impairment While Working

End point title	Change from Baseline to Months 6, 12 and EoT in WPAI:SHP Score: Percent Impairment While Working

End point description:

The WPAI:SHP is a self-administered questionnaire with 6 questions (Q1=Employment status; Q2=Hours absent from work due to the bladder condition; Q3=Hours absent from work due to other reasons; Q4=Hours actually worked; Q5=Impact of the bladder condition on productivity while working; Q6=Impact of the bladder condition on productivity while doing regular daily activities other than work) and a 1-week recall period. WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity, i.e., worse outcomes. A negative change from baseline indicates improvement. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. Only participants with both baseline and post-baseline values and who were employed during the study are included in the analysis. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 6,12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	135	461	
Units: percentage of impairment while working				
arithmetic mean (standard deviation)				
Month 6 [N=85, 111, 372]	-16.94 (± 24.10)	-12.97 (± 21.05)	-13.41 (± 24.37)	
Month 12 [N=83, 108, 349]	-19.16 (± 23.38)	-14.72 (± 27.32)	-16.68 (± 24.16)	
EoT [N=96, 123, 414]	-17.81 (± 23.45)	-13.90 (± 27.18)	-15.63 (± 25.61)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Months 6, 12 in WPAI:SHP Score: Percent Overall Work Impairment

End point title	Change From Baseline to Months 6, 12 in WPAI:SHP Score: Percent Overall Work Impairment

End point description:

The WPAI:SHP is a self-administered questionnaire with 6 questions (Q1=Employment status; Q2=Hours absent from work due to the bladder condition; Q3=Hours absent from work due to other reasons; Q4=Hours actually worked; Q5=Impact of the bladder condition on productivity while working; Q6=Impact of the bladder condition on productivity while doing regular daily activities other than work) and a 1-week recall period. WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity, i.e., worse outcomes. A negative change from baseline indicated improvement. N is the number of participants analyzed with data available at each time point. Only participants with both baseline and post-baseline values and who were employed during the study are included in the analysis. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 6, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	135	461	
Units: percentage of overall work impairment				
arithmetic mean (standard deviation)				
Month 6 [N= 85, 111, 372]	-16.33 (± 27.58)	-12.09 (± 22.26)	-13.99 (± 26.04)	
Month 12 [N= 83, 108, 349]	-17.83 (± 26.90)	-15.38 (± 27.97)	-17.27 (± 27.25)	
EoT [N= 96, 123, 414]	-16.83 (± 27.63)	-14.16 (± 27.51)	-16.15 (± 28.51)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Months 6, 12 in WPAI:SHP Score: Percent Activity Impairment

End point title	Change From Baseline to Months 6, 12 in WPAI:SHP Score: Percent Activity Impairment

End point description:

The WPAI:SHP is a self-administered questionnaire with 6 questions (Q1=Employment status; Q2=Hours absent from work due to the bladder condition; Q3=Hours absent from work due to other reasons; Q4=Hours actually worked; Q5=Impact of the bladder condition on productivity while working; Q6=Impact of the bladder condition on productivity while doing regular daily activities other than work) and a 1-week recall period. WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity, i.e., worse outcomes. A negative change from baseline indicated improvement. N is the number of participants analyzed with data available at each time point. Only participants with both baseline and post-baseline values during the study are included in the analysis. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 6, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	292	285	1167	
Units: percentage of activity impairment				
arithmetic mean (standard deviation)				
Month 6 [N= 258, 272, 1105]	-15.04 (± 27.08)	-16.25 (± 24.78)	-16.94 (± 28.49)	

Month 12 [N= 248, 255, 1045]	-16.85 (± 27.57)	-14.12 (± 29.87)	-18.91 (± 29.26)	
EoT [N= 274, 281, 1124]	-16.02 (± 27.63)	-14.02 (± 30.29)	-18.75 (± 29.14)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Zero Incontinence Episodes per 24 Hours Using the Last 3 Diary Days at Months 1, 3, 6, 9, 12 and EoT

End point title	Percentage of Participants with Zero Incontinence Episodes per 24 Hours Using the Last 3 Diary Days at Months 1, 3, 6, 9, 12 and EoT

End point description:

An incontinence episode was defined as the complaint of any involuntary leakage of urine. The percentage of participants with no incontinence episodes recorded during the last 3 days of the 7-day micturition diary is reported. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: percentage of participants				
number (not applicable)				
Month 1 [N=291, 288, 1158]	24.4	39.9	38.3	
Month 3 [N=282, 288, 1137]	40.1	44.8	49.6	
Month 6 [N=266, 273, 1107]	40.6	50.5	54.7	
Month 9 [N=264, 261, 1070]	47.0	54.4	55.8	
Month 12 [N=258, 256, 1048]	51.6	55.5	61.2	
EoT [N=301, 297, 1184]	47.8	53.2	58.8	

Statistical analyses

Statistical analysis title	Odds ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours during the last 3 days as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg

Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.26
upper limit	2.15

Statistical analysis title	Odds ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours during the last 3 days as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.08
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.67

Secondary: Percentage of Participants with ≥ 10 Points Improvement from Baseline in the OAB-q Symptom Bother Score at Months 1, 3, 6, 9, 12 and EoT

End point title	Percentage of Participants with ≥ 10 Points Improvement from Baseline in the OAB-q Symptom Bother Score at Months 1, 3, 6, 9, 12 and EoT

End point description:

The OAB-q is a self-reported questionnaire with items relating to symptom bother and HRQoL. The symptom bother portion consists of 8 items, rated on a 6-point Likert scale (1 through 6). The total symptom bother score was calculated from the 8 answers and then transformed to range from 0 (least severity) to 100 (worst severity). A negative change from baseline indicated an improvement. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: percentage of participants				
number (not applicable)				
Month 1 [N=281, 286, 1132]	63.7	67.5	72.8	
Month 3 [N=278, 286, 1137]	69.1	71.3	81.8	
Month 6 [N=260, 272, 1108]	70.4	74.6	80.5	
Month 9 [N=261, 264, 1077]	70.1	76.1	82.9	
Month 12 [N=250, 255, 1049]	72.8	74.1	84.4	
EoT [N=290, 294, 1163]	70.7	72.4	82.9	

Statistical analyses

Statistical analysis title	Odds ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline OAB-q subscale as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.37
upper limit	2.57

Statistical analysis title	Odds ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline OAB-q subscale as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg

Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	2.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.49
upper limit	2.78

Secondary: Percentage of Participants with ≥ 10 Points Improvement from Baseline in HRQoL Total Score at Months 1, 3, 6, 9, 12 and EoT

End point title	Percentage of Participants with ≥ 10 Points Improvement from Baseline in HRQoL Total Score at Months 1, 3, 6, 9, 12 and EoT

End point description:

The OAB-q is a self-reported questionnaire with items relating to symptom bother and HRQoL. The HRQoL portion consists of 25 HRQoL items comprising 4 HRQoL subscales (Coping, Concern, Sleep, and Social Interaction), each item was scored 1-6. The total score was calculated by adding the 4 HRQoL subscale scores and transforming to a scale from 0 to 100, with higher scores indicating better quality of life. A positive change from baseline indicated an improvement. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: percentage of participants				
number (not applicable)				
Month 1 [N=281, 286, 1132]	46.6	53.8	57.0	
Month 3 [N=278, 286, 1137]	53.6	59.4	64.6	
Month 6 [N=260, 272, 1108]	56.9	62.9	66.1	
Month 9 [N=261, 264, 1077]	57.1	62.9	67.7	
Month 12 [N=250, 255, 1049]	58.4	62.4	69.0	
EoT [N=290, 294, 1163]	56.2	61.6	68.4	

Statistical analyses

Statistical analysis title	Odds ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline OAB-q subscale as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	1.92

Statistical analysis title	Odds ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline OAB-q subscale as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.36
upper limit	2.43

Secondary: Percentage of Participants with 50% Reduction in Mean Number of Incontinence Episodes per 24 Hours at Months 1, 3, 6, 9, 12 and EoT

End point title	Percentage of Participants with 50% Reduction in Mean Number of Incontinence Episodes per 24 Hours at Months 1, 3, 6, 9, 12 and EoT

End point description:

An incontinence episode was defined as the complaint of any involuntary leakage of urine. The mean number of incontinence episodes per 24 hours was calculated from data recorded by the participant in a micturition diary for 7 days prior to each visit. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: percentage of participants				
number (not applicable)				
Month 1 [N=291, 288, 1158]	46.7	55.2	62.0	
Month 3 [N=282, 288, 1137]	58.2	67.0	73.3	
Month 6 [N=266, 273, 1107]	63.2	71.8	76.6	
Month 9 [N=264, 261, 1070]	67.0	73.6	77.8	
Month 12 [N=258, 256, 1048]	72.9	75.4	81.3	
EoT [N=301, 297, 1184]	69.1	73.1	79.5	

Statistical analyses

Statistical analysis title	Odds ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.34
upper limit	2.41

Statistical analysis title	Odds ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg

Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.019
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	1.95

Secondary: Percentage of Participants with Zero Incontinence Episodes per 24 Hours Using the Last 7 Diary Days at Months 1, 3, 6, 9, 12 and EoT

End point title	Percentage of Participants with Zero Incontinence Episodes per 24 Hours Using the Last 7 Diary Days at Months 1, 3, 6, 9, 12 and EoT

End point description:

An incontinence episode was defined as the complaint of any involuntary leakage of urine. The percentage of participants with no incontinence episodes recorded during the 7-day micturition diary is reported. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: percentage of participants				
number (not applicable)				
Month 1 [N=291, 288, 1158]	17.2	26.4	27.9	
Month 3 [N=282, 288, 1137]	27.0	35.1	40.0	
Month 6 [N=266, 273, 1107]	32.3	39.9	44.7	
Month 9 [N=264, 261, 1070]	37.1	43.7	46.9	
Month 12 [N=258, 256, 1048]	41.9	47.3	52.5	
EoT [N=301, 297, 1184]	38.9	45.1	49.7	

Statistical analyses

Statistical analysis title	Odds ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.133
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.62

Statistical analysis title	Odds ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.26
upper limit	2.19

Secondary: Percentage of Participants with Micturition Frequency Normalization at Months 1, 3, 6, 9, 12 and EoT

End point title	Percentage of Participants with Micturition Frequency Normalization at Months 1, 3, 6, 9, 12 and EoT

End point description:

The percentage of participants with micturition frequency normalization was defined as any participant who had ≥ 8 micturitions/24 hours at baseline and < 8 micturitions/24 h postbaseline at months 1, 3, 6, 9, 12 and EoT. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. Participants with less < 8 micturitions per 24 hours at baseline were not included in the analysis. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: percentage of participants				
number (not applicable)				
Month 1 [N=290, 287, 1155]	34.5	29.3	36.8	
Month 3 [N=281, 287, 1135]	36.7	36.6	46.6	
Month 6 [N=265, 272, 1105]	42.3	43.4	51.4	
Month 9 [N=263, 260, 1069]	44.5	41.9	52.5	
Month 12 [N=257, 255, 1047]	46.3	44.7	56.4	
EoT [N=300, 296, 1181]	46.0	46.3	55.9	

Statistical analyses

Statistical analysis title	Odds ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of micturitions per 24 hours as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.18
upper limit	2.03

Statistical analysis title	Odds ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of micturitions per 24 hours as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg

Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	1.95

Secondary: Percentage of Participants with ≥ 1 Point Improvement from Baseline in PPBC at Months 1, 3, 6, 9, 12 and EoT

End point title	Percentage of Participants with ≥ 1 Point Improvement from Baseline in PPBC at Months 1, 3, 6, 9, 12 and EoT

End point description:

The PPBC is a validated, global assessment tool using a 6-point Likert scale on which participants rated their subjective impression of their current bladder condition. Participants assessed their bladder condition using this scale: 1. Does not cause me any problems at all; 2. Causes me some very minor problems; 3. Causes me some minor problems; 4. Causes me (some) moderate problems; 5. Causes me severe problems; 6. Causes me many severe problems. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: percentage of participants				
number (not applicable)				
Month 1 [N=281, 287, 1133]	53.0	59.2	64.1	
Month 3 [N=278, 286, 1137]	61.9	65.7	72.5	
Month 6 [N=260, 272, 1108]	64.6	68.8	73.8	
Month 9 [N=261, 264, 1077]	65.5	68.9	75.1	
Month 12 [N=251, 255, 1049]	69.7	73.7	76.9	
EoT [N=290, 294, 1163]	66.2	71.4	76.0	

Statistical analyses

Statistical analysis title	Odds ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline PPBC as a covariate.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.24
upper limit	2.29

Statistical analysis title	Odds ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline PPBC as a covariate.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.109
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.77

Secondary: Percentage of Participants with Major (≥ 2 points) Improvement from Baseline in PPBC at Months 1, 3, 6, 9, 12 and EoT

End point title	Percentage of Participants with Major (≥ 2 points) Improvement from Baseline in PPBC at Months 1, 3, 6, 9, 12 and EoT

End point description:

The PPBC is a validated, global assessment tool using a 6-point Likert scale on which participants rated their subjective impression of their current bladder condition. Participants assessed their bladder condition using this scale: 1. Does not cause me any problems at all; 2. Causes me some very minor problems; 3. Causes me some minor problems; 4. Causes me (some) moderate problems; 5. Causes me severe problems; 6. Causes me many severe problems. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: percentage of participants				
number (not applicable)				
Month 1 [N=281, 287, 1133]	24.9	28.2	30.7	
Month 3 [N=278, 286, 1137]	31.3	33.9	42.8	
Month 6 [N=260, 272, 1108]	35.0	38.2	45.4	
Month 9 [N=261, 264, 1077]	37.5	40.9	47.0	
Month 12 [N=251, 255, 1049]	40.6	40.4	51.9	
EoT [N=290, 294, 1163]	38.3	39.8	50.3	

Statistical analyses

Statistical analysis title	Odds ratio vs. Mirabegron 50 mg (EoT)
Statistical analysis description:	
Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline PPBC as a covariate.	
Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.26
upper limit	2.25

Statistical analysis title	Odds ratio vs. Solifenacin 5 mg (EoT)
Statistical analysis description:	
Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline PPBC as a covariate.	
Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg

Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.22
upper limit	2.16

Secondary: Percentage of Participants Who Were Double Responders (≥ 50% Reduction in Mean Number of Incontinence Episodes per 24 Hours and at Least 10 Points Improvement on OAB-q Symptom Bother Scale) at Months 1, 3, 6, 9, 12 and EoT

End point title	Percentage of Participants Who Were Double Responders (≥ 50% Reduction in Mean Number of Incontinence Episodes per 24 Hours and at Least 10 Points Improvement on OAB-q Symptom Bother Scale) at Months 1, 3, 6, 9, 12 and EoT

End point description:

An incontinence episode was defined as the complaint of any involuntary leakage of urine. The mean number of incontinence episodes per 24 hours was calculated from data recorded by the participant in a micturition diary for 7 days prior to each visit. The OAB-q is a self-reported questionnaire with items relating to symptom bother and HRQoL. The symptom bother portion consists of 8 items, rated on a 6-point Likert scale (1 through 6). The total symptom bother score was calculated from the 8 answers and then transformed to range from 0 (least severity) to 100 (worst severity). A negative change from baseline indicated an improvement. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: percentage of participants				
number (not applicable)				
Month 1 [N=274, 279, 1115]	36.1	46.6	52.6	
Month 3 [N=270, 281, 1109]	47.8	55.5	65.1	
Month 6 [N=250, 267, 1080]	50.4	56.9	65.8	
Month 9 [N=254, 252, 1048]	53.1	61.9	69.2	
Month 12 [N=245, 248, 1018]	59.2	60.9	73.2	
EoT [N=289, 292, 1156]	55.7	58.2	70.8	

Statistical analyses

Statistical analysis title	Odds ratio vs. Mirabegron 50 mg (EoT)
Statistical analysis description:	
Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours and baseline OAB-q symptom bother scale as covariates.	
Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	2.62

Statistical analysis title	Odds ratio vs. Solifenacin 5 mg (EoT)
Statistical analysis description:	
Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours and baseline OAB-q symptom bother scale as covariates.	
Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.35
upper limit	2.36

Secondary: Percentage of Participants Who Were Double Responders (≥ 50%

Reduction in Mean Number of Incontinence Episodes per 24 Hours and at Least 10 Points Improvement on OAB-q HRQL Total Score) at Months 1, 3, 6, 9, 12 and EoT	
End point title	Percentage of Participants Who Were Double Responders (≥ 50% Reduction in Mean Number of Incontinence Episodes per 24 Hours and at Least 10 Points Improvement on OAB-q HRQL Total Score) at Months 1, 3, 6, 9, 12 and EoT

End point description:

An incontinence episode was defined as the complaint of any involuntary leakage of urine. The mean number of incontinence episodes per 24 hours was calculated from data recorded by the participant in a micturition diary for 7 days prior to each visit. The OAB-q is a self-reported questionnaire with items relating to symptom bother and HRQoL. The HRQoL portion consists of 25 HRQoL items comprising 4 HRQoL subscales (Coping, Concern, Sleep, and Social Interaction), each item was scored 1-6. The total score was calculated by adding the 4 HRQoL subscale scores and transforming to a scale from 0 to 100, with higher scores indicating better quality of life. A positive change from baseline indicated an improvement. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: percentage of participants				
number (not applicable)				
Month 1 [N=274, 279, 1115]	28.5	36.6	40.9	
Month 3 [N=270, 281, 1109]	39.6	43.8	52.3	
Month 6 [N=250, 267, 1080]	41.6	47.9	55.3	
Month 9 [N=254, 252, 1048]	43.7	51.2	57.6	
Month 12 [N=245, 248, 1018]	46.9	50.4	60.6	
EoT [N=289, 292, 1156]	44.3	49.0	59.2	

Statistical analyses

Statistical analysis title	Odds ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours and baseline OAB-q HRQL total score as covariates.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.93

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.46
upper limit	2.54

Statistical analysis title	Odds ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours and baseline OAB-q HRQL total score as covariates.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	2.09

Secondary: Percentage of Participants Who Were Double Responders (≥ 50% Reduction in Mean Number of Incontinence Episodes per 24 Hours and at Least 1 Point Improvement on PPBC) at Months 1, 3, 6, 9, 12 and EoT

End point title	Percentage of Participants Who Were Double Responders (≥ 50% Reduction in Mean Number of Incontinence Episodes per 24 Hours and at Least 1 Point Improvement on PPBC) at Months 1, 3, 6, 9, 12 and EoT

End point description:

An incontinence episode was defined as the complaint of any involuntary leakage of urine. The mean number of incontinence episodes per 24 hours was calculated from data recorded by the participant in a micturition diary for 7 days prior to each visit. The PPBC is a validated, global assessment tool using a 6-point Likert scale on which participants rated their subjective impression of their current bladder condition. Participants assessed their bladder condition using this scale: 1. Does not cause me any problems at all; 2. Causes me some very minor problems; 3. Causes me some minor problems; 4. Causes me (some) moderate problems; 5. Causes me severe problems; 6. Causes me many severe problems. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: percentage of participants				
number (not applicable)				
Month 1 [N=274, 280, 1116]	32.1	37.1	46.0	
Month 3 [N=270, 281, 1109]	43.3	47.7	57.6	
Month 6 [N=250, 267, 1080]	46.8	52.1	60.6	
Month 9 [N=254, 252, 1048]	49.6	53.2	63.0	
Month 12 [N=245, 248, 1018]	57.6	60.1	67.0	
EoT [N=289, 292, 1156]	52.9	57.5	65.1	

Statistical analyses

Statistical analysis title	Odds ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours and baseline PPBC as covariates.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.019
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	1.86

Statistical analysis title	Odds ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours and baseline PPBC as covariates.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.28
upper limit	2.26

Secondary: Percentage of Participants Who Were Triple Responders (≥ 50% Reduction in Mean Number of Incontinence Episodes per 24 Hours, ≥ 10 Points Improvement on OAB-q Symptom Bother Scale and ≥1 Point Improvement on PPBC) at Months 1, 3, 6, 9, 12 and EoT

End point title	Percentage of Participants Who Were Triple Responders (≥ 50% Reduction in Mean Number of Incontinence Episodes per 24 Hours, ≥ 10 Points Improvement on OAB-q Symptom Bother Scale and ≥1 Point Improvement on PPBC) at Months 1, 3, 6, 9, 12 and EoT

End point description:

The mean number of incontinence episodes per 24 hours was calculated from data recorded by the participant in a micturition diary for 7 days prior to each visit. The symptom bother portion of the OAB-q consists of 8 items, rated on a 6-point Likert scale (1 through 6). The total symptom bother score was calculated from the 8 answers and then transformed to range from 0 (least severity) to 100 (worst severity). A negative change from baseline indicated an improvement. The PPBC is a validated, global assessment tool using a 6-point Likert scale on which participants rated their subjective impression of their current bladder condition. Participants assessed their bladder condition using a scale (1-6). The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: percentage of participants				
number (not applicable)				
Month 1 [N=274, 279, 1115]	29.9	35.5	42.8	
Month 3 [N=270, 281, 1109]	38.9	44.8	54.1	
Month 6 [N=250, 267, 1080]	42.4	46.1	55.9	
Month 9 [N=254, 252, 1048]	46.5	50.8	59.2	
Month 12 [N=245, 248, 1018]	51.4	53.6	63.7	
EoT [N=289, 292, 1156]	47.4	51.4	61.7	

Statistical analyses

Statistical analysis title	Odds ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65

years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours, baseline OAB-q symptom bother scale and baseline PPBC as covariates.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.19
upper limit	2.09

Statistical analysis title	Odds ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours, baseline OAB-q symptom bother scale and baseline PPBC as covariates.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	2.46

Secondary: Percentage of Participants Who Were Triple Responders (≥ 50% Reduction in Mean Number of Incontinence Episodes per 24 Hours, ≥ 10 Points Improvement on OAB-q HRQL Total Score and ≥ 1 Point Improvement on PPBC) at Months 1, 3, 6, 9, 12 and EoT

End point title	Percentage of Participants Who Were Triple Responders (≥ 50% Reduction in Mean Number of Incontinence Episodes per 24 Hours, ≥ 10 Points Improvement on OAB-q HRQL Total Score and ≥ 1 Point Improvement on PPBC) at Months 1, 3, 6, 9, 12 and EoT

End point description:

The mean number of incontinence episodes per 24 hours was calculated from data recorded by the participant in a micturition diary for 7 days prior to each visit. The symptom bother portion of the OAB-q consists of 8 items, rated on a 6-point Likert scale (1 through 6). The total symptom bother score was

calculated from the 8 answers and then transformed to range from 0 (least severity) to 100 (worst severity). A negative change from baseline indicated an improvement. The PPBC is a validated, global assessment tool using a 6-point Likert scale on which participants rated their subjective impression of their current bladder condition. Participants assessed their bladder condition using a scale (1-6). The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	302	299	1193	
Units: percentage of participants				
number (not applicable)				
Month 1 [N=274, 279, 1115]	25.2	29.0	35.5	
Month 3 [N=270, 281, 1109]	33.3	39.1	45.9	
Month 6 [N=250, 267, 1080]	36.8	41.2	49.6	
Month 9 [N=254, 252, 1048]	39.0	44.0	51.3	
Month 12 [N=245, 248, 1018]	44.1	47.6	54.6	
EoT [N=289, 292, 1156]	40.1	45.2	53.3	

Statistical analyses

Statistical analysis title	Odds ratio vs. Solifenacin 5 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours, baseline OAB-q HRQL total score and baseline PPBC as covariates.

Comparison groups	Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	1.89

Statistical analysis title	Odds ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours, baseline OAB-q HRQL total score and baseline PPBC as covariates.

Comparison groups	Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg
Number of subjects included in analysis	1495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.33
upper limit	2.34

Secondary: Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Postvoid Residual (PVR) Volume

End point title	Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Postvoid Residual (PVR) Volume

End point description:

PVR volume was assessed by ultrasonography or a bladder scanner. The analysis population was the SAF. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12

End point values	Mirabegron 50 mg	Solifenacin 5 mg	Solifenacin 5 mg + mirabegron 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	305	303	1206	
Units: mL				
arithmetic mean (standard deviation)				
Month 1 [N=295, 298, 1170]	3.179 (± 27.491)	4.549 (± 33.973)	7.894 (± 38.369)	
Month 3 [N=293, 292, 1175]	4.686 (± 29.354)	3.233 (± 32.679)	7.033 (± 37.328)	
Month 6 [N=280, 282, 1144]	1.596 (± 29.399)	3.418 (± 31.864)	6.708 (± 35.881)	
Month 9 [N=272, 268, 1111]	3.074 (± 32.897)	3.436 (± 32.170)	8.229 (± 40.313)	
Month 12 [N=263, 266, 1084]	2.002 (± 32.453)	4.818 (± 33.764)	7.946 (± 38.118)	
EoT [N=300, 302, 1194]	1.747 (± 32.400)	7.382 (± 42.916)	8.522 (± 39.501)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of double-blind study drug up to 30 days after last dose of double-blind study drug (up to 56 weeks)	
Adverse event reporting additional description:	
The total number of deaths (all causes) includes deaths reported after the time frame above.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	Mirabegron 50 mg
Reporting group description:	
Participants who received mirabegron 50 mg once a day for 52 weeks.	
Reporting group title	Solifenacin 5 mg + mirabegron 50 mg
Reporting group description:	
Participants who received solifenacin 5 mg and mirabegron 50 mg once a day for 52 weeks.	
Reporting group title	Solifenacin 5 mg
Reporting group description:	
Participants who received solifenacin 5 mg once a day for 52 weeks.	

Serious adverse events	Mirabegron 50 mg	Solifenacin 5 mg + mirabegron 50 mg	Solifenacin 5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 305 (2.62%)	51 / 1206 (4.23%)	8 / 303 (2.64%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 305 (0.00%)	3 / 1206 (0.25%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			
subjects affected / exposed	1 / 305 (0.33%)	0 / 1206 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bowen's disease			

subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer female			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer recurrent			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma in situ			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic uterine cancer			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 305 (0.00%)	0 / 1206 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			

subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Appendicectomy			
subjects affected / exposed	1 / 305 (0.33%)	0 / 1206 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystectomy			
subjects affected / exposed	0 / 305 (0.00%)	2 / 1206 (0.17%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon polypectomy			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystocele repair			
subjects affected / exposed	1 / 305 (0.33%)	0 / 1206 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hysterectomy			
subjects affected / exposed	1 / 305 (0.33%)	0 / 1206 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fusion surgery			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal operation			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Non-cardiac chest pain			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 305 (0.33%)	0 / 1206 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Hysterocele			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic pain			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine prolapse			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal haemorrhage			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 305 (0.33%)	0 / 1206 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			

subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 305 (0.00%)	0 / 1206 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Cervical vertebral fracture			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 305 (0.00%)	2 / 1206 (0.17%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Incisional hernia			
subjects affected / exposed	0 / 305 (0.00%)	0 / 1206 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sternal fracture			
subjects affected / exposed	0 / 305 (0.00%)	0 / 1206 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 305 (0.33%)	2 / 1206 (0.17%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Coronary artery occlusion			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			

subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Long thoracic nerve palsy			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 305 (0.33%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 305 (0.00%)	0 / 1206 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diverticulum intestinal			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocele			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorder			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal sphincter insufficiency			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Cholelithiasis			
subjects affected / exposed	0 / 305 (0.00%)	2 / 1206 (0.17%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Cervical spinal stenosis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exostosis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 1206 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 1206 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteitis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 305 (0.00%)	2 / 1206 (0.17%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			

subjects affected / exposed	1 / 305 (0.33%)	2 / 1206 (0.17%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 305 (0.00%)	0 / 1206 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma infection			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 305 (0.33%)	2 / 1206 (0.17%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superinfection bacterial			
subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			

subjects affected / exposed	0 / 305 (0.00%)	1 / 1206 (0.08%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Mirabegron 50 mg	Solifenacin 5 mg + mirabegron 50 mg	Solifenacin 5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 305 (8.85%)	115 / 1206 (9.54%)	33 / 303 (10.89%)
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	12 / 305 (3.93%)	74 / 1206 (6.14%)	18 / 303 (5.94%)
occurrences (all)	12	77	20
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	16 / 305 (5.25%)	43 / 1206 (3.57%)	15 / 303 (4.95%)
occurrences (all)	16	46	16

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 November 2013	The changes for this amendment is summarized as: (1) Inclusion criterion 3 relating to female patients of childbearing potential and inclusion criterion 13 relating to the number of urgency episodes per 24 h, respectively, were clarified; (2) The sample size justification for change from baseline in mean number of incontinence episodes per 24 h was modified to accommodate the 7-day eDiary period; (3) The efficacy analysis was modified. If clear evidence for a normal distribution of change from baseline in mean number of incontinence episodes per 24 h was identified prior to hard locking of the database, then primary hypothesis testing for this variable would be performed within an analysis of covariance (ANCOVA) model; (4) Expected adverse drug reactions (ADRs) and expected risks (i.e., urinary retention) were updated in line with the company core data sheets; (5) Antidepressant drugs with anticholinergic ADRs were moved from the list of restricted medications to prohibited medications as these drugs are sometimes used to treat OAB. Nonsubstantial changes were also implemented.
11 December 2014	The changes for this amendment is summarized as: (1) Exclusion criteria 4, 10 and 24 relating to neurological cause for detrusor overactivity, QT interval corrected using Fridericia's correction formula (QTcF) and UTI, respectively, were clarified; and (2) The list of prohibited or restricted medications was updated and removed from Appendix 1 of the protocol and was provided to investigational sites via separate communications. Nonsubstantial changes were also implemented.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported