Clinical trial results:
A Randomized, Double-Blind, Multicenter Study to Evaluate the Efficacy and Safety of Adding Mirabegron to Solifenacin in Incontinent OAB Patients who have Received Solifenacin for 4 Weeks and Warrant Additional Relief for their OAB Symptoms

Summary

EudraCT number	2012-005401-41
Trial protocol	SK CZ GB SE IE BE PT NO AT FI GR HU ES SI NL DK PL
Global end of trial date	25 November 2014

Results information

Result version number	v3 (current)
This version publication date	28 April 2018
First version publication date	21 July 2016
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	905-EC-012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01908829
WHO universal trial number (UTN)	-
Other trial identifiers	Acronym: BESIDE

Notes:

Sponsors

Sponsor organisation name	Astellas Pharma Europe Ltd
Sponsor organisation address	2000 Hillswood Drive, Chertsey, United Kingdom, KT16 0RS
Public contact	Clinical Trial Disclosure, Astellas Pharma Europe Ltd, Astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Trial Disclosure, Astellas Pharma Europe Ltd, 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	25 November 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 November 2014
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 efficacy of solifenacin 5 mg in combination with mirabegron 50 mg (referred to as combination therapy from here on) vs solifenacin 5 mg monotherapy.

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	10 July 2013
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	Algeria: 15
Country: Number of subjects enrolled	Armenia: 52
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Austria: 24
Country: Number of subjects enrolled	Belgium: 24
Country: Number of subjects enrolled	Canada: 57
Country: Number of subjects enrolled	Czech Republic: 129
Country: Number of subjects enrolled	Denmark: 39
Country: Number of subjects enrolled	Egypt: 11
Country: Number of subjects enrolled	Finland: 6
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Georgia: 23
Country: Number of subjects enrolled	Germany: 106
Country: Number of subjects enrolled	Greece: 53
Country: Number of subjects enrolled	Hungary: 53
Country: Number of subjects enrolled	Ireland: 8
Country: Number of subjects enrolled	Israel: 43

Country: Number of subjects enrolled	Italy: 49
Country: Number of subjects enrolled	Kazakhstan: 23
Country: Number of subjects enrolled	Norway: 9
Country: Number of subjects enrolled	Poland: 234
Country: Number of subjects enrolled	Portugal: 12
Country: Number of subjects enrolled	Romania: 84
Country: Number of subjects enrolled	Russian Federation: 241
Country: Number of subjects enrolled	Slovakia: 93
Country: Number of subjects enrolled	Slovenia: 26
Country: Number of subjects enrolled	Spain: 76
Country: Number of subjects enrolled	Sweden: 54
Country: Number of subjects enrolled	Switzerland: 11
Country: Number of subjects enrolled	Turkey: 164
Country: Number of subjects enrolled	Ukraine: 28
Country: Number of subjects enrolled	United Kingdom: 78
Country: Number of subjects enrolled	United States: 320
Country: Number of subjects enrolled	Netherlands: 15
Worldwide total number of subjects	2174
EEA total number of subjects	1183

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)	1492
From 65 to 84 years	671
85 years and over	11

Subject disposition

Recruitment

Recruitment details:

This multicenter study was conducted at 281 centers globally. Randomization was stratified by sex, age group (< 65, ≥ 65 years), 4-week incontinence episode reduction group (< 50%, ≥ 50%) and geographic region.

Pre-assignment

Screening details:

Participants who met the screening inclusion/exclusion criteria went through a two week wash-out period and maintained a micturition diary during that the wash-out period. A total of 3815 participants were screened of which 2401 participants received solifenacin 5 mg run-in medication. A total of 2174 participants were randomized.

Pre-assignment period milestones

Number of subjects started	3815[1]
Intermediate milestone: Number of subjects	Received 1 dose, single-blind run-in: 2401
Number of subjects completed	2174

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Discontinued before run-in solifenacin 5 mg: 1414
Reason: Number of subjects	Exclusion/inclusion criteria not met: 169
Reason: Number of subjects	Patient withdrawn: 32
Reason: Number of subjects	Adverse event: 16
Reason: Number of subjects	Other reasons: 7
Reason: Number of subjects	Lost to follow-up: 3

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of participants included in the pre-assignment period were the total number screened. The number of participants included in the worldwide number enrolled were the total number of participants randomized.

Period 1

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

Blinding implementation details:

The study was comprised of a 12 week double-blind treatment period (participants were randomized into the double-blind period if they experienced 1 or more incontinence episodes over the 3-day diary period prior to randomization to double-blind period and warranted additional relief for their OAB symptoms). There was 2 week safety follow up period (placebo administered). The active and placebo tablets were made indistinguishable by using a double-dummy packaging system.

Arms

Are arms mutually exclusive?	Yes

Arm title	Combination (solifenacin + mirabegron)

Arm description:

Participants received solifenacin 5 mg, mirabegron 25 mg and solifenacin 10 mg matching placebo once daily for the first 4 weeks of double-blind period. For the last 8 weeks of the double-blind treatment period, the 25 mg mirabegron tablet was replaced by a 50 mg mirabegron tablet. Placebo was given for the 2 week single-blind safety follow-up period.

Arm type	Experimental
Investigational medicinal product name	solifenacin 5 mg
Investigational medicinal product code	YM905
Other name	Vesicare, Vesitrim, Vesikur, solifenacin succinate
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Solifenacin was provided as the marketed formulation in the 5 mg strength. Medication was taken orally with a glass of water, with or without food.

Investigational medicinal product name	solifenacin 10 mg matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of solifenacin succinate 10 mg tablets was supplied. Medication was taken orally with a glass of water, with or without food.

Investigational medicinal product name	mirabegron 25 mg
Investigational medicinal product code	YM178
Other name	Betanis, Betmiga, Myrbetriq
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Mirabegron was supplied as the marketed formulation in the 25 mg OCAS (Oral Controlled Absorption System) modified release tablets. Medication was taken orally with a glass of water, with or without food.

Investigational medicinal product name	mirabegron 50 mg
Investigational medicinal product code	YM178
Other name	Betanis, Betmiga, Myrbetriq
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Mirabegron was supplied as the marketed formulation in the 50 mg OCAS (Oral Controlled Absorption System) modified release tablets. Medication was taken orally with a glass of water, with or without food.

Arm title	Solifenacin 5 mg

Arm description:

Participants received solifenacin 5 mg, mirabegron 25 mg matching placebo and solifenacin 10 mg matching placebo once daily. For the last 8 weeks of the double-blind treatment period, the 25 mg mirabegron matching placebo tablet was replaced by a 50 mg mirabegron matching placebo tablet (to maintain the blind). Placebo was given for the 2 week single-blind safety follow-up period.

Arm type	Active comparator
Investigational medicinal product name	solifenacin 5 mg
Investigational medicinal product code	YM905
Other name	Vesicare, Vesitrim, Vesikur, solifenacin succinate
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Solifenacin was provided as the marketed formulation in the 5 mg strength. Medication was taken orally

with a glass of water, with or without food.

Investigational medicinal product name	solifenacin 10 mg matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of solifenacin succinate 10 mg tablets was supplied. Medication was taken orally with a glass of water, with or without food.

Investigational medicinal product name	mirabegron 25 mg matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of mirabegron OCAS 25 mg tablets was supplied. Medication was taken orally with a glass of water, with or without food.

Investigational medicinal product name	mirabegron 50 mg matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of mirabegron OCAS 50 mg tablets was supplied. Medication was taken orally with a glass of water, with or without food.

Arm title	Solifenacin 10 mg

Arm description:

Participants received solifenacin 5 mg matching placebo, mirabegron 25 mg matching placebo and solifenacin 10 mg once daily. For the last 8 weeks of the double-blind treatment period, the 25 mg mirabegron matching placebo tablet was replaced by a 50 mg mirabegron matching placebo tablet (to maintain the blind). Placebo was given for the 2 week single-blind safety follow-up period.

Arm type	Active comparator
Investigational medicinal product name	solifenacin 5 mg matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of solifenacin succinate 5 mg tablets was supplied. Medication was taken orally with a glass of water, with or without food.

Investigational medicinal product name	solifenacin 10 mg
Investigational medicinal product code	YM905
Other name	Vesicare, Vesitrim, Vesikur, solifenacin succinate
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Solifenacin was provided as the marketed formulation in the 10 mg strength. Medication was taken orally with a glass of water, with or without food.

Investigational medicinal product name	mirabegron 25 mg matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of mirabegron OCAS 25 mg tablets was supplied. Medication was taken orally with a glass of water, with or without food.

Investigational medicinal product name	mirabegron 50 mg matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of mirabegron OCAS 50 mg tablets was supplied. Medication was taken orally with a glass of water, with or without food.

Number of subjects in period 1	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg
Started	727	728	719
Treated with double-blind drug	725	728	719
Completed	678	679	680
Not completed	49	49	39
Randomized no double-blind drug received	1	-	1
Discontinued (no EoT page)	2	-	-
Miscellaneous	-	2	-
Adverse event	13	11	13
Protocol Violation	2	2	-
Lost to follow-up	4	2	1
Lack of efficacy	1	3	2
Withdrawal by subject	26	29	22

Baseline characteristics

Reporting groups	
Reporting group title	Combination (solifenacin + mirabegron)
Reporting group description:	
Participants received solifenacin 5 mg, mirabegron 25 mg and solifenacin 10 mg matching placebo once daily for the first 4 weeks of double-blind period. For the last 8 weeks of the double-blind treatment period, the 25 mg mirabegron tablet was replaced by a 50 mg mirabegron tablet. Placebo was given for the 2 week single-blind safety follow-up period.	
Reporting group title	Solifenacin 5 mg
Reporting group description:	
Participants received solifenacin 5 mg, mirabegron 25 mg matching placebo and solifenacin 10 mg matching placebo once daily. For the last 8 weeks of the double-blind treatment period, the 25 mg mirabegron matching placebo tablet was replaced by a 50 mg mirabegron matching placebo tablet (to maintain the blind). Placebo was given for the 2 week single-blind safety follow-up period.	
Reporting group title	Solifenacin 10 mg
Reporting group description:	
Participants received solifenacin 5 mg matching placebo, mirabegron 25 mg matching placebo and solifenacin 10 mg once daily. For the last 8 weeks of the double-blind treatment period, the 25 mg mirabegron matching placebo tablet was replaced by a 50 mg mirabegron matching placebo tablet (to maintain the blind). Placebo was given for the 2 week single-blind safety follow-up period.	

Reporting group values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg
Number of subjects	727	728	719
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	58.2	56.9	57.4
standard deviation	± 13.1	± 13.5	± 13.2
Gender categorical			
Units:			
Male	123	124	119
Female	604	604	600

Reporting group values	Total		
Number of subjects	2174		
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units:			
Male	366		
Female	1808		

End points

End points reporting groups

Reporting group title	Combination (solifenacin + mirabegron)

Reporting group description:

Participants received solifenacin 5 mg, mirabegron 25 mg and solifenacin 10 mg matching placebo once daily for the first 4 weeks of double-blind period. For the last 8 weeks of the double-blind treatment period, the 25 mg mirabegron tablet was replaced by a 50 mg mirabegron tablet. Placebo was given for the 2 week single-blind safety follow-up period.

Reporting group title	Solifenacin 5 mg

Reporting group description:

Participants received solifenacin 5 mg, mirabegron 25 mg matching placebo and solifenacin 10 mg matching placebo once daily. For the last 8 weeks of the double-blind treatment period, the 25 mg mirabegron matching placebo tablet was replaced by a 50 mg mirabegron matching placebo tablet (to maintain the blind). Placebo was given for the 2 week single-blind safety follow-up period.

Reporting group title	Solifenacin 10 mg

Reporting group description:

Participants received solifenacin 5 mg matching placebo, mirabegron 25 mg matching placebo and solifenacin 10 mg once daily. For the last 8 weeks of the double-blind treatment period, the 25 mg mirabegron matching placebo tablet was replaced by a 50 mg mirabegron matching placebo tablet (to maintain the blind). Placebo was given for the 2 week single-blind safety follow-up period.

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:

The mean number of incontinence episodes (complaint of any involuntary leakage of urine) per day was derived from number of incontinence episodes recorded on valid diary days during the 3-day micturition diary period divided by the number of valid diary days during the 3-day micturition diary period. The analysis population consisted of the Full Analysis Set (FAS) which comprised of all the Randomized Analysis Set's (RAS) participants who met the following criteria: took at least 1 dose of double-blind study drug after randomization, reported at least 1 micturition in the baseline diary & at least 1 micturition postbaseline & reported at least 1 incontinence episode in the baseline diary. For participants who withdrew before EoT (week 12) and have no measurement available for that diary period, the Last Observation Carried Forward (LOCF) value during the double-blind study period was used as EoT value to derive the primary variable.

End point type	Primary

End point timeframe:

Baseline and end of treatment (up to 12 weeks)

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	706	704	697	
Units: incontinence episodes				
least squares mean (standard error)	-1.8 (± 0.08)	-1.53 (± 0.08)	-1.67 (± 0.08)	

Statistical analyses

Statistical analysis title	Adjusted Difference Combination vs Solifenacin 5mg

Statistical analysis description:

Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group based on ANCOVA model. Means (LS means) and 95% Confidence Intervals (CIs) are from an ANCOVA model with sex, age group (< 65, ≥ 65 years), geographic region, and 4-week incontinence episode reduction group as fixed factors and mean number of incontinence episodes per 24 hours at baseline as a covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1410
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [1]
Method	stratified rank ANCOVA
Parameter estimate	Least Squares (LS) Means
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	-0.05
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[1] - P values for pairwise comparisons were from the stratified rank ANCOVA model. P < 0.05 indicated superiority in favor of treatment group with the largest improvement.

Secondary: Change from Baseline to Weeks 4, 8 & 12 in Mean Number of Incontinence Episodes per 24 Hours

End point title	Change from Baseline to Weeks 4, 8 & 12 in Mean Number of Incontinence Episodes per 24 Hours

End point description:

The mean number of incontinence episodes (complaint of any involuntary leakage of urine) per day was derived from number of incontinence episodes recorded on valid diary days during the 3-day micturition diary period divided by the number of valid diary days during the 3-day micturition diary period. The analysis population consisted of the FAS. N=number of participants with available data (applicable for all secondary endpoints).

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8 & 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: incontinence episodes				
least squares mean (standard error)				
Week 4 (N= 690, 690, 679)	-1.24 (± 0.07)	-0.91 (± 0.07)	-1.12 (± 0.07)	
Week 8 (N= 661, 674, 673)	-1.68 (± 0.07)	-1.29 (± 0.07)	-1.49 (± 0.07)	
Week 12 (N= 653, 645, 664)	-1.81 (± 0.08)	-1.57 (± 0.08)	-1.67 (± 0.08)	

Statistical analyses

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group based on ANCOVA model. Means (LS means) and 95% Confidence Intervals (CIs) are from an ANCOVA model with sex, age group (< 65, ≥ 65 years), geographic region, and 4-week incontinence episode reduction group as fixed factors and mean number of incontinence episodes per 24 hours at baseline as a covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [2]
Method	stratified rank ANCOVA
Parameter estimate	LS Means
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.52
upper limit	-0.14
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[2] - P values for pairwise comparisons are from the stratified rank ANCOVA model. P < 0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group based on ANCOVA model. Means (LS means) and 95% Confidence Intervals (CIs) are from an ANCOVA model with sex, age group (< 65, ≥ 65 years), geographic region, and 4-week incontinence episode reduction group as fixed factors and mean number of incontinence episodes per 24 hours at baseline as a covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [3]
Method	stratified rank ANCOVA
Parameter estimate	LS Means
Point estimate	-0.39

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	-0.18
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[3] - P values for pairwise comparisons are from the stratified rank ANCOVA model. P < 0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group based on ANCOVA model. Means (LS means) and 95% Confidence Intervals (CIs) are from an ANCOVA model with sex, age group (< 65, ≥ 65 years), geographic region, and 4-week incontinence episode reduction group as fixed factors and mean number of incontinence episodes per 24 hours at baseline as a covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [4]
Method	stratified rank ANCOVA
Parameter estimate	LS Means
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	-0.03
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[4] - P-values for pairwise comparisons are from the stratified rank ANCOVA model. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Secondary: Change from Baseline in Mean Number of Micturitions per 24 Hours

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

End point description:

The average number of micturitions (voluntary urinations (excluding incontinence only episodes)) per 24 hours was derived from number of micturitions recorded on valid diary days during the 3-day micturition diary period divided by the number of valid diary days during the 3-day micturition diary period (excluding incontinence only episodes). LOCF was used for EoT. The analysis population included the FAS.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8 & 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: micturitions				
least squares mean (standard error)				
Week 4 (N= 690, 690, 679)	-0.95 (± 0.07)	-0.69 (± 0.07)	-0.79 (± 0.07)	
Week 8 (N= 661, 674, 673)	-1.36 (± 0.08)	-0.94 (± 0.08)	-1.00 (± 0.08)	
Week 12 (N= 653, 645, 664)	-1.63 (± 0.08)	-1.16 (± 0.09)	-1.11 (± 0.08)	
EoT (N= 706, 704, 697)	-1.59 (± 0.08)	-1.14 (± 0.08)	-1.12 (± 0.08)	

Statistical analyses

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs and p-value were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01 [5]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	-0.06
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[5] - P-values for pairwise comparisons are from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs and p-value were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [6]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	-0.19
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[6] - P-values for pairwise comparisons are from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs and p-value were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [7]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	-0.23
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[7] - P-values for pairwise comparisons are from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs and p-value were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [8]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.67
upper limit	-0.22
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[8] - P-values for pairwise comparisons are from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Secondary: Number of Incontinence Episodes Reported During the 3-Day Diary

End point title	Number of Incontinence Episodes Reported During the 3-Day Diary

End point description:

The number of incontinence episodes (complaint of any involuntary leakage of urine) per day was derived from total number of incontinence episodes on valid diary days recorded during the 3-day micturition diary period. LOCF was used for EoT. The analysis population included the FAS.

End point type	Secondary

End point timeframe:

Weeks 4, 8 and 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: incontinence episodes				
arithmetic mean (standard error)				
Week 4 (N= 690, 690, 679)	5.81 (± 0.30)	6.68 (± 0.31)	6.41 (± 0.33)	
Week 8 (N= 661, 674, 673)	4.55 (± 0.30)	5.43 (± 0.30)	5.28 (± 0.32)	
Week 12 (N= 653, 645, 664)	4.03 (± 0.29)	4.56 (± 0.28)	4.62 (± 0.31)	
EoT (N= 706, 704, 697)	4.25 (± 0.29)	4.87 (± 0.28)	4.72 (± 0.31)	

Statistical analyses

Statistical analysis title	Rate Ratio Combination vs 5 mg Solifenacin Week 4

Statistical analysis description:

Rate ratio, 95% CIs, & p-value for number of incontinence episodes during EoT 3-day diary between combination & solifenacin treatment was calculated from Mixed Effects Poisson (negative binomial) regression model including treatment group, sex, age group (<65, >=65 years), geographic region & 4-week incontinence episode reduction group as factors, log of (number of incontinence episodes/valid

diary days) at baseline as covariate & log of number of valid diary days as the offset variable.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005 [9]
Method	Mixed Effects Poisson
Parameter estimate	Rate Ratio
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	0.96
Variability estimate	Standard error of the mean
Dispersion value	0.05

Notes:

[9] - p<0.05 indicates superiority in favor of treatment group with lowest rate of incontinence episodes.

Statistical analysis title	Rate Ratio Combination vs 5 mg Solifenacin Week 8

Statistical analysis description:

Rate ratio, 95% CIs, & p-value for number of incontinence episodes during EoT 3-day diary between combination & solifenacin treatment was calculated from Mixed Effects Poisson (negative binomial) regression model including treatment group, sex, age group (<65, >=65 years), geographic region & 4-week incontinence episode reduction group as factors, log of (number of incontinence episodes/valid diary days) at baseline as covariate & log of number of valid diary days as the offset variable.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [10]
Method	Mixed Effects Poisson
Parameter estimate	Rate Ratio
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	0.86
Variability estimate	Standard error of the mean
Dispersion value	0.07

Notes:

[10] - p<0.05 indicates superiority in favor of treatment group with lowest rate of incontinence episodes.

Statistical analysis title	Rate Ratio Combination vs 5 mg Solifenacin Week 12

Statistical analysis description:

Rate ratio, 95% CIs, & p-value for number of incontinence episodes during EoT 3-day diary between combination & solifenacin treatment was calculated from Mixed Effects Poisson (negative binomial) regression model including treatment group, sex, age group (<65, >=65 years), geographic region & 4-week incontinence episode reduction group as factors, log of (number of incontinence episodes/valid diary days) at baseline as covariate & log of number of valid diary days as the offset variable.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.021 [11]
Method	Mixed Effects Poisson
Parameter estimate	Rate Ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.97
Variability estimate	Standard error of the mean
Dispersion value	0.08

Notes:

[11] - p<0.05 indicates superiority in favor of treatment group with lowest rate of incontinence episodes.

Statistical analysis title	Rate Ratio Combination vs 5 mg Solifenacin EoT

Statistical analysis description:

Rate ratio, 95% CIs, & p-value for number of incontinence episodes during EoT 3-day diary between combination & solifenacin treatment was calculated from Mixed Effects Poisson (negative binomial) regression model including treatment group, sex, age group (<65, >=65 years), geographic region & 4-week incontinence episode reduction group as factors, log of (number of incontinence episodes/valid diary days) at baseline as covariate & log of number of valid diary days as the offset variable.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014 [12]
Method	Mixed Effects Poisson
Parameter estimate	Rate Ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	0.96
Variability estimate	Standard error of the mean
Dispersion value	0.08

Notes:

[12] - p<0.05 indicates superiority in favor of treatment group with lowest rate of incontinence episodes.

Secondary: Change from Baseline in Mean Volume Voided (MVV) per Micturition

End point title	Change from Baseline in Mean Volume Voided (MVV) per Micturition

End point description:

MVV per micturition was defined as MVV (mL) per micturition during last 3 days of the 3-day micturition diary period. MVV per micturition was calculated as the sum of each volume voided for each record with volume voided > 0 on valid diary days divided by the total number of records with a volume voided > 0 on valid diary days during the 3-day micturition diary period. LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8 & 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: mL				
least squares mean (standard error)				
Week 4 (N= 665, 669, 664)	15.06 (± 1.55)	11.20 (± 1.55)	14.99 (± 1.55)	
Week 8 (N= 638, 648, 655)	25.21 (± 1.89)	14.02 (± 1.87)	21.08 (± 1.86)	
Week 12 (N= 627, 617, 642)	29.54 (± 2.06)	17.16 (± 2.08)	20.99 (± 2.04)	
EoT (N= 680, 682, 682)	28.05 (± 1.97)	16.52 (± 1.97)	20.30 (± 1.97)	

Statistical analyses

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs and p-value were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.078 [13]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	3.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.43
upper limit	8.16
Variability estimate	Standard error of the mean
Dispersion value	2.19

Notes:

[13] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs and p-value were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [14]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	11.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.98
upper limit	16.4
Variability estimate	Standard error of the mean
Dispersion value	2.66

Notes:

[14] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs and p-value were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [15]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	12.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.65
upper limit	18.12
Variability estimate	Standard error of the mean
Dispersion value	2.92

Notes:

[15] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs and p-value were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [16]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	11.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.06
upper limit	16.99
Variability estimate	Standard error of the mean
Dispersion value	2.79

Notes:

[16] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Secondary: Change from Baseline to EoT in Corrected Micturition Frequency (CMF)

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

End point description:

CMF was defined as the mean number of micturitions per 24 hours that participants would have at EoT if their fluid intake had remained unchanged since baseline. This was calculated by the MVV per Micturition at baseline multiplied by the mean number of micturitions per 24 hours at baseline divided by the MVV per micturition at EoT. LOCF was used. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and EoT (up to 12 weeks)

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	706	704	697	
Units: micturitions				
least squares mean (standard error)	-0.96 (± 0.10)	-0.52 (± 0.10)	-0.71 (± 0.10)	

Statistical analyses

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs and p-value were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1410
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [17]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	-0.16
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[17] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Secondary: Change from Baseline in Mean Number of Urgency Incontinence (UI) Episodes per 24 Hours

End point title	Change from Baseline in Mean Number of Urgency Incontinence (UI) Episodes per 24 Hours

End point description:

UI was defined as the complaint of involuntary urine leakage accompanied by or immediately preceded by urgency. UI was measured using the Patient Perception of Intensity of Urgency Scale (PPIUS), a patient reported outcome validated 5-point categorical scale rating the degree of associated urinary urgency severity (0=No urgency, I felt no need to empty my bladder, but did so for other reasons. 1=Mild, I could postpone voiding as long as necessary, without fear of wetting myself. 2= Moderate, I could postpone voiding for a short while, without fear of wetting myself. 3=Severe, I could not postpone voiding, but had to rush to the toilet in order not to wet myself. 4=Urgency incontinence, I leaked before arriving to the toilet). One urgency incontinence episode was counted for each record of the diary in which the following occurred: incontinence episode or 'both' was recorded & severity of urinary urgency recorded was 3 or 4. LOCF was used for EoT. FAS population.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8 & 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: UI episodes				
least squares mean (standard error)				
Week 4 (N= 676, 670, 650)	-1.26 (± 0.07)	-0.91 (± 0.07)	-1.14 (± 0.07)	
Week 8 (N= 649, 654, 645)	-1.70 (± 0.07)	-1.25 (± 0.07)	-1.45 (± 0.07)	
Week 12 (N= 643, 627, 635)	-1.84 (± 0.07)	-1.58 (± 0.07)	-1.62 (± 0.07)	
EoT (N= 691, 683, 666)	-1.82 (± 0.07)	-1.54 (± 0.07)	-1.63 (± 0.07)	

Statistical analyses

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[18]
P-value	< 0.001 [19]
Method	stratified rank ANCOVA
Parameter estimate	LS Means
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	-0.17
Variability estimate	Standard error of the mean
Dispersion value	0.09

Notes:

[18] - Only participants with at least one UI episode reported in baseline diary were included.

[19] - P-values for pairwise comparisons were from stratified rank ANCOVA model. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[20]
P-value	< 0.001 [21]
Method	stratified rank ANCOVA
Parameter estimate	LS Means
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	-0.25
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[20] - Only participants with at least one UI episode reported in baseline diary were included.

[21] - P-values for pairwise comparisons were from stratified rank ANCOVA model. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[22]
P-value	= 0.004 [23]
Method	stratified rank ANCOVA
Parameter estimate	LS Means
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	-0.05
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[22] - Only participants with at least one UI episode reported in baseline diary were included.

[23] - P-values for pairwise comparisons were from stratified rank ANCOVA model. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[24]
P-value	= 0.003 [25]
Method	stratified rank ANCOVA
Parameter estimate	LS Means
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	-0.07
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[24] - Only participants with at least one UI episode reported in baseline diary were included.

[25] - P-values for pairwise comparisons were from stratified rank ANCOVA model. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Secondary: Number of UI Episodes Reported During the 3-Day Diary

End point title	Number of UI Episodes Reported During the 3-Day Diary

End point description:

Number of UI episodes was calculated using the number of UI episodes recorded on valid diary days during the 3-day micturition diary period. NOTE: Only urgency incontinence episodes recorded on a valid diary day were counted. LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Weeks 4, 8 and 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: UI episodes				
arithmetic mean (standard error)				
Week 4 (N= 676, 670, 650)	4.96 (± 0.27)	5.86 (± 0.29)	5.50 (± 0.30)	
Week 8 (N= 649, 654, 645)	3.55 (± 0.25)	4.76 (± 0.27)	4.50 (± 0.30)	
Week 12 (N= 643, 627, 635)	3.10 (± 0.24)	3.78 (± 0.25)	3.91 (± 0.30)	
EoT (N= 691, 683, 666)	3.33 (± 0.24)	4.00 (± 0.25)	3.96 (± 0.29)	

Statistical analyses

Statistical analysis title	Rate Ratio Combination vs 5 mg Solifenacin Week 4

Statistical analysis description:

Rate ratio, 95% CIs, and p-value for number of UI episodes during EoT 3-day diary between combination and solifenacin treatment was calculated from a Mixed Effects Poisson (negative binomial) regression model including treatment group, sex, age group (<65, >=65 years), geographic region and 4-week incontinence episode reduction group as factors, log of (number of UI episodes/number of valid diary days) at baseline as covariate and log of number of valid diary as the offset variable.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[26]
P-value	= 0.003 [27]
Method	Mixed Effects Poisson
Parameter estimate	Rate Ratio
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	0.94
Variability estimate	Standard error of the mean
Dispersion value	0.05

Notes:

[26] - Only participants with at least one UI episode reported in baseline diary were included.

[27] - p<0.05 indicates superiority in favor of treatment group with lowest rate of UI episodes.

Statistical analysis title	Rate Ratio Combination vs 5 mg Solifenacin Week 8

Statistical analysis description:

Rate ratio, 95% CIs, and p-value for number of UI episodes during EoT 3-day diary between combination and solifenacin treatment was calculated from a Mixed Effects Poisson (negative binomial) regression model including treatment group, sex, age group (<65, >=65 years), geographic region and 4-week incontinence episode reduction group as factors, log of (number of UI episodes/number of valid diary days) at baseline as covariate and log of number of valid diary as the offset variable.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[28]
P-value	< 0.001 [29]
Method	Mixed Effects Poisson
Parameter estimate	Rate Ratio
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	0.86
Variability estimate	Standard error of the mean
Dispersion value	0.08

Notes:

[28] - Only participants with at least one UI episode reported in baseline diary were included.

[29] - p<0.05 indicates superiority in favor of treatment group with lowest rate of UI episodes.

Statistical analysis title	Rate Ratio Combination vs 5 mg Solifenacin Week 12

Statistical analysis description:

Rate ratio, 95% CIs, and p-value for number of UI episodes during EoT 3-day diary between combination and solifenacin treatment was calculated from a Mixed Effects Poisson (negative binomial) regression model including treatment group, sex, age group (<65, >=65 years), geographic region and 4-week incontinence episode reduction group as factors, log of (number of UI episodes/number of valid diary days) at baseline as covariate and log of number of valid diary as the offset variable.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[30]
P-value	= 0.038 [31]
Method	Mixed Effects Poisson
Parameter estimate	Rate Ratio
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	0.99
Variability estimate	Standard error of the mean
Dispersion value	0.09

Notes:

[30] - Only participants with at least one UI episode reported in baseline diary were included.

[31] - p<0.05 indicates superiority in favor of treatment group with lowest rate of UI episodes.

Statistical analysis title	Rate Ratio Combination vs 5 mg Solifenacin EoT

Statistical analysis description:

Rate ratio, 95% CIs, and p-value for number of UI episodes during EoT 3-day diary between

combination and solifenacin treatment was calculated from a Mixed Effects Poisson (negative binomial) regression model including treatment group, sex, age group (<65, >=65 years), geographic region and 4-week incontinence episode reduction group as factors, log of (number of UI episodes/number of valid diary days) at baseline as covariate and log of number of valid diary as the offset variable.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[32]
P-value	= 0.022 [33]
Method	Mixed Effects Poisson
Parameter estimate	Rate Ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	0.97
Variability estimate	Standard error of the mean
Dispersion value	0.09

Notes:

[32] - Only participants with at least one UI episode reported in baseline diary were included.

[33] - p<0.05 indicates superiority in favor of treatment group with lowest rate of UI episodes.

Secondary: Change from Baseline in Mean Number of Urgency Episodes (Grade 3 and/or 4) per 24 Hours

End point title	Change from Baseline in Mean Number of Urgency Episodes (Grade 3 and/or 4) per 24 Hours

End point description:

An urgency episode was defined as the complaint of a sudden, compelling desire to pass urine, which is difficult to defer. The mean number of urgency episodes (severity of 3 or 4) per 24 hours was defined as the average number of times a participant recorded an urgency episode (severity of 3 or 4) with or without incontinence per day during the 3-day micturition diary period. Measured using the PPIUS scale. This was calculated using the sum of each record with an urgency episode (severity of 3 or 4) recorded on a valid diary day divided by the number of valid diary days during the 3-day micturition diary period. LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8 & 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: urgency episodes				
least squares mean (standard error)				
Week 4 (N= 684, 681, 663)	-1.84 (± 0.09)	-1.39 (± 0.09)	-1.74 (± 0.10)	
Week 8 (N= 654, 665, 659)	-2.64 (± 0.10)	-2.00 (± 0.10)	-2.29 (± 0.10)	
Week 12 (N= 647, 638, 648)	-2.97 (± 0.11)	-2.44 (± 0.11)	-2.55 (± 0.11)	
EoT (N= 699, 694, 680)	-2.95 (± 0.10)	-2.41 (± 0.10)	-2.54 (± 0.11)	

Statistical analyses

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[34]
P-value	= 0.001 [35]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.72
upper limit	-0.19
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[34] - Only participants with at least one urgency episode reported in baseline diary were included.

[35] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[36]
P-value	< 0.001 [37]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.64

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	-0.35
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[36] - Only participants with at least one urgency episode reported in baseline diary were included.

[37] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[38]
P-value	= 0.001 [39]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.82
upper limit	-0.22
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[38] - Only participants with at least one urgency episode reported in baseline diary were included.

[39] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[40]
P-value	< 0.001 [41]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.54

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.83
upper limit	-0.25
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[40] - Only participants with at least one urgency episode reported in baseline diary were included.

[41] - P-values for pairwise comparisons were from the ANCOVA model described above. $p<0.05$ indicates superiority in favor of treatment group with the largest improvement.

Secondary: Change from Baseline in Mean Number of Pads per 24 hours

End point title	Change from Baseline in Mean Number of Pads per 24 hours

End point description:

The mean number of pads per 24 hours was defined as the average number of times a participant recorded a new pad used per day during the 3-day micturition diary period. This was calculated using the number of new pads used during valid diary days during the 3-day micturition diary period divided by the number of valid diary days during the 3-day micturition diary period. LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8 & 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: pads				
least squares mean (standard error)				
Week 4 (N= 497, 467, 474)	-1.12 (± 0.07)	-0.86 (± 0.07)	-1.04 (± 0.07)	
Week 8 (N= 482, 459, 469)	-1.50 (± 0.07)	-1.17 (± 0.08)	-1.36 (± 0.08)	
Week 12 (N= 477, 440, 468)	-1.65 (± 0.07)	-1.38 (± 0.07)	-1.43 (± 0.07)	
EoT (N= 510, 476, 487)	-1.66 (± 0.07)	-1.35 (± 0.07)	-1.43 (± 0.07)	

Statistical analyses

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group & geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[42]
P-value	= 0.008 [43]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	-0.07
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[42] - Only participants with reported use of at least one pad reported in baseline diary were included.

[43] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group & geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[44]
P-value	= 0.002 [45]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	-0.13
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[44] - Only participants with reported use of at least one pad reported in baseline diary were included.

[45] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group & geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[46]
P-value	= 0.006 [47]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	-0.08
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[46] - Only participants with reported use of at least one pad reported in baseline diary were included.

[47] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group & geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[48]
P-value	= 0.002 [49]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.51
upper limit	-0.12
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[48] - Only participants with reported use of at least one pad reported in baseline diary were included.

[49] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Secondary: Number of Pads Used During the 3-Day Diary

End point title	Number of Pads Used During the 3-Day Diary

End point description:

The number of pads used was defined as the number of times a participant recorded a new pad used during the 3-day micturition diary period. This was calculated using the sum of each record with new pad checked. Only records with new pad checked on a valid diary day were counted. LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:
Weeks 4, 8 and 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: pads				
arithmetic mean (standard error)				
Week 4 (N= 497, 467, 474)	4.80 (± 0.28)	5.69 (± 0.36)	5.41 (± 0.29)	
Week 8 (N= 482, 459, 469)	3.64 (± 0.24)	4.71 (± 0.37)	4.50 (± 0.29)	
Week 12 (N= 477, 440, 468)	3.23 (± 0.22)	4.13 (± 0.28)	4.07 (± 0.28)	
EoT (N= 510, 476, 487)	3.29 (± 0.22)	4.27 (± 0.28)	4.17 (± 0.29)	

Statistical analyses

Statistical analysis title	Rate Ratio Combination vs 5 mg Solifenacin Week 4

Statistical analysis description:

Rate ratio, 95% CIs, and p-value for number of pads used during the 3-day diary between combination & solifenacin treatment was calculated from a Mixed Effects Poisson (negative binomial) regression model including treatment group, sex, age group (<65, >=65 years), geographic region and 4-week incontinence episode reduction group as factors, log of (number of pads used/number of valid diary days) at baseline as covariate and log of number of valid diary days as the offset variable.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[50]
P-value	= 0.545 [51]
Method	Mixed Effects Poisson
Parameter estimate	Rate Ratio
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.08
Variability estimate	Standard error of the mean
Dispersion value	0.06

Notes:

[50] - Only participants who reported use of at least one pad in baseline diary were included.

[51] - p<0.05 indicates superiority in favor of treatment group with lowest rate of pads used.

Statistical analysis title	Rate Ratio Combination vs 5 mg Solifenacin Week 8

Statistical analysis description:

Rate ratio, 95% CIs, and p-value for number of pads used during the 3-day diary between combination & solifenacin treatment was calculated from a Mixed Effects Poisson (negative binomial) regression model including treatment group, sex, age group (<65, >=65 years), geographic region and 4-week incontinence episode reduction group as factors, log of (number of pads used/number of valid diary

days) at baseline as covariate and log of number of valid diary days as the offset variable.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[52]
P-value	= 0.01 [53]
Method	Mixed Effects Poisson
Parameter estimate	Rate Ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.95
Variability estimate	Standard error of the mean
Dispersion value	0.08

Notes:

[52] - Only participants who reported use of at least one pad in baseline diary were included.

[53] - p<0.05 indicates superiority in favor of treatment group with lowest rate of pads used.

Statistical analysis title	Rate Ratio Combination vs 5 mg Solifenacin Week 12

Statistical analysis description:

Rate ratio, 95% CIs, and p-value for number of pads used during the 3-day diary between combination & solifenacin treatment was calculated from a Mixed Effects Poisson (negative binomial) regression model including treatment group, sex, age group (<65, >=65 years), geographic region and 4-week incontinence episode reduction group as factors, log of (number of pads used/number of valid diary days) at baseline as covariate and log of number of valid diary days as the offset variable.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[54]
P-value	= 0.007 [55]
Method	Mixed Effects Poisson
Parameter estimate	Rate Ratio
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	0.94
Variability estimate	Standard error of the mean
Dispersion value	0.09

Notes:

[54] - Only participants who reported use of at least one pad in baseline diary were included.

[55] - p<0.05 indicates superiority in favor of treatment group with lowest rate of pads used.

Statistical analysis title	Rate Ratio Combination vs 5 mg Solifenacin EoT

Statistical analysis description:

Rate ratio, 95% CIs, and p-value for number of pads used during the 3-day diary between combination & solifenacin treatment was calculated from a Mixed Effects Poisson (negative binomial) regression model including treatment group, sex, age group (<65, >=65 years), geographic region and 4-week incontinence episode reduction group as factors, log of (number of pads used/number of valid diary days) at baseline as covariate and log of number of valid diary days as the offset variable.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[56]
P-value	= 0.003 [57]
Method	Mixed Effects Poisson
Parameter estimate	Rate Ratio
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	0.92
Variability estimate	Standard error of the mean
Dispersion value	0.08

Notes:

[56] - Only participants who reported use of at least one pad in baseline diary were included.

[57] - p<0.05 indicates superiority in favor of treatment group with lowest rate of pads used.

Secondary: Change from Baseline in Mean Number of Nocturia Episodes

End point title	Change from Baseline in Mean Number of Nocturia Episodes

End point description:

Mean number of nocturia episodes was defined as the number of times a participant urinated (excluding incontinence only episodes) while sleeping during the 3-day diary period, divided by the number of valid diary days during the diary period. Night time episode of incontinence only was not considered a nocturia episode. Nocturia episodes were counted for each micturition record which occurred between the date/time of going to bed with intention to sleep and the date/time of getting up with intention to stay awake on a valid diary day & which was accompanied by a sleep interruption. Nocturia only determined for those who were not night-shift workers. LOCF used for EoT.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8 & 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: nocturia episodes				
least squares mean (standard error)				
Week 4 (N= 526, 514, 517)	-0.28 (± 0.03)	-0.27 (± 0.03)	-0.29 (± 0.03)	
Week 8 (N= 500, 501, 514)	-0.37 (± 0.03)	-0.35 (± 0.03)	-0.37 (± 0.03)	
Week 12 (N= 492, 480, 510)	-0.46 (± 0.03)	-0.38 (± 0.03)	-0.41 (± 0.03)	
EoT (N= 537, 523, 531)	-0.43 (± 0.03)	-0.37 (± 0.03)	-0.41 (± 0.03)	

Statistical analyses

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs and p-value were generated from an ANCOVA

model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[58]
P-value	= 0.836 [59]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.08
Variability estimate	Standard error of the mean
Dispersion value	0.05

Notes:

[58] - Only participants with at least one nocturia episode reported in baseline diary were included. The analysis population consisted of the FAS.
[59] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs and p-value were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[60]
P-value	= 0.617 [61]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.07
Variability estimate	Standard error of the mean
Dispersion value	0.05

Notes:

[60] - Only participants with at least one nocturia episode reported in baseline diary were included. The analysis population consisted of the FAS.
[61] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs and p-value were generated from an ANCOVA

model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[62]
P-value	= 0.134 [63]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.17
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.05

Notes:

[62] - Only participants with at least one nocturia episode reported in baseline diary were included. The analysis population consisted of the FAS.
[63] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs and p-value were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[64]
P-value	= 0.174 [65]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.05

Notes:

[64] - Only participants with at least one nocturia episode reported in baseline diary were included. The analysis population consisted of the FAS.
[65] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicates superiority in favor of treatment group with the largest improvement.

Secondary: Number of Nocturia Episodes Reported Over 3-Day Diary

End point title	Number of Nocturia Episodes Reported Over 3-Day Diary

End point description:

The number of nocturia episodes was defined as the number of times a participant urinated (excluding incontinence only episodes) during sleeping time during the 3-day micturition diary period. This was calculated using the sum of each nocturia episode recorded on valid diary days during the 3-day micturition diary period. LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Weeks 4, 8 and 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: nocturia episodes				
arithmetic mean (standard error)				
Week 4 (N= 526, 514, 517)	3.63 (± 0.12)	3.59 (± 0.12)	3.58 (± 0.12)	
Week 8 (N= 500, 501, 514)	3.33 (± 0.12)	3.35 (± 0.12)	3.32 (± 0.12)	
Week 12 (N= 492, 480, 510)	3.12 (± 0.13)	3.26 (± 0.12)	3.23 (± 0.12)	
EoT (N= 537, 523, 531)	3.16 (± 0.12)	3.28 (± 0.11)	3.19 (± 0.12)	

Statistical analyses

Statistical analysis title	Rate Ratio Combination vs 5 mg Solifenacin Week 4

Statistical analysis description:

Rate ratio, 95% CIs, & p-value for number of nocturia episodes during the 3-day diary between combination & solifenacin treatment was calculated from a Mixed Effects Poisson (negative binomial) regression model including treatment group, sex, age group (<65, >=65 years), geographic region & 4-week incontinence episode reduction group as factors, log of (number of nocturia episodes/number of valid diary days) at baseline as covariate and log of number of valid diary days as the offset variable.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[66]
P-value	= 0.993 [67]
Method	Mixed Effects Poisson
Parameter estimate	Rate Ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.08
Variability estimate	Standard error of the mean
Dispersion value	0.04

Notes:

[66] - Only participants with at least one nocturia episode reported in baseline diary were included.

[67] - p<0.05 indicates superiority in favor of treatment group with lowest rate of nocturia episodes.

Statistical analysis title	Rate Ratio Combination vs 5 mg Solifenacin Week 8

Statistical analysis description:

Rate ratio, 95% CIs, & p-value for number of nocturia episodes during the 3-day diary between combination & solifenacin treatment was calculated from a Mixed Effects Poisson (negative binomial) regression model including treatment group, sex, age group (<65, >=65 years), geographic region & 4-week incontinence episode reduction group as factors, log of (number of nocturia episodes/number of valid diary days) at baseline as covariate and log of number of valid diary days as the offset variable.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[68]
P-value	= 0.736 [69]
Method	Mixed Effects Poisson
Parameter estimate	Rate Ratio
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.07
Variability estimate	Standard error of the mean
Dispersion value	0.04

Notes:

[68] - Only participants with at least one nocturia episode reported in baseline diary were included.

[69] - p<0.05 indicates superiority in favor of treatment group with lowest rate of nocturia episodes.

Statistical analysis title	Rate Ratio Combination vs 5 mg Solifenacin Week 12

Statistical analysis description:

Rate ratio, 95% CIs, & p-value for number of nocturia episodes during the 3-day diary between combination & solifenacin treatment was calculated from a Mixed Effects Poisson (negative binomial) regression model including treatment group, sex, age group (<65, >=65 years), geographic region & 4-week incontinence episode reduction group as factors, log of (number of nocturia episodes/number of valid diary days) at baseline as covariate and log of number of valid diary days as the offset variable.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[70]
P-value	= 0.121 [71]
Method	Mixed Effects Poisson
Parameter estimate	Rate Ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.02
Variability estimate	Standard error of the mean
Dispersion value	0.05

Notes:

[70] - Only participants with at least one nocturia episode reported in baseline diary were included.

[71] - p<0.05 indicates superiority in favor of treatment group with lowest rate of nocturia episodes.

Statistical analysis title	Rate Ratio Combination vs 5 mg Solifenacin EoT

Statistical analysis description:

Rate ratio, 95% CIs, & p-value for number of nocturia episodes during the 3-day diary between combination & solifenacin treatment was calculated from a Mixed Effects Poisson (negative binomial) regression model including treatment group, sex, age group (<65, >=65 years), geographic region & 4-week incontinence episode reduction group as factors, log of (number of nocturia episodes/number of valid diary days) at baseline as covariate and log of number of valid diary days as the offset variable.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority[72]
P-value	= 0.172 [73]
Method	Mixed Effects Poisson
Parameter estimate	Rate Ratio
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.03
Variability estimate	Standard error of the mean
Dispersion value	0.04

Notes:

[72] - Only participants with at least one nocturia episode reported in baseline diary were included.

[73] - p<0.05 indicates superiority in favor of treatment group with lowest rate of nocturia episodes.

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

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

End point description:

The EQ-5D is an international, standardized, nondisease specific instrument for describing and valuing health status. It has 5 dimensions: Mobility, Self-care, Usual Activities, Pain/Discomfort, and Anxiety/Depression. Each dimension has 5 response levels: level 1=no problem or none; level 2=slight problems; level 3=moderate problems; level 4=severe problems; level 5=unable to perform activity. LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and EoT (up to 12 weeks)

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: participants				
number (not applicable)				
No problems -> no problems	409	370	374	
No problems -> slight problems	33	35	36	
No problems -> moderate problems	14	11	11	
No problems -> severe problems	0	7	4	
No problems -> extreme problems	0	1	0	
No problems -> no data	2	4	5	

Slight problems -> no problems	52	58	60	
Slight problems -> slight problems	43	46	40	
Slight problems -> moderate problems	15	28	16	
Slight problems -> severe problems	1	3	3	
Slight problems -> extreme problems	0	0	0	
Slight problems -> no data	2	0	0	
Moderate problems -> no problems	24	36	25	
Moderate problems -> slight problems	25	18	23	
Moderate problems -> moderate problems	28	28	40	
Moderate problems -> severe problems	2	3	7	
Moderate problems -> extreme problems	0	1	0	
Moderate problems -> no data	1	0	0	
Severe problems -> no problems	7	8	2	
Severe problems -> slight problems	6	7	7	
Severe problems -> moderate problems	17	11	11	
Severe problems -> severe problems	12	10	14	
Severe problems -> extreme problems	0	0	0	
Severe problems -> no data	1	1	0	
Extreme problems -> no problems	3	2	2	
Extreme problems -> slight problems	1	0	0	
Extreme problems -> moderate problems	1	1	1	
Extreme problems -> severe problems	1	0	0	
Extreme problems -> extreme problems	0	0	0	
Extreme problems -> no data	0	0	0	
No data -> no problems	4	9	13	
No data -> slight problems	2	4	1	
No data -> moderate problems	0	3	3	
No data -> severe problems	0	0	0	
No data -> extreme problems	0	0	0	
No data -> no data	1	0	0	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The EQ-5D is an international, standardized, nondisease specific instrument for describing and valuing health status. It has 5 dimensions: Mobility, Self-care, Usual Activities, Pain/Discomfort, and Anxiety/Depression. Each dimension has 5 response levels: level 1=no problem or none; level 2=slight problems; level 3=moderate problems; level 4=severe problems; level 5=unable to perform activity. LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and EoT (up to 12 weeks)

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: participants				
number (not applicable)				
No problems -> no problems	548	541	548	
No problems -> slight problems	28	26	25	
No problems -> moderate problems	0	14	7	
No problems -> severe problems	3	0	2	
No problems -> extreme problems	0	0	0	
No problems -> no data	6	5	4	
Slight problems -> no problems	37	25	32	
Slight problems -> slight problems	23	24	22	
Slight problems -> moderate problems	9	7	9	
Slight problems -> severe problems	1	0	0	
Slight problems -> extreme problems	0	0	0	
Slight problems -> no data	0	0	1	
Moderate problems -> no problems	12	16	7	
Moderate problems -> slight problems	9	9	5	
Moderate problems -> moderate problems	11	7	12	
Moderate problems -> severe problems	0	2	2	
Moderate problems -> extreme problems	0	0	0	
Moderate problems -> no data	0	0	0	
Severe problems -> no problems	7	5	0	
Severe problems -> slight problems	2	2	2	
Severe problems -> moderate problems	2	1	2	
Severe problems -> severe problems	1	4	1	
Severe problems -> extreme problems	0	0	0	
Severe problems -> no data	0	0	0	
Extreme problems -> no problems	0	0	0	
Extreme problems -> slight problems	0	1	0	
Extreme problems -> moderate problems	0	0	0	
Extreme problems -> severe problems	1	0	0	
Extreme problems -> extreme problems	0	0	0	
Extreme problems -> no data	0	0	0	
No data -> no problems	6	14	17	
No data -> slight problems	0	2	0	
No data -> moderate problems	0	0	0	
No data -> severe problems	0	0	0	
No data -> extreme problems	0	0	0	
No data -> no data	1	0	0	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The EQ-5D is an international, standardized, nondisease specific instrument for describing and valuing health status. It has 5 dimensions: Mobility, Self-care, Usual Activities, Pain/Discomfort, and Anxiety/Depression. Each dimension has 5 response levels: level 1=no problem or none; level 2=slight problems; level 3=moderate problems; level 4=severe problems; level 5=unable to perform activity. LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and EoT (up to 12 weeks)

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: participants				
number (not applicable)				
No problems -> no problems	397	384	379	
No problems -> slight problems	38	30	42	
No problems -> moderate problems	12	19	11	
No problems -> severe problems	1	4	1	
No problems -> extreme problems	0	0	1	
No problems -> no data	4	3	3	
Slight problems -> no problems	75	81	78	
Slight problems -> slight problems	46	45	37	
Slight problems -> moderate problems	12	16	15	
Slight problems -> severe problems	1	1	3	
Slight problems -> extreme problems	0	1	0	
Slight problems -> no data	0	1	2	
Moderate problems -> no problems	29	35	25	
Moderate problems -> slight problems	22	20	28	
Moderate problems -> moderate problems	22	18	21	
Moderate problems -> severe problems	3	3	4	
Moderate problems -> extreme problems	1	0	0	
Moderate problems -> no data	2	1	0	
Severe problems -> no problems	9	8	12	
Severe problems -> slight problems	7	5	1	
Severe problems -> moderate problems	7	6	9	
Severe problems -> severe problems	5	7	9	
Severe problems -> extreme problems	0	0	0	
Severe problems -> no data	0	0	0	
Extreme problems -> no problems	2	0	0	

Extreme problems -> slight problems	1	0	0	
Extreme problems -> moderate problems	3	1	0	
Extreme problems -> severe problems	1	0	0	
Extreme problems -> extreme problems	0	0	0	
Extreme problems -> no data	0	0	0	
No data -> no problems	5	11	15	
No data -> slight problems	1	4	1	
No data -> moderate problems	0	1	1	
No data -> severe problems	0	0	0	
No data -> extreme problems	0	0	0	
No data -> no data	1	0	0	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The EQ-5D is an international, standardized, nondisease specific instrument for describing and valuing health status. It has 5 dimensions: Mobility, Self-care, Usual Activities, Pain/Discomfort, and Anxiety/Depression. Each dimension has 5 response levels: level 1=no problem or none; level 2=slight problems; level 3=moderate problems; level 4=severe problems; level 5=unable to perform activity. LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and EoT (up to 12 weeks)

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: participants				
number (not applicable)				
No pain -> no pain	299	290	283	
No pain -> slight pain	45	62	51	
No pain -> moderate pain	12	14	17	
No pain -> severe pain	3	9	2	
No pain -> extreme pain	0	0	1	
No pain -> no data	4	4	3	
Slight pain -> no pain	79	82	81	
Slight pain -> slight pain	58	64	55	
Slight pain -> moderate pain	28	17	31	
Slight pain -> severe pain	0	2	5	
Slight pain -> extreme pain	1	2	0	

Slight pain -> no data	0	0	2	
Moderate pain -> no pain	39	36	21	
Moderate pain -> slight pain	37	36	39	
Moderate pain -> moderate pain	34	30	39	
Moderate pain -> severe pain	7	4	8	
Moderate pain -> extreme pain	0	1	0	
Moderate pain -> no data	2	1	0	
Severe pain -> no pain	7	4	10	
Severe pain -> slight pain	12	7	4	
Severe pain -> moderate pain	11	16	16	
Severe pain -> severe pain	10	4	9	
Severe pain -> extreme pain	0	1	1	
Severe pain -> no data	0	0	0	
Extreme pain -> no pain	4	1	0	
Extreme pain -> slight pain	0	1	1	
Extreme pain -> moderate pain	1	0	1	
Extreme pain -> severe pain	6	1	1	
Extreme pain -> extreme pain	1	0	0	
Extreme pain -> no data	0	0	0	
No data -> no pain	4	8	11	
No data -> slight pain	1	3	4	
No data -> moderate pain	1	5	2	
No data -> severe pain	0	0	0	
No data -> extreme pain	0	0	0	
No data -> no data	1	0	0	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The EQ-5D is an international, standardized, nondisease specific instrument for describing and valuing health status. It has 5 dimensions: Mobility, Self-care, Usual Activities, Pain/Discomfort, and Anxiety/Depression. Each dimension has 5 response levels: level 1=no problem or none; level 2=slight problems; level 3=moderate problems; level 4=severe problems; level 5=unable to perform activity. LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and EoT (up to 12 weeks)

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: participants				
number (not applicable)				
Not anxious -> not anxious	322	300	307	
Not anxious -> slightly anxious	43	39	43	
Not anxious -> moderately anxious	11	17	15	
Not anxious -> severely anxious	2	2	3	
Not anxious-> extremely anxious	0	0	0	
Not anxious -> no data	4	3	3	
Slightly anxious -> not anxious	107	99	90	
Slightly anxious -> slightly anxious	56	60	69	
Slightly anxious -> moderately anxious	13	11	23	
Slightly anxious -> severely anxious	1	2	2	
Slightly anxious -> extremely anxious	0	0	0	
Slightly anxious -> no data	1	2	2	
Moderately anxious -> not anxious	36	38	34	
Moderately anxious -> slightly anxious	36	40	33	
Moderately anxious -> moderately anxious	22	26	17	
Moderately anxious -> severely anxious	3	7	1	
Moderately anxious -> extremely anxious	0	3	1	
Moderately anxious -> no data	0	0	0	
Severely anxious -> not anxious	10	8	8	
Severely anxious -> slightly anxious	9	5	5	
Severely anxious -> moderately anxious	6	6	11	
Severely anxious -> severely anxious	5	8	7	
Severely anxious -> extremely anxious	0	3	0	
Severely anxious -> no data	0	0	0	
Extremely anxious -> not anxious	1	4	1	
Extremely anxious -> slightly anxious	2	1	1	
Extremely anxious -> moderately anxious	4	2	3	
Extremely anxious -> severely anxious	4	1	1	
Extremely anxious -> extremely anxious	1	2	1	
Extremely anxious -> no data	1	0	0	
No data -> not anxious	5	13	11	
No data -> slightly anxious	0	2	5	
No data -> moderately anxious	1	1	1	
No data -> severely anxious	0	0	0	
No data -> extremely anxious	0	0	0	
No data -> no data	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Overactive Bladder Symptom (OAB-q) Symptom Bother Score

End point title	Change from Baseline in Overactive Bladder Symptom (OAB-q) Symptom Bother Score

End point description:

The OAB-q was a self-reported questionnaire comprising 33-items each rated on a 6-point Likert scale. The questionnaire consisted of an 8-item symptom bother scale and 25 health-related QoL (HRQL) items comprising 4 HRQL subscales (Coping, Concern, Sleep, and Social Interaction). Symptom Bother score ranges from 0 (least severity) to 100 (worst severity). LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8 & 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: units on a scale				
least squares mean (standard error)				
Week 4 (N= 682, 677, 669)	-16.68 (± 0.65)	-13.79 (± 0.65)	-15.82 (± 0.65)	
Week 8 (N= 670, 660, 658)	-22.86 (± 0.68)	-18.36 (± 0.69)	-19.34 (± 0.69)	
Week 12 (N= 644, 641, 647)	-27.90 (± 0.71)	-22.31 (± 0.71)	-24.09 (± 0.71)	
EoT (N= 694, 683, 676)	-26.89 (± 0.69)	-21.93 (± 0.70)	-23.59 (± 0.70)	

Statistical analyses

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [74]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-2.89

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.68
upper limit	-1.1
Variability estimate	Standard error of the mean
Dispersion value	0.91

Notes:

[74] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [75]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.4
upper limit	-2.6
Variability estimate	Standard error of the mean
Dispersion value	0.97

Notes:

[75] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [76]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-5.59

Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.56
upper limit	-3.62
Variability estimate	Standard error of the mean
Dispersion value	1

Notes:

[76] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [77]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-4.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.88
upper limit	-3.04
Variability estimate	Standard error of the mean
Dispersion value	0.98

Notes:

[77] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Secondary: Change from Baseline in OAB-q Health-Related Quality of Life (HRQL) Total Score

End point title	Change from Baseline in OAB-q Health-Related Quality of Life (HRQL) Total Score

End point description:

The OAB-q was a self-reported questionnaire comprising 33-items each rated on a 6-point Likert scale. The questionnaire consisted of an 8-item symptom bother scale and 25 health-related QoL (HRQL) items comprising 4 HRQL subscales (Coping, Concern, Sleep, and Social Interaction). HRQL subscales (coping, concern, sleep and social) and total score range from 0 (worst quality of life) to 100 (best quality of life). LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8 & 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: units on a scale				
least squares mean (standard error)				
Week 4 (N= 682, 677, 669)	12.95 (± 0.59)	11.03 (± 0.59)	12.44 (± 0.59)	
Week 8 (N= 670, 660, 658)	17.58 (± 0.63)	15.26 (± 0.63)	14.60 (± 0.64)	
Week 12 (N= 644, 641, 647)	21.40 (± 0.66)	17.91 (± 0.67)	17.72 (± 0.66)	
EoT (N= 694, 683, 676)	20.78 (± 0.65)	17.63 (± 0.65)	17.40 (± 0.65)	

Statistical analyses

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.021
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	3.55
Variability estimate	Standard error of the mean
Dispersion value	0.83

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01 [78]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	2.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	4.06
Variability estimate	Standard error of the mean
Dispersion value	0.89

Notes:

[78] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [79]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	3.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.65
upper limit	5.33
Variability estimate	Standard error of the mean
Dispersion value	0.94

Notes:

[79] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [80]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	3.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.35
upper limit	4.95
Variability estimate	Standard error of the mean
Dispersion value	0.92

Notes:

[80] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Secondary: Change from Baseline in OAB-q HRQL Subscale Score: Coping

End point title	Change from Baseline in OAB-q HRQL Subscale Score: Coping

End point description:

The OAB-q was a self-reported questionnaire comprising 33-items each rated on a 6-point Likert scale. The questionnaire consisted of an 8-item symptom bother scale and 25 health-related QoL (HRQL) items comprising 4 HRQL subscales (Coping, Concern, Sleep, and Social Interaction). HRQL subscales (coping, concern, sleep and social) and total score range from 0 (worst quality of life) to 100 (best quality of life). LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8 & 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: units on a scale				
least squares mean (standard error)				
Week 4 (N= 682, 677, 669)	15.17 (± 0.68)	12.27 (± 0.68)	14.25 (± 0.68)	
Week 8 (N= 670, 660, 658)	20.82 (± 0.74)	17.47 (± 0.74)	16.87 (± 0.74)	
Week 12 (N= 644, 641, 647)	25.16 (± 0.78)	20.45 (± 0.78)	20.20 (± 0.78)	
EoT (N= 694, 683, 676)	24.48 (± 0.75)	20.19 (± 0.76)	19.90 (± 0.76)	

Statistical analyses

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means

were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [81]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	4.78
Variability estimate	Standard error of the mean
Dispersion value	0.96

Notes:

[81] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [82]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	3.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.29
upper limit	5.4
Variability estimate	Standard error of the mean
Dispersion value	1.05

Notes:

[82] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [83]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	4.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.55
upper limit	6.87
Variability estimate	Standard error of the mean
Dispersion value	1.1

Notes:

[83] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [84]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	4.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.2
upper limit	6.39
Variability estimate	Standard error of the mean
Dispersion value	1.07

Notes:

[84] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Secondary: Change from Baseline in OAB-q HRQL Subscale Score: Concern

End point title	Change from Baseline in OAB-q HRQL Subscale Score: Concern

End point description:

The OAB-q was a self-reported questionnaire comprising 33-items each rated on a 6-point Likert scale. The questionnaire consisted of an 8-item symptom bother scale and 25 health-related QoL (HRQL) items comprising 4 HRQL subscales (Coping, Concern, Sleep, and Social Interaction). HRQL subscales (coping, concern, sleep and social) and total score range from 0 (worst quality of life) to 100 (best quality of life). LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8 & 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: units on a scale				
least squares mean (standard error)				
Week 4 (N= 682, 677, 669)	13.79 (± 0.68)	11.85 (± 0.68)	13.82 (± 0.69)	
Week 8 (N= 670, 660, 658)	18.87 (± 0.70)	16.36 (± 0.71)	15.88 (± 0.71)	
Week 12 (N= 644, 641, 647)	22.85 (± 0.74)	19.24 (± 0.75)	19.67 (± 0.74)	
Week EoT (N= 694, 683, 676)	22.28 (± 0.72)	19.00 (± 0.73)	19.28 (± 0.73)	

Statistical analyses

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044 [85]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	1.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	3.83
Variability estimate	Standard error of the mean
Dispersion value	0.96

Notes:

[85] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012 [86]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	4.46
Variability estimate	Standard error of the mean
Dispersion value	1

Notes:

[86] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [87]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	3.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.54
upper limit	5.67
Variability estimate	Standard error of the mean
Dispersion value	1.05

Notes:

[87] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [88]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	3.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.27
upper limit	5.29
Variability estimate	Standard error of the mean
Dispersion value	1.03

Notes:

[88] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Secondary: Change from Baseline in OAB-q HRQL Subscale Score: Sleep

End point title	Change from Baseline in OAB-q HRQL Subscale Score: Sleep

End point description:

The OAB-q was a self-reported questionnaire comprising 33-items each rated on a 6-point Likert scale. The questionnaire consisted of an 8-item symptom bother scale and 25 health-related QoL (HRQL) items comprising 4 HRQL subscales (Coping, Concern, Sleep, and Social Interaction). HRQL subscales (coping, concern, sleep and social) and total score range from 0 (worst quality of life) to 100 (best quality of life). LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8 & 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: units on a scale				
least squares mean (standard error)				
Week 4 (N= 682, 677, 669)	11.58 (± 0.68)	11.04 (± 0.68)	11.16 (± 0.69)	
Week 8 (N= 670, 660, 658)	16.18 (± 0.71)	14.57 (± 0.71)	13.72 (± 0.71)	
Week 12 (N= 644, 641, 647)	20.00 (± 0.74)	17.74 (± 0.74)	16.84 (± 0.74)	
Week EoT (N= 694, 683, 676)	19.16 (± 0.72)	17.30 (± 0.73)	16.55 (± 0.73)	

Statistical analyses

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means

were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.575 [89]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.35
upper limit	2.43
Variability estimate	Standard error of the mean
Dispersion value	0.96

Notes:

[89] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.109 [90]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	3.58
Variability estimate	Standard error of the mean
Dispersion value	1

Notes:

[90] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.032 [91]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	2.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	4.32
Variability estimate	Standard error of the mean
Dispersion value	1.05

Notes:

[91] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.069 [92]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	1.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	3.87
Variability estimate	Standard error of the mean
Dispersion value	1.02

Notes:

[92] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Secondary: Change from Baseline in OAB-q HRQL Subscale Score: Social Interaction

End point title	Change from Baseline in OAB-q HRQL Subscale Score: Social Interaction

End point description:

The OAB-q was a self-reported questionnaire comprising 33-items each rated on a 6-point Likert scale. The questionnaire consisted of an 8-item symptom bother scale and 25 health-related QoL (HRQL) items comprising 4 HRQL subscales (Coping, Concern, Sleep, and Social Interaction). HRQL subscales (coping, concern, sleep and social) and total score range from 0 (worst quality of life) to 100 (best quality of life). LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8 & 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: units on a scale				
least squares mean (standard error)				
Week 4 (N= 682, 677, 669)	9.58 (± 0.59)	7.85 (± 0.59)	8.95 (± 0.59)	
Week 8 (N= 670, 660, 658)	11.93 (± 0.60)	10.84 (± 0.60)	10.16 (± 0.60)	
Week 12 (N= 644, 641, 647)	14.70 (± 0.61)	12.08 (± 0.61)	11.98 (± 0.61)	
Week EoT (N= 694, 683, 676)	14.39 (± 0.60)	11.91 (± 0.60)	11.72 (± 0.61)	

Statistical analyses

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.037 [93]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	3.36
Variability estimate	Standard error of the mean
Dispersion value	0.83

Notes:

[93] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.199 [94]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	2.76
Variability estimate	Standard error of the mean
Dispersion value	0.85

Notes:

[94] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [95]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	2.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	4.31
Variability estimate	Standard error of the mean
Dispersion value	0.87

Notes:

[95] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Adjusted change from baseline values as well as 95% CIs & p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors & baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [96]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	2.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	4.15
Variability estimate	Standard error of the mean
Dispersion value	0.85

Notes:

[96] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Secondary: Change from Baseline in Treatment Satisfaction - Visual Analogue Scale (TS-VAS) Score

End point title	Change from Baseline in Treatment Satisfaction - Visual Analogue Scale (TS-VAS) Score

End point description:

The TS-VAS rated participant satisfaction with treatment on a scale from 0 (No, not at all) to 10 (Yes, completely). LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8 & 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: units on a scale				
least squares mean (standard error)				
Week 4 (N= 680, 677, 668)	1.2 (± 0.1)	0.8 (± 0.1)	1.1 (± 0.1)	
Week 8 (N= 668, 660, 656)	1.5 (± 0.1)	1.2 (± 0.1)	1.3 (± 0.1)	
Week 12 (N= 644, 641, 646)	1.9 (± 0.1)	1.4 (± 0.1)	1.6 (± 0.1)	
EoT (N= 693, 683, 675)	1.8 (± 0.1)	1.4 (± 0.1)	1.6 (± 0.1)	

Statistical analyses

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Adjusted change from baseline values as well as the 95% CIs and p-value were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from

adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [97]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[97] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Adjusted change from baseline values as well as the 95% CIs and p-value were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.019 [98]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[98] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Adjusted change from baseline values as well as the 95% CIs and p-value were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [99]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[99] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Adjusted change from baseline values as well as the 95% CIs and p-value were generated from an ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Differences of adjusted means were calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [100]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[100] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Secondary: Change from Baseline in Patient Perception Bladder Control (PPBC) Score

End point title	Change from Baseline in Patient Perception Bladder Control (PPBC) Score

End point description:

The PPBC was a validated, global assessment tool using a 6-point Likert scale on which participants rated their subjective impression of their current bladder condition. PPBC score: 1-no problem, 2- some very minor problems, 3-some minor problems, 4-moderate problems, 5-severe problems, 6-many severe problems. LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8 & 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: units on a scale				
least squares mean (standard error)				
Week 4 (N= 687, 685, 677)	-0.9 (± 0.0)	-0.6 (± 0.0)	-0.7 (± 0.0)	
Week 8 (N= 673, 667, 669)	-1.2 (± 0.0)	-1.0 (± 0.0)	-1.0 (± 0.0)	
Week 12 (N= 647, 648, 655)	-1.5 (± 0.0)	-1.2 (± 0.0)	-1.3 (± 0.0)	
EoT (N= 697, 688, 683)	-1.5 (± 0.0)	-1.2 (± 0.0)	-1.3 (± 0.0)	

Statistical analyses

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Adjusted change from baseline values as well as the 95% CIs and p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Difference of adjusted mean was calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [101]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[101] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Adjusted change from baseline values as well as the 95% CIs and p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Difference of adjusted mean was calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [102]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[102] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Adjusted change from baseline values as well as the 95% CIs and p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Difference of adjusted mean was calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [103]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[103] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Statistical analysis title	Adj. Diff. Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Adjusted change from baseline values as well as the 95% CIs and p-value were generated from ANCOVA model with treatment group, sex, age group (<65, >=65 years), 4-week incontinence reduction group and geographic region as fixed factors and baseline value as a covariate. Difference of adjusted mean was calculated by subtracting adjusted mean of solifenacin monotherapy groups from adjusted mean of combination group.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [104]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[104] - P-values for pairwise comparisons were from the ANCOVA model described above. p<0.05 indicated superiority in favor of treatment group with the largest improvement.

Secondary: Number of Participants in Each Category of Patient and Clinician Global Impression of Change Scales (PGIC and CGIC)

End point title	Number of Participants in Each Category of Patient and Clinician Global Impression of Change Scales (PGIC and CGIC)

End point description:

The PGIC was a 2-part questionnaire, assessing both the change in the participant's overall condition (Patient Impression in General Health (PIBS)) and change in bladder condition since the start of the study (Patient Impression in General Health (PIGH)) (from very much worse to very much improved). The CGIC was a single questionnaire assessing the participant's change in bladder condition since the beginning of the study (Clinician Impression in Bladder Symptoms (CIBS)). LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

End of treatment (up to 12 weeks)

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: participants				
number (not applicable)				
PIBS Very Much Improved	227	152	171	
PIBS Much Improved	257	264	284	
PIBS Minimally Improved	135	170	152	
PIBS No Change	25	55	56	
PIBS Minimally Worse	7	11	4	
PIBS Much Worse	4	4	6	
PIBS Very Much Worse	0	1	1	
PIGH Very Much Improved	144	104	108	
PIGH Much Improved	239	236	244	
PIGH Minimally Improved	143	147	146	
PIGH No Change	113	142	160	
PIGH Minimally Worse	14	23	10	

PIGH Much Worse	1	4	4	
PIGH Very Much Worse	1	1	2	
CIBS Very Much Improved	184	118	141	
CIBS Much Improved	311	316	329	
CIBS Minimally Improved	141	164	155	
CIBS No Change	23	56	40	
CIBS Minimally Worse	4	8	5	
CIBS Much Worse	4	3	5	
CIBS Very Much Worse	3	3	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with at Least a 50% Decrease from Baseline in Mean Number of Incontinence Episodes per 24 Hours

End point title	Percentage of Participants with at Least a 50% Decrease from Baseline in Mean Number of Incontinence Episodes per 24 Hours

End point description:

Incontinence was defined as any involuntary leakage of urine. LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Weeks 4, 8 and 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: percentage of participants				
number (not applicable)				
Week 4 (N= 690, 690, 679)	52.5	43.3	49.0	
Week 8 (N= 661, 674, 673)	66.9	57.6	61.8	
Week 12 (N= 653, 645, 664)	72.4	64.0	66.9	
EoT (N= 706, 704, 697)	71.2	63.1	66.6	

Statistical analyses

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [105]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.19
upper limit	1.84

Notes:

[105] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [106]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.25
upper limit	1.98

Notes:

[106] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [107]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.54

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.21
upper limit	1.95

Notes:

[107] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [108]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	1.9

Notes:

[108] - p<0.05 indicated superiority in favor of treatment group with highest response.

Secondary: Percentage of Participants with Zero Incontinence Episodes Postbaseline

End point title	Percentage of Participants with Zero Incontinence Episodes Postbaseline

End point description:

Incontinence was defined as any involuntary leakage of urine. LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Weeks 4, 8 and 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: percentage of participants				
number (not applicable)				
Week 4 (N= 690, 690, 679)	23.5	20.0	22.1	
Week 8 (N= 661, 674, 673)	40.4	31.6	34.3	
Week 12 (N= 653, 645, 664)	47.3	39.5	40.7	

EoT (N= 706, 704, 697)	46.0	37.9	40.2	

Statistical analyses

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.119 [109]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.63

Notes:

[109] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [110]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	1.98

Notes:

[110] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [111]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.14
upper limit	1.82

Notes:

[111] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [112]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	1.84

Notes:

[112] - p<0.05 indicated superiority in favor of treatment group with highest response.

Secondary: Percentage of Participants with a Mean of at Least 8 Micturitions per 24 Hours at Baseline and Less than 8 Micturitions per 24 Hours Postbaseline

End point title	Percentage of Participants with a Mean of at Least 8 Micturitions per 24 Hours at Baseline and Less than 8 Micturitions per 24 Hours Postbaseline

End point description:

Micturitions were defined as voluntary urinations (excluding incontinence only episodes). LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Weeks 4, 8 and 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: percentage of participants				
number (not applicable)				
Week 4 (N= 690, 690, 679)	21.0	18.7	20.2	
Week 8 (N= 661 674, 673)	28.1	22.4	26.3	
Week 12 (N= 653, 645, 664)	31.4	24.8	28.0	
EoT (N= 706, 704, 697)	30.2	25.0	27.7	

Statistical analyses

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.305 [113]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.5

Notes:

[113] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014 [114]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	1.76

Notes:

[114] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012 [115]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	1.76

Notes:

[115] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036 [116]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.29

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.64

Notes:

[116] - p<0.05 indicated superiority in favor of treatment group with highest response.

Secondary: Percentage of Participants with at Least a 10-Point Improvement from Baseline in OAB-q Symptom Bother Score

End point title	Percentage of Participants with at Least a 10-Point Improvement from Baseline in OAB-q Symptom Bother Score

End point description:

The OAB-q was a self-reported questionnaire comprising 33-items each rated on a 6-point Likert scale. The questionnaire consisted of an 8-item symptom bother scale and 25 health-related QoL (HRQL) items comprising 4 HRQL subscales (Coping, Concern, Sleep, and Social Interaction). Symptom Bother score ranges from 0 (least severity) to 100 (worst severity). LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Weeks 4, 8 and 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: percentage of participants				
number (not applicable)				
Week 4 (N= 682, 677, 669)	67.9	58.2	61.9	
Week 8 (N= 670, 660, 658)	77.2	66.4	69.1	
Week 12 (N= 644, 641, 647)	83.5	72.1	75.4	
EoT (N= 694, 683, 676)	81.7	71.7	74.6	

Statistical analyses

Statistical analysis title	OAB-q Odds Ratio Comb. vs Solifenacin 5mg Week 4

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [117]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.49

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.18
upper limit	1.88

Notes:

[117] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	OAB-q Odds Ratio Comb. vs Solifenacin 5mg Week 8

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [118]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.31
upper limit	2.18

Notes:

[118] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	OAB-q Odds Ratio Comb. vs Solifenacin 5mg Week 12

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [119]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.47
upper limit	2.61

Notes:

[119] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	OAB-q Odds Ratio Comb. vs Solifenacin 5mg EoT

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [120]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.34
upper limit	2.3

Notes:

[120] - p<0.05 indicated superiority in favor of treatment group with highest response.

Secondary: Percentage of Participants with at Least a 10-Point Improvement from Baseline in HRQL Total Score

End point title	Percentage of Participants with at Least a 10-Point Improvement from Baseline in HRQL Total Score

End point description:

HRQL subscales (coping, concern, sleep and social) and total score range from 0 (worst quality of life) to 100 (best quality of life). LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Weeks 4, 8 and 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: percentage of participants				
number (not applicable)				
Week 4 (N= 682, 677, 669)	52.6	44.5	48.1	
Week 8 (N= 670, 660, 658)	63.6	54.8	53.8	
Week 12 (N= 644, 641, 647)	70.5	60.8	60.4	
EoT (N= 694, 683, 676)	68.6	60.6	60.1	

Statistical analyses

Statistical analysis title	HRQL Odds Ratio Comb. vs Solifenacin 5mg Week 4

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model

including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [121]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.14
upper limit	1.82

Notes:

[121] - p<0.05 indicates superiority in favor of treatment group with highest response.

Statistical analysis title	HRQL Odds Ratio Comb. vs Solifenacin 5mg Week 8

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [122]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.18
upper limit	1.93

Notes:

[122] - p<0.05 indicates superiority in favor of treatment group with highest response.

Statistical analysis title	HRQL Odds Ratio Comb. vs Solifenacin 5mg Week 12

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [123]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.64

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.27
upper limit	2.13

Notes:

[123] - p<0.05 indicates superiority in favor of treatment group with highest response.

Statistical analysis title	HRQL Odds Ratio Comb. vs Solifenacin 5mg EoT

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [124]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	1.91

Notes:

[124] - p<0.05 indicates superiority in favor of treatment group with highest response.

Secondary: Percentage of Participants with at Least a 1-Point Improvement from Baseline in PPBC

End point title	Percentage of Participants with at Least a 1-Point Improvement from Baseline in PPBC

End point description:

The PPBC was a validated, global assessment tool using a 6-point Likert scale on which participants rated their subjective impression of their current bladder condition. LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Weeks 4, 8 and 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: percentage of participants				
number (not applicable)				
Week 4 (N= 687, 685, 677)	61.1	52.1	56.3	
Week 8 (N= 673, 667, 669)	70.1	62.1	64.6	

Week 12 (N= 647, 648, 655)	77.9	70.4	72.7	
EoT (N= 697, 688, 683)	76.5	69.5	71.9	

Statistical analyses

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [125]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	1.79

Notes:

[125] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [126]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	1.84

Notes:

[126] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [127]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.15
upper limit	1.96

Notes:

[127] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006 [128]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	1.84

Notes:

[128] - p<0.05 indicated superiority in favor of treatment group with highest response.

Secondary: Percentage of Participants with Major (at Least 2-Point) Improvement from Baseline in PPBC

End point title	Percentage of Participants with Major (at Least 2-Point) Improvement from Baseline in PPBC

End point description:

The PPBC was a validated, global assessment tool using a 6-point Likert scale on which participants rated their subjective impression of their current bladder condition. LOCF was used for EoT. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Weeks 4, 8 and 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	707	705	698	
Units: percentage of participants				
number (not applicable)				
Week 4 (N= 687, 685, 677)	26.6	21.6	21.6	
Week 8 (N= 673, 667, 669)	39.5	31.5	31.8	
Week 12 (N= 647, 648, 655)	51.8	39.8	43.8	
EoT (N= 697, 688, 683)	49.8	39.1	43.2	

Statistical analyses

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg Week 4

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.065 [129]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.66

Notes:

[129] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg Week 8

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg

Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [130]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	1.79

Notes:

[130] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg Week 12

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [131]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	2.07

Notes:

[131] - p<0.05 indicated superiority in favor of treatment group with highest response.

Statistical analysis title	Odds Ratio Combination vs Solifenacin 5mg EoT

Statistical analysis description:

Odds ratios, 95% Two sided CIs for Odds ratios and p-values were from a logistic regression model including treatment group, sex, age group (<65, >=65 years), 4-week incontinence episode reduction group, geographic region as factors and baseline value as covariate.

Comparison groups	Combination (solifenacin + mirabegron) v Solifenacin 5 mg
Number of subjects included in analysis	1412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [132]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.55

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.24
upper limit	1.94

Notes:

[132] - p<0.05 indicated superiority in favor of treatment group with highest response.

Secondary: Number of Participants with Adverse Events (AEs)

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

End point description:

AE was defined as any untoward medical occurrence in a participant administered a study drug or has undergone study procedures & which does not necessarily have a causal relationship with this treatment. Treatment-Emergent Adverse Event (TEAE) referred to an adverse event which started or worsened in the period from first double-blind medication intake until 30 days after the last double-blind medication intake. The analysis population consisted of the Safety Analysis Set, the SAF comprised all randomized participants who received at least 1 dose of double-blind treatment.

End point type	Secondary

End point timeframe:

From first dose of double blind treatment until 30 days after last dose (up to 16 weeks)

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	725	728	719	
Units: participants				
AEs	260	241	283	
Drug-related AEs	141	125	161	
Serious Adverse Events (SAEs)	13	10	15	
Drug-related SAEs	1	0	3	
AEs Leading to Perm. Disc. of Study Drug	11	11	11	
Drug-related AEs Leading to Perm. Disc. of Drug	9	10	9	
Deaths	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Post Void Residual (PVR) Volume

End point title	Change From Baseline in Post Void Residual (PVR) Volume

End point description:

PVR Volume was assessed by bladder scan. The analysis population consisted of the SAF with data available at each time point.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8 & 12

End point values	Combination (solifenacin + mirabegron)	Solifenacin 5 mg	Solifenacin 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	725	728	719	
Units: mL				
arithmetic mean (standard deviation)				
Week 4 (N= 705, 712, 704)	1.545 (± 40.313)	2.821 (± 38.588)	7.308 (± 72.122)	
Week 8 (N= 683, 694, 690)	2.245 (± 38.347)	1.117 (± 36.470)	7.232 (± 60.096)	
Week 12 (N= 669, 680, 681)	6.356 (± 51.067)	2.337 (± 42.147)	6.552 (± 48.505)	
EoT (N= 706, 713, 707)	5.478 (± 51.595)	3.046 (± 43.499)	7.354 (± 54.121)	

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 treatment until 30 days after last dose (up to 16 weeks)

Adverse event reporting additional description:

Population consisted of the SAF. An AE was defined as any untoward medical occurrence in a participant administered a study drug or who had undergone study procedures and did not necessarily have a causal relationship with this treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Combination (solifenacin + mirabegron)

Reporting group description:

Participants received solifenacin 5 mg, mirabegron 25 mg and solifenacin 10 mg matching placebo once daily for the first 4 weeks of double-blind period. For the last 8 weeks of the double-blind treatment period, the 25 mg mirabegron tablet was replaced by a 50 mg mirabegron tablet. Placebo was given for the 2 week single-blind safety follow-up period.

Reporting group title	Solifenacin 10 mg

Reporting group description:

Participants received solifenacin 5 mg matching placebo, mirabegron 25 mg matching placebo and solifenacin 10 mg once daily. For the last 8 weeks of the double-blind treatment period, the 25 mg mirabegron matching placebo tablet was replaced by a 50 mg mirabegron matching placebo tablet (to maintain the blind). Placebo was given for the 2 week single-blind safety follow-up period.

Reporting group title	Solifenacin 5 mg

Reporting group description:

Participants received solifenacin 5 mg, mirabegron 25 mg matching placebo and solifenacin 10 mg matching placebo once daily. For the last 8 weeks of the double-blind treatment period, the 25 mg mirabegron matching placebo tablet was replaced by a 50 mg mirabegron matching placebo tablet (to maintain the blind). Placebo was given for the 2 week single-blind safety follow-up period.

Serious adverse events	Combination (solifenacin + mirabegron)	Solifenacin 10 mg	Solifenacin 5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 725 (1.79%)	15 / 719 (2.09%)	10 / 728 (1.37%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adrenal adenoma			
subjects affected / exposed	0 / 725 (0.00%)	1 / 719 (0.14%)	0 / 728 (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
Anal cancer			

subjects affected / exposed	1 / 725 (0.14%)	0 / 719 (0.00%)	0 / 728 (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
Intraductal proliferative breast lesion			
subjects affected / exposed	1 / 725 (0.14%)	0 / 719 (0.00%)	0 / 728 (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
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 725 (0.00%)	1 / 719 (0.14%)	0 / 728 (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
Thrombosis			
subjects affected / exposed	0 / 725 (0.00%)	0 / 719 (0.00%)	1 / 728 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Joint resurfacing surgery			
subjects affected / exposed	0 / 725 (0.00%)	1 / 719 (0.14%)	0 / 728 (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
Skin neoplasm excision			
subjects affected / exposed	0 / 725 (0.00%)	0 / 719 (0.00%)	1 / 728 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Adhesion			
subjects affected / exposed	0 / 725 (0.00%)	0 / 719 (0.00%)	1 / 728 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 725 (0.14%)	1 / 719 (0.14%)	0 / 728 (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

Pyrexia			
subjects affected / exposed	1 / 725 (0.14%)	0 / 719 (0.00%)	0 / 728 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 725 (0.14%)	0 / 719 (0.00%)	0 / 728 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Cervix haemorrhage uterine			
subjects affected / exposed	0 / 725 (0.00%)	0 / 719 (0.00%)	1 / 728 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory tract oedema			
subjects affected / exposed	1 / 725 (0.14%)	0 / 719 (0.00%)	0 / 728 (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
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 725 (0.14%)	0 / 719 (0.00%)	0 / 728 (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
Arteriogram coronary normal			
subjects affected / exposed	1 / 725 (0.14%)	0 / 719 (0.00%)	0 / 728 (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
Arthroscopy			
subjects affected / exposed	0 / 725 (0.00%)	1 / 719 (0.14%)	0 / 728 (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
Aspartate aminotransferase increased			

subjects affected / exposed	1 / 725 (0.14%)	0 / 719 (0.00%)	0 / 728 (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
Colonoscopy			
subjects affected / exposed	0 / 725 (0.00%)	1 / 719 (0.14%)	0 / 728 (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
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 725 (0.14%)	0 / 719 (0.00%)	0 / 728 (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
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 725 (0.00%)	1 / 719 (0.14%)	0 / 728 (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
Multiple fractures			
subjects affected / exposed	1 / 725 (0.14%)	0 / 719 (0.00%)	0 / 728 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 725 (0.00%)	1 / 719 (0.14%)	0 / 728 (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
Atrial fibrillation			
subjects affected / exposed	0 / 725 (0.00%)	0 / 719 (0.00%)	1 / 728 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	1 / 725 (0.14%)	0 / 719 (0.00%)	0 / 728 (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

Nervous system disorders			
Polyneuropathy			
subjects affected / exposed	1 / 725 (0.14%)	0 / 719 (0.00%)	0 / 728 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 725 (0.00%)	1 / 719 (0.14%)	0 / 728 (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 disorders			
Abdominal hernia			
subjects affected / exposed	0 / 725 (0.00%)	0 / 719 (0.00%)	1 / 728 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 725 (0.00%)	1 / 719 (0.14%)	0 / 728 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 725 (0.00%)	0 / 719 (0.00%)	1 / 728 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 725 (0.14%)	0 / 719 (0.00%)	0 / 728 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 725 (0.00%)	0 / 719 (0.00%)	1 / 728 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic pain			

subjects affected / exposed	0 / 725 (0.00%)	1 / 719 (0.14%)	0 / 728 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver disorder			
subjects affected / exposed	0 / 725 (0.00%)	1 / 719 (0.14%)	0 / 728 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 725 (0.00%)	1 / 719 (0.14%)	0 / 728 (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
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 725 (0.00%)	0 / 719 (0.00%)	1 / 728 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 725 (0.00%)	0 / 719 (0.00%)	1 / 728 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture pain			
subjects affected / exposed	0 / 725 (0.00%)	1 / 719 (0.14%)	0 / 728 (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
Mobility decreased			
subjects affected / exposed	1 / 725 (0.14%)	0 / 719 (0.00%)	0 / 728 (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
Infections and infestations			
Appendicitis			

subjects affected / exposed	1 / 725 (0.14%)	1 / 719 (0.14%)	1 / 728 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis herpes			
subjects affected / exposed	1 / 725 (0.14%)	0 / 719 (0.00%)	0 / 728 (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
Pneumonia			
subjects affected / exposed	1 / 725 (0.14%)	0 / 719 (0.00%)	0 / 728 (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

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

Non-serious adverse events	Combination (solifenacin + mirabegron)	Solifenacin 10 mg	Solifenacin 5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 725 (5.93%)	68 / 719 (9.46%)	41 / 728 (5.63%)
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	43 / 725 (5.93%)	68 / 719 (9.46%)	41 / 728 (5.63%)
occurrences (all)	44	70	44

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

One participant was randomized to the Combination arm, but actually received Solifenacin 10 mg. In terms of actual treatment received, the participant was allocated to the solifenacin 10 mg arm.

Notes: