



Clinical trial results:

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

Summary

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

Results information

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

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | 178-CL-102 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02045862 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 08 September 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 September 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 17 March 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

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

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

Notes:

Subjects enrolled per age group

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

Subject disposition

Recruitment

Recruitment details:

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

Pre-assignment

Screening details:

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

Period 1

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

Arms

| | |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Mirabegron 50 mg |

Arm description:

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

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

Dosage and administration details:

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

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

Dosage and administration details:

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

| | |
|------------------|------------------|
| Arm title | Solifenacin 5 mg |
|------------------|------------------|

Arm description:

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

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

Dosage and administration details:

Participants received solifenacin 5 mg orally once a day at the same time each day.

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

Dosage and administration details:

Participants received placebo to match mirabegron 50 mg orally once a day at the same time each day. This intervention was given to maintain the blind during the study.

| | |
|------------------|-------------------------------------|
| Arm title | Solifenacin 5 mg + mirabegron 50 mg |
|------------------|-------------------------------------|

Arm description:

Participants received solifenacin 5 mg and mirabegron 50 mg once a day for 52 weeks.

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

Dosage and administration details:

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

| | |
|--|--|
| Investigational medicinal product name | Solifenacin succinate |
| Investigational medicinal product code | YM905 |
| Other name | Solifenacin, Vesicare, Vesikur, Vesitrim |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received solifenacin 5 mg orally once a day at the same time each day.

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

Baseline characteristics

Reporting groups

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

| Reporting group values | Mirabegron 50 mg | Solifenacin 5 mg | Solifenacin 5 mg + mirabegron 50 mg |
|------------------------|------------------|------------------|-------------------------------------|
| Number of subjects | 306 | 305 | 1218 |
| Age categorical | | | |
| Units: Subjects | | | |

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

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

| | | | |
|---|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 1829 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Randomized analysis set (RAS), comprised of all randomized participants. | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| RAS | | | |
| Units: | | | |
| Male | 368 | | |
| Female | 1461 | | |
| Mean Number of Incontinence Episodes per 24 Hours | | | |
| RAS; data only available for 1818 participants [306, 303, 1209]. | | | |
| Units: incontinence episodes | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Mean Number of Micturitions per 24 Hours | | | |
| RAS; data only available for 1818 participants [306, 303, 1209]. | | | |
| Units: micturitions | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Mean Volume Voided per Micturition | | | |
| RAS; data only available for 1815 participants [306, 303, 1206]. | | | |
| Units: mL | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Number of Incontinence Episodes per Week | | | |
| RAS; data only available for 1818 participants [306, 303, 1209]. | | | |
| Units: incontinence episodes/week | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Mean Number of Urgency Incontinence Episodes per 24 Hours | | | |
| RAS; data only available for 1809 participants [306, 301, 1202]. Only participants with ≥ 1 urgency incontinence episode at baseline were included. An urgency incontinence episode is defined as the involuntary leakage of urine accompanied by or immediately proceeded by urgency. | | | |
| Units: urgency incontinence episodes | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Number of Urgency Incontinence Episodes per Week | | | |
| RAS; data only available for 1809 participants [306, 301, 1202]. Only participants with ≥ 1 urgency incontinence episode at baseline were included. | | | |
| Units: urgency incontinence episodes/week | | | |
| arithmetic mean | | | |
| standard deviation | - | | |

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

End points

End points reporting groups

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

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

| | |
|--|--|
| End point title | Number of Participants with Treatment-Emergent Adverse Events (TEAEs) ^[1] |
| End point description: | |
| A TEAE is defined as an adverse event (AE) observed after taking the first dose of double-blind treatment until 14 days after taking the last dose of double-blind treatment for non-serious AEs and until 30 days after taking the last dose of double-blind treatment for serious adverse events (SAEs). This includes abnormal laboratory tests, vital signs or electrocardiogram data that were defined as AEs if the abnormality induced clinical signs or symptoms, required active intervention, interruption or discontinuation of study drug or was clinically significant in the investigator's opinion. The severity of an AE was measured by: Mild (No disruption of normal daily activities); Moderate (Affected normal daily activities) and Severe (Inability to perform daily activities). The analysis population was the Safety Analysis Set (SAF), which consisted of all participants who received ≥ 1 dose of double-blind study drug and excluded participants from one site due to protocol noncompliance. | |
| End point type | Primary |
| End point timeframe: | |
| From first dose of double-blind study drug up to 30 days after last dose of double-blind study drug (up to 56 weeks) | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

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

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

| | | | | |
|---|---|---|----|--|
| Drug-related TEAEs leading to discontinuation of drug | 4 | 4 | 17 | |
| TEAEs leading to death | 0 | 0 | 1 | |

Statistical analyses

No statistical analyses for this end point

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

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

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

Statistical analyses

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

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

Notes:

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

| | |
|-----------------------------------|---------------------------------|
| Statistical analysis title | Difference vs. Solifenacin 5 mg |
|-----------------------------------|---------------------------------|

Statistical analysis description:

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

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

Notes:

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

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and Week 52

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

Statistical analyses

| Statistical analysis title | Difference vs. Mirabegron 50 mg |
|-----------------------------------|---------------------------------|
|-----------------------------------|---------------------------------|

Statistical analysis description:

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

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

Notes:

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

| Statistical analysis title | Difference vs. Solifenacin 5 mg |
|-----------------------------------|---------------------------------|
|-----------------------------------|---------------------------------|

Statistical analysis description:

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

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

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

Notes:

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Week 52

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

Statistical analyses

| | |
|----------------------------|---------------------------------|
| Statistical analysis title | Difference vs. Solifenacin 5 mg |
|----------------------------|---------------------------------|

Statistical analysis description:

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

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

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

| | |
|-----------------------------------|---------------------------------|
| Statistical analysis title | Difference vs. Mirabegron 50 mg |
|-----------------------------------|---------------------------------|

Statistical analysis description:

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

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

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

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

End point description:

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

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

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

Statistical analyses

| Statistical analysis title | Difference vs. Mirabegron 50 mg |
|---|--|
| Statistical analysis description: | |
| Difference of the adjusted mean (i.e., least squares mean) was calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, \geq 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1453 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least squares mean difference |
| Point estimate | -7.55 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.05 |
| upper limit | -5.05 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.27 |

| Statistical analysis title | Difference vs. Solifenacin 5 mg |
|--|--|
| Statistical analysis description: | |
| Difference of the adjusted mean (i.e., least squares mean) was calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, \geq 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |

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

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

| | |
|---|--|
| End point title | Change from Baseline to EoT in the Patient's Assessment of Treatment Satisfaction-Visual Analogue Scale (TS-VAS) |
| End point description: | |
| The TS-VAS is a visual analogue scale which asks participants to rate their satisfaction with the treatment by placing a vertical mark on a line that runs from 0 (No, not at all) on the left to 10 (Yes, completely) on the right. A positive change from baseline indicated improvement. The analysis population was the FAS, with baseline and at least one post-baseline measurement. LOCF was used for EoT. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 52 | |

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

Statistical analyses

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

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

| | |
|-----------------------------------|---------------------------------|
| Statistical analysis title | Difference vs. Solifenacin 5 mg |
|-----------------------------------|---------------------------------|

Statistical analysis description:

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Months 1, 3, 6, 9, 12

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

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

Statistical analyses

| Statistical analysis title | Rate ratio vs. Mirabegron 50 mg (EoT) |
|---|--|
| Statistical analysis description: | |
| Rate ratio of number of incontinence episodes during the EoT 7-day diary between the combination therapy group and the mirabegron monotherapy group is calculated from a negative binomial regression model incl. treatment group, sex, age group (< 65, \geq 65 years), geographic region and previous study history as factors, log(number of incontinence episodes divided by number of valid diary days) at baseline included as a covariate and number of valid diary day at EoT as the offset variable. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1495 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed Effects Poisson-negative binomial |
| Parameter estimate | Rate ratio |
| Point estimate | 0.67 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.54 |
| upper limit | 0.84 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.12 |

| Statistical analysis title | Rate ratio vs. Solifenacin 5 mg (EoT) |
|--|--|
| Statistical analysis description: | |
| Rate ratio of number of incontinence episodes during the EoT 7-day diary between the combination therapy group and the solifenacin monotherapy group is calculated from a negative binomial regression model incl. treatment group, sex, age group (< 65, \geq 65 years), geographic region and previous study history as factors, log(number of incontinence episodes divided by number of valid diary days) at baseline included as a covariate and number of valid diary day at EoT as the offset variable. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1492 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.029 |
| Method | Mixed Effects Poisson-negative binomial |
| Parameter estimate | Rate ratio |
| Point estimate | 0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.61 |
| upper limit | 0.97 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.12 |

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

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

Statistical analysis description:

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

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

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

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

Statistical analysis description:

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

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

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

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

End point description:

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

| | |
|-----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Months 1, 3, 6, 9, 12 | |

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

Statistical analyses

| Statistical analysis title | Odds ratio vs. Mirabegron 50 mg (EoT) |
|---|--|
| Statistical analysis description: | |
| Odds ratio is from a overdispersed binomial regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and log transformed baseline mean number of incontinence episodes per 24 hours as a covariate. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1495 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Overdispersed binomial regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.26 |
| upper limit | 2.01 |

| Statistical analysis title | Odds ratio vs. Solifenacin 5 mg (EoT) |
|---|--|
| Statistical analysis description: | |
| Odds ratio is from a overdispersed binomial regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and log transformed baseline mean number of incontinence episodes per 24 hours as a covariate. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Months 1, 3, 6, 9, 12

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

Statistical analyses

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

Statistical analysis description:

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

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

Statistical analysis title

Odds ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

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

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

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

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

End point description:

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

| | |
|------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Months 1, 3, 6, 9, 12 | |

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

Statistical analyses

| Statistical analysis title | Difference vs. Mirabegron 50 mg (EoT) |
|--|--|
| Statistical analysis description: | |
| Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 ^[6] |
| Method | Stratified rank ANCOVA |
| Parameter estimate | Least squares mean difference |
| Point estimate | -0.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.65 |
| upper limit | -0.21 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.11 |

Notes:

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

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

Statistical analysis description:

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

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

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

Notes:

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Months 1, 3, 6, 9, 12

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

Statistical analyses

| Statistical analysis title | Rate ratio vs. Mirabegron 50 mg (EoT) |
|--|--|
| Statistical analysis description: | |
| Rate ratio of number of incontinence episodes during the EoT 7-day diary between the combination therapy group and the mirabegron monotherapy group is calculated from a negative binomial regression model incl. treatment group, sex, age group (< 65, ≥65 years), geographic region and previous study history as factors, log(number of urgency incontinence episodes divided by number of valid diary days) included as a covariate and post baseline number of valid diary days at EoT as the offset variable. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Negative binomial regression |
| Parameter estimate | Rate ratio |
| Point estimate | 0.62 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.48 |
| upper limit | 0.79 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.13 |

| Statistical analysis title | Rate ratio vs. Solifenacin 5 mg (EoT) |
|--|--|
| Statistical analysis description: | |
| Rate ratio of number of incontinence episodes during the EoT 7-day diary between the combination therapy group and the solifenacin monotherapy group is calculated from a negative binomial regression model incl. treatment group, sex, age group (< 65, ≥ 65 years), geographic region and previous study history as factors, log(number of urgency incontinence episodes divided by number of valid diary days) included as a covariate and post baseline number of valid diary day at EoT as the offset variable | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1484 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.023 |
| Method | Negative binomial regression |
| Parameter estimate | Rate ratio |
| Point estimate | 0.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.58 |
| upper limit | 0.96 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.13 |

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

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

Statistical analysis description:

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

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

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

Notes:

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

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

Statistical analysis description:

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

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

Notes:

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

No statistical analyses for this end point

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

| | |
|--|--|
| End point title | Number of Days with < 8 Micturitions per Day Reported During the 7-Day Micturition Diary Period Prior to Each Visit (at Months 1, 3, 6, 9, 12 and EoT) |
| End point description: | |
| The number of days with < 8 micturitions was the number of valid diary days during the 7-day micturition diary period with with less than 8 micturitions per day. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT. | |
| End point type | Secondary |
| End point timeframe: | |
| Months 1, 3, 6, 9, 12 | |

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

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Odds ratio vs. Solifenacin 5 mg (EoT) |
| Statistical analysis description: | |
| Odds ratio is from a overdispersed binomial regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of micturitions per 24 hours as a covariate. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1492 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.007 |
| Method | Overdispersed binomial regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.37 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.09 |
| upper limit | 1.73 |

| | |
|--|--|
| Statistical analysis title | Odds ratio vs. Mirabegron 50 mg (EoT) |
| Statistical analysis description: | |
| Odds ratio is from a overdispersed binomial regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of micturitions per 24 hours as a covariate. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1495 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | Overdispersed binomial regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.14 |
| upper limit | 1.8 |

Secondary: Change from Baseline to EoT in Corrected Micturition Frequency

| | |
|--|--|
| End point title | Change from Baseline to EoT in Corrected Micturition Frequency |
| End point description: Corrected micturition frequency was defined as the mean number of micturitions per 24 hours that participants had at end of treatment if their fluid intake had remained unchanged since baseline. Corrected micturition frequency was calculated as the baseline mean volume voided per micturition multiplied by the baseline mean number of micturitions per 24 hours divided by the mean volume voided per micturition at EoT. The analysis population was the FAS. LOCF was used for EoT. | |
| End point type | Secondary |
| End point timeframe: Baseline and Month 12 | |

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

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Difference vs. Mirabegron 50 mg (EoT) |
| Statistical analysis description: Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline mean number of micturitions per 24 hours as a covariate. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1485 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least squares mean difference |
| Point estimate | -0.78 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.16 |
| upper limit | -0.41 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.19 |

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

Statistical analysis description:

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Months 3, 6, 12

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

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

Statistical analysis description:

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

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

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

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

Statistical analysis description:

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

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

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

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

End point description:

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

| | |
|------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Months 1, 3, 6, 9, 12 | |

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

Statistical analyses

| Statistical analysis title | Difference vs. Solifenacin 5 mg (EoT) |
|---|--|
| Statistical analysis description: | |
| Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1279 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.068 |
| Method | ANCOVA |
| Parameter estimate | Least squares mean difference |
| Point estimate | -0.09 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.19 |
| upper limit | 0.01 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.05 |

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

Statistical analysis description:

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

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

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

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

| | |
|---|--|
| End point title | Number of Nocturia Episodes Reported During the 7-Day Micturition Diary Period Prior to Each Visit |
| End point description: | |
| A nocturia episode was defined as waking at night 1 or more times to void (i.e., any voiding associated with sleep disturbance between the time the participant goes to bed with the intention to sleep until the time the participant gets up in the morning with the intention to stay awake). The number of nocturia episodes was the number of times a participant recorded a nocturia episode during the 7-day micturition diary period prior to each visit. The analysis population was the FAS. Only participants with ≥ 1 nocturia episode at baseline were included in the analysis. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT. | |
| End point type | Secondary |
| End point timeframe: | |
| Months 1, 3, 6, 9, 12 | |

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

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Rate ratio vs. Mirabegron 50 mg (EoT) |
| Statistical analysis description: | |
| Rate ratio of number of nocturia episodes during the EoT 7-day diary between the combination therapy group and the mirabegron monotherapy group is calculated from a negative binomial regression model incl. treatment group, sex, age group (< 65, ≥ 65 years), geographic region and previous study history as factors, log(number of nocturia episodes divided by number of valid diary days) included as a covariate and post baseline number of valid diary days as the offset variable. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1289 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.067 |
| Method | Negative binomial regression |
| Parameter estimate | Rate ratio |
| Point estimate | 0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.81 |
| upper limit | 1.01 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.06 |

| | |
|--|--|
| Statistical analysis title | Rate ratio vs. Solifenacin 5 mg (EoT) |
| Statistical analysis description: | |
| Rate ratio of number of nocturia episodes during the EoT 7-day diary between the combination therapy group and the solifenacin monotherapy group is calculated from a negative binomial regression model incl. treatment group, sex, age group (< 65, ≥ 65 years), geographic region and previous study history as factors, log(number of nocturia episodes divided by number of valid diary days) included as a covariate and post baseline number of valid diary day as the offset variable. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1279 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.131 |
| Method | Negative binomial regression |
| Parameter estimate | Rate ratio |
| Point estimate | 0.92 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.82 |
| upper limit | 1.03 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.06 |

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

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

Statistical analysis description:

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

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

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

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

Statistical analysis description:

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

| Statistical analysis title | Difference vs. Mirabegron 50 mg (EoT) |
|--|--|
| Statistical analysis description: | |
| Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 972 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | ANCOVA |
| Parameter estimate | Least squares mean difference |
| Point estimate | -0.42 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.69 |
| upper limit | -0.16 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.13 |

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

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

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

| | |
|---|--|
| End point title | Number of Pads Used Reported During the 7-Day Micturition Diary Period Prior to Each Visit |
| End point description: | |
| The number of pads used was the number of times a participant recorded a new pad used during the 7-day micturition diary period prior to each visit. The analysis population was the FAS. Only participants with ≥ 1 pad used at baseline were included in the analysis. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT. | |
| End point type | Secondary |
| End point timeframe: | |
| Months 1, 3, 6, 9, 12 | |

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

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Rate ratio vs. Mirabegron 50 mg (EoT) |
| Statistical analysis description: | |
| Rate ratio of number of pads during the EoT 7-day diary between the combination therapy group and the mirabegron monotherapy group is calculated from a negative binomial regression model incl. treatment group, sex, age group (< 65, ≥ 65 years), geographic region and previous study history as factors, log(number of pads divided by number of valid diary days) included as a covariate and post baseline number of valid diary days as the offset variable. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 972 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Negative binomial regression |
| Parameter estimate | Rate ratio |
| Point estimate | 0.58 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.45 |
| upper limit | 0.76 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.14 |

| | |
|---|--|
| Statistical analysis title | Rate ratio vs. Solifenacin 5 mg (EoT) |
| Statistical analysis description: | |
| Rate ratio of number of pads during the EoT 7-day diary between the combination therapy group and the solifenacin monotherapy group is calculated from a negative binomial regression model incl. treatment group, sex, age group (< 65, ≥ 65 years), geographic region and previous study history as factors, log(number of pads divided by number of valid diary days) included as a covariate and post baseline number of valid diary days as the offset variable. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 964 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.044 |
| Method | Negative binomial regression |
| Parameter estimate | Rate ratio |
| Point estimate | 0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.58 |
| upper limit | 0.99 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.14 |

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

| | |
|---|---|
| End point title | Change from Baseline to Months 1, 3, 6, 9, 12 and EoT in Number of Pads Used Reported During the 7-Day Micturition Diary Period Prior to Each Visit |
| End point description: | |
| The number of pads used was the number of times a participant recorded a new pad used during the 7-day micturition diary period prior to each visit. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. Only participants with ≥ 1 pad used at baseline were included in the analysis. LOCF was used for EoT. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Months 1, 3, 6, 9, 12 | |

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

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Difference vs. Mirabegron 50 mg (EoT) |
| Statistical analysis description: | |
| Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65 , ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 972 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least squares mean difference |
| Point estimate | -2.98 |

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

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

Statistical analysis description:

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

| | | | | |
|------------------------|---------------------|---------------------|---------------------|--|
| EoT [N=290, 294, 1163] | 16.57 (\pm 1.00) | 18.47 (\pm 0.99) | 21.33 (\pm 0.50) | |
|------------------------|---------------------|---------------------|---------------------|--|

Statistical analyses

| Statistical analysis title | Difference vs. Mirabegron 50 mg (EoT) |
|---|--|
| Statistical analysis description: | |
| Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, \geq 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1495 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least squares mean difference |
| Point estimate | 4.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.56 |
| upper limit | 6.96 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.12 |

| Statistical analysis title | Difference vs. Solifenacin 5 mg (EoT) |
|--|--|
| Statistical analysis description: | |
| Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, \geq 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1492 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.01 |
| Method | ANCOVA |
| Parameter estimate | Least squares mean difference |
| Point estimate | 2.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.68 |
| upper limit | 5.04 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.11 |

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

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

Statistical analysis description:

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

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

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

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

Statistical analysis description:

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

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

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

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

End point description:

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

| | |
|------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Months 1, 3, 6, 9, 12 | |

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

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Difference vs. Mirabegron 50 mg (EoT) |
| Statistical analysis description: | |
| Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1495 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least squares mean difference |
| Point estimate | 5.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.65 |
| upper limit | 7.38 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.21 |

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

Statistical analysis description:

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

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Difference vs. Mirabegron 50 mg (EoT) |
| Statistical analysis description: | |
| Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1495 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least squares mean difference |
| Point estimate | 5.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.47 |
| upper limit | 7.83 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.36 |

| | |
|---|--|
| Statistical analysis title | Difference vs. Solifenacin 5 mg (EoT) |
| Statistical analysis description: | |
| Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1492 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.016 |
| Method | ANCOVA |
| Parameter estimate | Least squares mean difference |
| Point estimate | 3.27 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.62 |
| upper limit | 5.93 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.35 |

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

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

Statistical analysis description:

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

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

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

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

Statistical analysis description:

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

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

Statistical analyses

| Statistical analysis title | Difference vs. Mirabegron 50 mg (EoT) |
|--|--|
| Statistical analysis description: | |
| Difference of the adjusted mean is calculated by subtracting the adjusted mean of the mirabegron monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1495 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least squares mean difference |
| Point estimate | -0.32 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.47 |
| upper limit | -0.16 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.08 |

| Statistical analysis title | Difference vs. Solifenacin 5 mg (EoT) |
|---|--|
| Statistical analysis description: | |
| Difference of the adjusted mean is calculated by subtracting the adjusted mean of the solifenacin monotherapy group from the adjusted mean of the combination therapy group (solifenacin 5 mg + mirabegron 50 mg) based on the ANCOVA model with treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as fixed factors and baseline value as a covariate. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1492 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.011 |
| Method | ANCOVA |
| Parameter estimate | Least squares mean difference |
| Point estimate | -0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.36 |
| upper limit | -0.05 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.08 |

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 12

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

Statistical analyses

No statistical analyses for this end point

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

in General Health at Month 12 and EoT

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 12

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Month 12

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Month 12

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

Statistical analyses

No statistical analyses for this end point

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

| | |
|---|--|
| End point title | Number of Participants With Change from Baseline to EoT in EQ-5D Questionnaire Subscale Score: Pain/Discomfort |
| End point description: | |
| The EQ-5D questionnaire is an international, standardized, nondisease specific instrument for describing and valuing health status, and has 5 dimensions: Mobility, Self-care, Usual Activities, Pain/Discomfort, and Anxiety/Depression. Each dimension has 5 response levels ranging from level 1 (no problem or none) to level 5 (unable to perform activity). The analysis population was the FAS. LOCF was used for EoT. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Month 12 | |

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

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

Statistical analyses

No statistical analyses for this end point

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

| | |
|---|---|
| End point title | Number of Participants With Change from Baseline to EoT in EQ-5D Questionnaire Subscale Score: Anxiety/Depression |
| End point description: | |
| The EQ-5D questionnaire is an international, standardized, nondisease specific instrument for describing and valuing health status, and has 5 dimensions: Mobility, Self-care, Usual Activities, Pain/Discomfort, and Anxiety/Depression. Each dimension has 5 response levels ranging from level 1 (no problem or none) to level 5 (unable to perform activity). The analysis population was the FAS. LOCF was used for EoT. | |
| End point type | Secondary |

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------------|--------------------------|
| End point type | Secondary |
| End point timeframe: | Baseline and Months 6,12 |

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

Statistical analyses

No statistical analyses for this end point

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

| | |
|---|--|
| End point title | Change from Baseline to Months 6, 12 and EoT in WPAI:SHP Score: Percent Impairment While Working |
| End point description: The WPAI:SHP is a self-administered questionnaire with 6 questions (Q1=Employment status; Q2=Hours absent from work due to the bladder condition; Q3=Hours absent from work due to other reasons; Q4=Hours actually worked; Q5=Impact of the bladder condition on productivity while working; Q6=Impact of the bladder condition on productivity while doing regular daily activities other than work) and a 1-week recall period. WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity, i.e., worse outcomes. A negative change from baseline indicates improvement. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. Only participants with both baseline and post-baseline values and who were employed during the study are included in the analysis. LOCF was used for EoT. | |
| End point type | Secondary |
| End point timeframe: Baseline and Months 6,12 | |

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

Statistical analyses

No statistical analyses for this end point

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

| | |
|--|---|
| End point title | Change From Baseline to Months 6, 12 in WPAI:SHP Score: Percent Overall Work Impairment |
| End point description: The WPAI:SHP is a self-administered questionnaire with 6 questions (Q1=Employment status; Q2=Hours absent from work due to the bladder condition; Q3=Hours absent from work due to other reasons; Q4=Hours actually worked; Q5=Impact of the bladder condition on productivity while working; Q6=Impact of the bladder condition on productivity while doing regular daily activities other than work) and a 1-week recall period. WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity, i.e., worse outcomes. A negative change from baseline indicated improvement. N is the number of participants analyzed with data available at each time point. Only participants with both baseline and post-baseline values and who were employed during the study are included in the analysis. LOCF was used for EoT. | |
| End point type | Secondary |
| End point timeframe: Baseline and Months 6, 12 | |

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

Statistical analyses

No statistical analyses for this end point

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

| | |
|--|---|
| End point title | Change From Baseline to Months 6, 12 in WPAI:SHP Score: Percent Activity Impairment |
| End point description: | |
| The WPAI:SHP is a self-administered questionnaire with 6 questions (Q1=Employment status; Q2=Hours absent from work due to the bladder condition; Q3=Hours absent from work due to other reasons; Q4=Hours actually worked; Q5=Impact of the bladder condition on productivity while working; Q6=Impact of the bladder condition on productivity while doing regular daily activities other than work) and a 1-week recall period. WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity, i.e., worse outcomes. A negative change from baseline indicated improvement. N is the number of participants analyzed with data available at each time point. Only participants with both baseline and post-baseline values during the study are included in the analysis. LOCF was used for EoT. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Months 6, 12 | |

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Months 1, 3, 6, 9, 12

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

Statistical analyses

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

Statistical analysis description:

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

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

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

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

Statistical analysis description:

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

| Statistical analysis title | Odds ratio vs. Solifenacin 5 mg (EoT) |
|--|--|
| Statistical analysis description: | |
| Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline OAB-q subscale as a covariate. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1492 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.37 |
| upper limit | 2.57 |

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Odds ratio vs. Solifenacin 5 mg (EoT) |
| Statistical analysis description: | |
| Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline OAB-q subscale as a covariate. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1492 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.014 |
| Method | Logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.08 |
| upper limit | 1.92 |

| | |
|--|--|
| Statistical analysis title | Odds ratio vs. Mirabegron 50 mg (EoT) |
| Statistical analysis description: | |
| Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline OAB-q subscale as a covariate. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1495 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.36 |
| upper limit | 2.43 |

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

| | |
|--|---|
| End point title | Percentage of Participants with 50% Reduction in Mean Number of Incontinence Episodes per 24 Hours at Months 1, 3, 6, 9, 12 and EoT |
| End point description: | |
| An incontinence episode was defined as the complaint of any involuntary leakage of urine. The mean number of incontinence episodes per 24 hours was calculated from data recorded by the participant in a micturition diary for 7 days prior to each visit. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT. | |
| End point type | Secondary |

End point timeframe:

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

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

Statistical analyses

| Statistical analysis title | Odds ratio vs. Mirabegron 50 mg (EoT) |
|--|--|
| Statistical analysis description: Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours as a covariate. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1495 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.34 |
| upper limit | 2.41 |

| Statistical analysis title | Odds ratio vs. Solifenacin 5 mg (EoT) |
|--|--|
| Statistical analysis description: Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours as a covariate. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Months 1, 3, 6, 9, 12

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

Statistical analyses

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

Statistical analysis description:

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

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

Statistical analysis title

Odds ratio vs. Mirabegron 50 mg (EoT)

Statistical analysis description:

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

| Statistical analysis title | Odds ratio vs. Mirabegron 50 mg (EoT) |
|--|--|
| Statistical analysis description: | |
| Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of micturitions per 24 hours as a covariate. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1495 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | Logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.55 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.18 |
| upper limit | 2.03 |

| Statistical analysis title | Odds ratio vs. Solifenacin 5 mg (EoT) |
|--|--|
| Statistical analysis description: | |
| Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of micturitions per 24 hours as a covariate. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Odds ratio vs. Mirabegron 50 mg (EoT) |
| Statistical analysis description: | |
| Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline PPBC as a covariate. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1495 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.68 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.24 |
| upper limit | 2.29 |

| | |
|--|--|
| Statistical analysis title | Odds ratio vs. Solifenacin 5 mg (EoT) |
| Statistical analysis description: | |
| Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline PPBC as a covariate. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1492 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.109 |
| Method | Logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.29 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.94 |
| upper limit | 1.77 |

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

| | |
|--|---|
| End point title | Percentage of Participants with Major (≥ 2 points) Improvement from Baseline in PPBC at Months 1, 3, 6, 9, 12 and EoT |
| End point description: | |
| The PPBC is a validated, global assessment tool using a 6-point Likert scale on which participants rated their subjective impression of their current bladder condition. Participants assessed their bladder condition using this scale: 1. Does not cause me any problems at all; 2. Causes me some very minor problems; 3. Causes me some minor problems; 4. Causes me (some) moderate problems; 5. Causes me severe problems; 6. Causes me many severe problems. The analysis population was the FAS. N is the number of participants analyzed with data available at each time point. LOCF was used for EoT. | |
| End point type | Secondary |

End point timeframe:

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

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

Statistical analyses

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

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

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

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

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

Reduction in Mean Number of Incontinence Episodes per 24 Hours and at Least 10 Points Improvement on OAB-q HRQL Total Score) at Months 1, 3, 6, 9, 12 and EoT

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

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

Statistical analysis description:

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

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

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

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

Statistical analysis description:

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

| Statistical analysis title | Odds ratio vs. Solifenacin 5 mg (EoT) |
|--|--|
| Statistical analysis description: | |
| Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours and baseline PPBC as covariates. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1492 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.019 |
| Method | Logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.06 |
| upper limit | 1.86 |

| Statistical analysis title | Odds ratio vs. Mirabegron 50 mg (EoT) |
|--|--|
| Statistical analysis description: | |
| Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours and baseline PPBC as covariates. | |
| Comparison groups | Mirabegron 50 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1495 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.7 |

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

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

Statistical analysis description:

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

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

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

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

Statistical analysis description:

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

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

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

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

End point description:

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

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

| | |
|------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Months 1, 3, 6, 9, 12 | |

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

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Odds ratio vs. Solifenacin 5 mg (EoT) |
| Statistical analysis description: | |
| Odds ratio is from a logistic regression model including treatment group, sex, age group (< 65, ≥ 65 years), previous study history and geographic region as factors and baseline mean number of incontinence episodes per 24 hours, baseline OAB-q HRQL total score and baseline PPBC as covariates. | |
| Comparison groups | Solifenacin 5 mg v Solifenacin 5 mg + mirabegron 50 mg |
| Number of subjects included in analysis | 1492 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.012 |
| Method | Logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.08 |
| upper limit | 1.89 |

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

Statistical analysis description:

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Adverse event reporting additional description:

The total number of deaths (all causes) includes deaths reported after the time frame above.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 16.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | Mirabegron 50 mg |
|-----------------------|------------------|

Reporting group description:

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

| | |
|-----------------------|-------------------------------------|
| Reporting group title | Solifenacin 5 mg + mirabegron 50 mg |
|-----------------------|-------------------------------------|

Reporting group description:

Participants who received solifenacin 5 mg and mirabegron 50 mg once a day for 52 weeks.

| | |
|-----------------------|------------------|
| Reporting group title | Solifenacin 5 mg |
|-----------------------|------------------|

Reporting group description:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

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

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported