



## Clinical trial results:

### An International Phase 3, Randomized, Double-Blind, Placebo- and Active (Tolterodine)-Controlled Multicenter Study to Evaluate the Safety and Efficacy of Vibegron in Patients with Symptoms of Overactive Bladder

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2017-003293-14   |
| Trial protocol           | LV HU EE BG LT   |
| Global end of trial date | 04 February 2019 |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1              |
| This version publication date  | 27 January 2021 |
| First version publication date | 27 January 2021 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | RVT-901-3003 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03492281 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Urovant Sciences GmbH  |
| Sponsor organisation address | Viaduktstrasse 8 4051, Basel, Switzerland,   |
| Public contact               | Clinical Trial Information Contact, Urovant Sciences GmbH, 41 (42) 2155999, info@urovant.com |
| Scientific contact           | Clinical Trial Information Contact, Urovant Sciences GmbH, 41 (42) 2155999, info@urovant.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                       | 05 October 2019  |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 10 January 2019  |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 04 February 2019 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

This study was conducted to evaluate the efficacy of vibegron compared to placebo in subjects with symptoms of overactive bladder (OAB), specifically the frequency of micturitions and frequency of urge urinary incontinence episodes, and to evaluate the safety and tolerability of treatment with vibegron.

Protection of trial subjects:

Each investigator obtained approval of the study from a properly constituted Institutional Review Board (IRB), Research Ethics Board (REB), or Independent Ethics Committee (IEC) prior to study initiation. This study was conducted in compliance with Good Clinical Practice (GCP). Prior to participating in any study procedures, the study was discussed with each subject and/or with the subject's legally authorized representative, and written informed consent was obtained.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 26 March 2018 |
| 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: 26          |
| Country: Number of subjects enrolled | Hungary: 27         |
| Country: Number of subjects enrolled | Latvia: 17          |
| Country: Number of subjects enrolled | Lithuania: 3        |
| Country: Number of subjects enrolled | Poland: 82          |
| Country: Number of subjects enrolled | United States: 1363 |
| Worldwide total number of subjects   | 1518                |
| EEA total number of subjects         | 129                 |

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)      | 871 |
| From 65 to 84 years       | 632 |
| 85 years and over         | 15  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Of 3149 subjects screened for this study, 1518 were randomized (after a 2-week, single-blind placebo Run-in Period), and 1515 received 1 dose of double-blind study drug in the Treatment Period (Safety Set: placebo, N = 540; vibegron, N = 545; tolterodine, N = 430).

### Period 1

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

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Placebo |

Arm description:

Subjects received matching placebo, orally, once daily for 12 weeks.

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

Dosage and administration details:

Placebo to match vibegron 75-mg tablet, administered as a single tablet, orally, once daily

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

Dosage and administration details:

Placebo to match tolterodine extended release (ER) 4-mg capsule, administered as a single capsule, orally, once daily

|                  |                |
|------------------|----------------|
| <b>Arm title</b> | Vibegron 75 mg |
|------------------|----------------|

Arm description:

Subjects received vibegron 75 milligrams (mg), orally, once daily for 12 weeks.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Vibegron     |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Vibegron 75-mg tablet, administered as a single tablet, orally, once daily

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | Tolterodine ER 4 mg |
|------------------|---------------------|

Arm description:

Subjects received tolterodine ER 4 mg, orally, once daily for 12 weeks.

|  |                   |
|--|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Tolterodine       |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Capsule           |
| Routes of administration               | Oral use          |

Dosage and administration details:

Tolterodine ER 4-mg capsule, administered as a single capsule, orally, once daily

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Placebo | Vibegron 75 mg | Tolterodine ER 4 mg |
|---|---------|----------------|---------------------|
| Started   | 540     | 545            | 430                 |
| Completed   | 486     | 502            | 385                 |
| Not completed                                       | 54      | 43             | 45                  |
| Withdrawn Due To Sponsor                            | 1       | -              | 1                   |
| Adverse event, serious fatal                        | -       | -              | 1                   |
| Physician decision                                  | 1       | -              | 3                   |
| Consent withdrawn by subject                        | 21      | 14             | 13                  |
| Adverse event, non-fatal                            | 6       | 8              | 13                  |
| Lost to follow-up                                   | 14      | 15             | 10                  |
| Captured As Other In Database                       | 8       | 6              | 3                   |
| Lack of efficacy                                    | 3       | -              | 1                   |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Of 3149 subjects screened for this study, 1518 were randomized, and 1515 received 1 dose of double-blind study drug in the Treatment Period (Safety Set). Baseline data are reported for members of the Safety Set.

## Baseline characteristics

### Reporting groups

|   |                     |
|---|---------------------|
| Reporting group title   | Placebo             |
| Reporting group description:  |                     |
| Subjects received matching placebo, orally, once daily for 12 weeks.            |                     |
| Reporting group title   | Vibegron 75 mg      |
| Reporting group description:  |                     |
| Subjects received vibegron 75 milligrams (mg), orally, once daily for 12 weeks. |                     |
| Reporting group title   | Tolterodine ER 4 mg |
| Reporting group description:  |                     |
| Subjects received tolterodine ER 4 mg, orally, once daily for 12 weeks.         |                     |

| Reporting group values | Placebo | Vibegron 75 mg | Tolterodine ER 4 mg |
|------------------------|---------|----------------|---------------------|
| Number of subjects     | 540     | 545            | 430                 |
| Age categorical        |         |                |                     |
| Units:                 |         |                |                     |

|  |         |         |         |
|--|---------|---------|---------|
| Age continuous   |         |         |         |
| Units: years   |         |         |         |
| arithmetic mean  | 59.9    | 60.4    | 59.8    |
| standard deviation   | ± 13.35 | ± 13.49 | ± 13.27 |
| Gender categorical   |         |         |         |
| Units: Subjects  |         |         |         |
| Female   | 459     | 463     | 364     |
| Male   | 81      | 82      | 66      |
| Race/Ethnicity, Customized   |         |         |         |
| Units: Subjects  |         |         |         |
| American Indian or Alaska  | 3       | 2       | 0       |
| Asian  | 30      | 28      | 27      |
| Black or African American  | 85      | 78      | 72      |
| White  | 418     | 435     | 326     |
| Puerto Rican   | 1       | 1       | 1       |
| White and Black or African American  | 1       | 0       | 0       |
| Hispanic   | 2       | 1       | 0       |
| Filipino   | 0       | 0       | 1       |
| Morrocan   | 0       | 0       | 1       |
| Multiracial  | 0       | 0       | 1       |
| White, Black or African American   | 0       | 0       | 1       |
| Average number of micturations per 24 hours in all overactive bladder (OAB) subjects   |         |         |         |
| A micturition/void was defined as "Urinated in Toilet" as indicated on the Patient Voiding Diary (PVD). The number of micturations was defined as the number of times a subject voided in the toilet as indicated on the PVD. The average daily number of micturations was calculated using the daily entries in the PVD (which was to be completed prior to each study visit) as the total number of micturations that occurred on a Complete Diary Day (CDD) divided by the number of CDDs in the PVD. 999999=population not analyzed. |         |         |         |
| Units: micturations  |         |         |         |
| arithmetic mean  |         |         |         |

|  |   |   |   |
|--|---|---|---|
| standard deviation   | ± | ± | ± |
| Average number of urge urinary incontinence (UUI) episodes per 24 hours in OAB Wet subjects  |   |   |   |
| The number of UUI episodes was defined as the number of times a subject had checked "urge" as the main reason for the leakage in the PVD, regardless of whether more than one reason for leakage in addition to "urge" was checked. OAB Wet subjects were those subjects with an average of ≥8.0 micturitions per Diary Day (DD); with an average of ≥1.0 UUI episodes per DD; and, if stress urinary incontinence was present, with a total number of UUI episodes greater than the total number of stress urinary incontinence episodes from the previous visit diary. 999999=population not analyzed. |   |   |   |
| Units: UUI episodes<br>arithmetic mean<br>standard deviation   | ± | ± | ± |
| Average number of urgency episodes over 24 hours in all OAB subjects   |   |   |   |
| An urgency episode was defined as the "Need to Urinate Immediately" as indicated on the PVD. "Over 24 hours" corresponds to one Diary Day (i.e., time between when the subject got up for the day each morning and time the subject got up for the day the next morning as recorded in the PVD). 999999=population not analyzed.   |   |   |   |
| Units: urgency episodes<br>arithmetic mean<br>standard deviation   | ± | ± | ± |
| Average number of total incontinence episodes over 24 hours in OAB Wet subjects  |   |   |   |
| Total incontinence was defined as having any reason for "Accidental Urine Leakage" and/or "Accidental Urine Leakage" checked, as indicated on the PVD. It is assumed that if the subject recorded a reason for leakage then the accidental urine leakage occurred. OAB Wet subjects were defined as those with an average of ≥8.0 micturitions per Diary Day; with an average of ≥1.0 UUI episodes per Diary Day; and, if stress urinary incontinence was present, with a total number of UUI episodes > the total number of stress urinary incontinence episodes from the previous visit diary.         |   |   |   |
| Units: total incontinence episodes<br>arithmetic mean<br>standard deviation  | ± | ± | ± |
| Coping Score from the OAB Questionnaire Long Form (OAB-q LF, 1-week recall) in all OAB subjects  |   |   |   |
| The OAB-q LF is a validated patient-reported outcome. 8 questions of the OAB-q LF ask subjects how well they have coped with their bladder symptoms during the previous week, as a measure of quality of life. Each question has a response ranging from "not coping" (=1) to "coping well" (=6). These questions make up the coping scale. The raw score (sum of question scores [ranging from 8 to 48]) is transformed to a unified score, ranging from 0 to 100. Higher scores correspond to a higher quality of life, and lower scores represent a lower quality of life. n=518, 524, 416.           |   |   |   |
| Units: Units on a scale<br>arithmetic mean<br>standard deviation   | ± | ± | ± |
| Average volume voided per micturition in all OAB subjects  |   |   |   |
| A micturition/void was defined as "Urinated in Toilet" as indicated on the PVD. The number of micturitions was defined as the number of times a subject voided in the toilet as indicated on the PVD. The average volume voided per micturition was calculated as the arithmetic mean of all voids for which a subject recorded the volume. 999999=population not analyzed. n=514, 524, 415 (only subjects with evaluable data were analyzed).   |   |   |   |
| Units: milliliters<br>arithmetic mean<br>standard deviation  | ± | ± | ± |
| Health-related Quality of Life (HRQL) TS from the OAB-q LF (1-week recall) in all OAB subjects   |   |   |   |
| TS=total score. The OAB-q LF is a validated patient-reported outcome. The 25 questions comprising the subscales of the OAB-q LF ask subjects how much their symptoms have affected their life over the last  |   |   |   |

week. Each question has a response ranging from "None of the time" (=1) to "All of the time" (=6). The raw score (sum of question scores for the 4 subscales [ranging from 25 to 150]) is transformed to a unified score, ranging from 0 to 100. Higher scores correspond to a higher quality of life, and lower scores represent a lower quality of life. n=518, 524, 416 (evaluable subjects).

|                         |   |   |   |
|-------------------------|---|---|---|
| Units: Units on a scale |   |   |   |
| arithmetic mean         |   |   |   |
| standard deviation      | ± | ± | ± |

|  |  |  |  |
|--|--|--|--|
| Symptom Bother Score from the OAB-q LF (1-week recall) in all OAB subjects |  |  |  |
|--|--|--|--|

The OAB-q LF is a validated patient-reported outcome. The first 8 questions of the OAB-q LF ask subjects how much they were bothered by their bladder symptoms during the previous week. Each question has a response ranging from "Not at all" (=1) to "A very great deal" (=6). These questions make up the symptom bother scale. The raw score (sum of question scores [ranging from 8 to 48]) is transformed to a unified score, ranging from 0 to 100. Higher scores correspond to the symptoms having a larger bother, and lower scores represent a lower amount of bother due to symptoms. n=518, 524, 416.

|                         |   |   |   |
|-------------------------|---|---|---|
| Units: Units on a scale |   |   |   |
| arithmetic mean         |   |   |   |
| standard deviation      | ± | ± | ± |

|  |  |  |  |
|--|--|--|--|
| Overall bladder symptoms based on PGI of Severity (PGI-Severity) in all OAB subjects |  |  |  |
|--|--|--|--|

The Patient Global Impression (PGI) questions are designed to assess a subject's overall impression of OAB. For the PGI-Severity score, subjects are asked to rate their OAB symptoms over the previous week with one of the following responses: 1 = none, 2 = mild, 3 = moderate, 4 = severe. 999999=population not analyzed. n=519, 525, 417 (only subjects with evaluable data were analyzed).

|                         |   |   |   |
|-------------------------|---|---|---|
| Units: Units on a scale |   |   |   |
| arithmetic mean         |   |   |   |
| standard deviation      | ± | ± | ± |

|   |  |  |  |
|---|--|--|--|
| Overall control over bladder symptoms based on PGI of Control (PGI-Control) in all OAB subjects |  |  |  |
|---|--|--|--|

The PGI questions are designed to assess a subject's overall impression of OAB. For the PGI-Control score, subjects were asked to rate how much control they had over their OAB symptoms over the previous week with one of the following responses: 1 = complete control, 2 = a lot of control, 3 = some control, 4 = only a little control, 5 = no control. 999999=population not analyzed. n=519, 525, 417 (only subjects with evaluable data were analyzed).

|                         |   |   |   |
|-------------------------|---|---|---|
| Units: Units on a scale |   |   |   |
| arithmetic mean         |   |   |   |
| standard deviation      | ± | ± | ± |

|                               |       |  |  |
|-------------------------------|-------|--|--|
| <b>Reporting group values</b> | Total |  |  |
| Number of subjects            | 1515  |  |  |
| Age categorical               |       |  |  |
| Units:                        |       |  |  |

|                            |      |  |  |
|----------------------------|------|--|--|
| Age continuous             |      |  |  |
| Units: years               |      |  |  |
| arithmetic mean            |      |  |  |
| standard deviation         | -    |  |  |
| Gender categorical         |      |  |  |
| Units: Subjects            |      |  |  |
| Female                     | 1286 |  |  |
| Male                       | 229  |  |  |
| Race/Ethnicity, Customized |      |  |  |
| Units: Subjects            |      |  |  |
| American Indian or Alaska  | 5    |  |  |



|  |      |  |  |
|--|------|--|--|
| Asian  | 85   |  |  |
| Black or African American  | 235  |  |  |
| White  | 1179 |  |  |
| Puerto Rican   | 3    |  |  |
| White and Black or African American  | 1    |  |  |
| Hispanic   | 3    |  |  |
| Filipino   | 1    |  |  |
| Moroccan   | 1    |  |  |
| Multiracial  | 1    |  |  |
| White, Black or African American   | 1    |  |  |
| Average number of micturitions per 24 hours in all overactive bladder (OAB) subjects   |      |  |  |
| A micturition/void was defined as "Urinated in Toilet" as indicated on the Patient Voiding Diary (PVD). The number of micturitions was defined as the number of times a subject voided in the toilet as indicated on the PVD. The average daily number of micturitions was calculated using the daily entries in the PVD (which was to be completed prior to each study visit) as the total number of micturitions that occurred on a Complete Diary Day (CDD) divided by the number of CDDs in the PVD. 999999=population not analyzed.   |      |  |  |
| Units: micturitions  |      |  |  |
| arithmetic mean  |      |  |  |
| standard deviation   | -    |  |  |
| Average number of urge urinary incontinence (UUI) episodes per 24 hours in OAB Wet subjects  |      |  |  |
| The number of UUI episodes was defined as the number of times a subject had checked "urge" as the main reason for the leakage in the PVD, regardless of whether more than one reason for leakage in addition to "urge" was checked. OAB Wet subjects were those subjects with an average of $\geq 8.0$ micturitions per Diary Day (DD); with an average of $\geq 1.0$ UUI episodes per DD; and, if stress urinary incontinence was present, with a total number of UUI episodes greater than the total number of stress urinary incontinence episodes from the previous visit diary. 999999=population not analyzed. |      |  |  |
| Units: UUI episodes  |      |  |  |
| arithmetic mean  |      |  |  |
| standard deviation   | -    |  |  |
| Average number of urgency episodes over 24 hours in all OAB subjects   |      |  |  |
| An urgency episode was defined as the "Need to Urinate Immediately" as indicated on the PVD. "Over 24 hours" corresponds to one Diary Day (i.e., time between when the subject got up for the day each morning and time the subject got up for the day the next morning as recorded in the PVD). 999999=population not analyzed.   |      |  |  |
| Units: urgency episodes  |      |  |  |
| arithmetic mean  |      |  |  |
| standard deviation   | -    |  |  |
| Average number of total incontinence episodes over 24 hours in OAB Wet subjects  |      |  |  |
| Total incontinence was defined as having any reason for "Accidental Urine Leakage" and/or "Accidental Urine Leakage" checked, as indicated on the PVD. It is assumed that if the subject recorded a reason for leakage then the accidental urine leakage occurred. OAB Wet subjects were defined as those with an average of $\geq 8.0$ micturitions per Diary Day; with an average of $\geq 1.0$ UUI episodes per Diary Day; and, if stress urinary incontinence was present, with a total number of UUI episodes > the total number of stress urinary incontinence episodes from the previous visit diary.         |      |  |  |
| Units: total incontinence episodes   |      |  |  |
| arithmetic mean  |      |  |  |
| standard deviation   | -    |  |  |
| Coping Score from the OAB Questionnaire Long Form (OAB-q LF, 1-week recall) in all OAB subjects  |      |  |  |
| The OAB-q LF is a validated patient-reported outcome. 8 questions of the OAB-q LF ask subjects how   |      |  |  |

|  |   |  |  |
|--|---|--|--|
| well they have coped with their bladder symptoms during the previous week, as a measure of quality of life. Each question has a response ranging from "not coping" (=1) to "coping well" (=6). These questions make up the coping scale. The raw score (sum of question scores [ranging from 8 to 48]) is transformed to a unified score, ranging from 0 to 100. Higher scores correspond to a higher quality of life, and lower scores represent a lower quality of life. n=518, 524, 416.  |   |  |  |
| Units: Units on a scale<br>arithmetic mean<br>standard deviation   | - |  |  |
| Average volume voided per micturition in all OAB subjects  |   |  |  |
| A micturition/void was defined as "Urinated in Toilet" as indicated on the PVD. The number of micturitions was defined as the number of times a subject voided in the toilet as indicated on the PVD. The average volume voided per micturition was calculated as the arithmetic mean of all voids for which a subject recorded the volume. 999999=population not analyzed. n=514, 524, 415 (only subjects with evaluable data were analyzed).   |   |  |  |
| Units: milliliters<br>arithmetic mean<br>standard deviation  | - |  |  |
| Health-related Quality of Life (HRQL) TS from the OAB-q LF (1-week recall) in all OAB subjects   |   |  |  |
| TS=total score. The OAB-q LF is a validated patient-reported outcome. The 25 questions comprising the subscales of the OAB-q LF ask subjects how much their symptoms have affected their life over the last week. Each question has a response ranging from "None of the time" (=1) to "All of the time" (=6). The raw score (sum of question scores for the 4 subscales [ranging from 25 to 150]) is transformed to a unified score, ranging from 0 to 100. Higher scores correspond to a higher quality of life, and lower scores represent a lower quality of life. n=518, 524, 416 (evaluable subjects).       |   |  |  |
| Units: Units on a scale<br>arithmetic mean<br>standard deviation   | - |  |  |
| Symptom Bother Score from the OAB-q LF (1-week recall) in all OAB subjects   |   |  |  |
| The OAB-q LF is a validated patient-reported outcome. The first 8 questions of the OAB-q LF ask subjects how much they were bothered by their bladder symptoms during the previous week. Each question has a response ranging from "Not at all" (=1) to "A very great deal" (=6). These questions make up the symptom bother scale. The raw score (sum of question scores [ranging from 8 to 48]) is transformed to a unified score, ranging from 0 to 100. Higher scores correspond to the symptoms having a larger bother, and lower scores represent a lower amount of bother due to symptoms. n=518, 524, 416. |   |  |  |
| Units: Units on a scale<br>arithmetic mean<br>standard deviation   | - |  |  |
| Overall bladder symptoms based on PGI of Severity (PGI-Severity) in all OAB subjects   |   |  |  |
| The Patient Global Impression (PGI) questions are designed to assess a subject's overall impression of OAB. For the PGI-Severity score, subjects are asked to rate their OAB symptoms over the previous week with one of the following responses: 1 = none, 2 = mild, 3 = moderate, 4 = severe. 999999=population not analyzed. n=519, 525, 417 (only subjects with evaluable data were analyzed).   |   |  |  |
| Units: Units on a scale<br>arithmetic mean<br>standard deviation   | - |  |  |
| Overall control over bladder symptoms based on PGI of Control (PGI-Control) in all OAB subjects  |   |  |  |
| The PGI questions are designed to assess a subject's overall impression of OAB. For the PGI-Control score, subjects were asked to rate how much control they had over their OAB symptoms over the previous week with one of the following responses: 1 = complete control, 2 = a lot of control, 3 = some control, 4 = only a little control, 5 = no control. 999999=population not analyzed. n=519, 525, 417 (only subjects with evaluable data were analyzed).   |   |  |  |
| Units: Units on a scale  |   |  |  |

|                    |   |  |  |
|--------------------|---|--|--|
| arithmetic mean    |   |  |  |
| standard deviation | - |  |  |

## Subject analysis sets

|                            |                            |
|----------------------------|----------------------------|
| Subject analysis set title | Placebo: Full Analysis Set |
| Subject analysis set type  | Full analysis              |

Subject analysis set description:

Subjects received matching placebo, orally, once daily for 12 weeks. The Full Analysis Set is defined as all randomized OAB subjects who took at least 1 dose of double-blind study treatment and had at least 1 evaluable change from baseline micturition measurement.

|                            |                                   |
|----------------------------|-----------------------------------|
| Subject analysis set title | Vibegron 75 mg: Full Analysis Set |
| Subject analysis set type  | Full analysis                     |

Subject analysis set description:

Subjects received vibegron 75 milligrams (mg), orally, once daily for 12 weeks. The Full Analysis Set is defined as all randomized OAB Subjects who took at least 1 dose of double-blind study treatment and had at least 1 evaluable change from baseline micturition measurement.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Tolterodine ER 4 mg: Full Analysis Set |
| Subject analysis set type  | Full analysis                          |

Subject analysis set description:

Subjects received tolterodine extended release (ER) 4 mg, orally, once daily for 12 weeks. The Full Analysis Set is defined as all randomized OAB subjects who took at least 1 dose of double-blind study treatment and had at least 1 evaluable change from baseline micturition measurement.

|                            |                  |
|----------------------------|------------------|
| Subject analysis set title | Placebo: OAB Wet |
| Subject analysis set type  | Full analysis    |

Subject analysis set description:

Subjects who met the definition of OAB Wet at study entry (based on the PVD) received matching placebo, orally, once daily for 12 weeks. OAB Wet subjects were defined as those with an average of  $\geq 8.0$  micturitions per Diary Day; with an average of  $\geq 1.0$  UUI episodes per Diary Day; and, if stress urinary incontinence was present, with a total number of UUI episodes greater than the total number of stress urinary incontinence episodes from the previous visit diary. Analysis was conducted in members of the Full Analysis Set for Incontinence (FAS-I) Population, comprised of all randomized OAB Wet subjects who took at least 1 dose of double-blind study treatment and had at least 1 evaluable change from the Baseline UUI measurement.

|                            |                         |
|----------------------------|-------------------------|
| Subject analysis set title | Vibegron 75 mg: OAB Wet |
| Subject analysis set type  | Full analysis           |

Subject analysis set description:

Subjects who met the definition of OAB Wet at study entry (based on the PVD) received vibegron 75 milligrams (mg), orally, once daily for 12 weeks. OAB Wet subjects were defined as those with an average of  $\geq 8.0$  micturitions per Diary Day; with an average of  $\geq 1.0$  UUI episodes per Diary Day; and, if stress urinary incontinence was present, with a total number of UUI episodes greater than the total number of stress urinary incontinence episodes from the previous visit diary. Analysis was conducted in members of the FAS-I Population, comprised of all randomized OAB Wet subjects who took at least 1 dose of double-blind study treatment and had at least 1 evaluable change from the Baseline UUI measurement.

|                            |                              |
|----------------------------|------------------------------|
| Subject analysis set title | Tolterodine ER 4 mg: OAB Wet |
| Subject analysis set type  | Full analysis                |

Subject analysis set description:

Subjects who met the definition of OAB Wet at study entry (based on the PVD) received tolterodine extended release (ER) 4 mg, orally, once daily for 12 weeks. OAB Wet subjects were defined as those with an average of  $\geq 8.0$  micturitions per Diary Day; with an average of  $\geq 1.0$  UUI episodes per Diary Day; and, if stress urinary incontinence was present, with a total number of UUI episodes greater than the total number of stress urinary incontinence episodes from the previous visit diary. Analysis was conducted in members of the FAS-I Population, comprised of all randomized OAB Wet subjects who took at least 1 dose of double-blind study treatment and had at least 1 evaluable change from the Baseline UUI measurement.

| Reporting group values    | Placebo: Full Analysis Set | Vibegron 75 mg: Full Analysis Set | Tolterodine ER 4 mg: Full Analysis Set |
|---------------------------|----------------------------|-----------------------------------|--|
| Number of subjects        | 520                        | 526                               | 417                                    |
| Age categorical<br>Units: |                            |                                   |  |

|  |                    |                    |                    |
|--|--------------------|--------------------|--------------------|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation  | ±                  | ±                  | ±                  |
| Gender categorical<br>Units: Subjects  |                    |                    |                    |
| Female   |                    |                    |                    |
| Male   |                    |                    |                    |
| Race/Ethnicity, Customized<br>Units: Subjects  |                    |                    |                    |
| American Indian or Alaska<br>Asian<br>Black or African American<br>White<br>Puerto Rican<br>White and Black or African American<br>Hispanic<br>Filipino<br>Morrocan<br>Multiracial<br>White, Black or African American   |                    |                    |                    |
| Average number of micturitions per 24 hours in all overactive bladder (OAB) subjects   |                    |                    |                    |
| A micturition/void was defined as "Urinated in Toilet" as indicated on the Patient Voiding Diary (PVD). The number of micturitions was defined as the number of times a subject voided in the toilet as indicated on the PVD. The average daily number of micturitions was calculated using the daily entries in the PVD (which was to be completed prior to each study visit) as the total number of micturitions that occurred on a Complete Diary Day (CDD) divided by the number of CDDs in the PVD. 999999=population not analyzed.   |                    |                    |                    |
| Units: micturitions<br>arithmetic mean<br>standard deviation   | 11.75<br>± 4.007   | 11.31<br>± 3.420   | 11.48<br>± 3.153   |
| Average number of urge urinary incontinence (UUI) episodes per 24 hours in OAB Wet subjects  |                    |                    |                    |
| The number of UUI episodes was defined as the number of times a subject had checked "urge" as the main reason for the leakage in the PVD, regardless of whether more than one reason for leakage in addition to "urge" was checked. OAB Wet subjects were those subjects with an average of ≥8.0 micturitions per Diary Day (DD); with an average of ≥1.0 UUI episodes per DD; and, if stress urinary incontinence was present, with a total number of UUI episodes greater than the total number of stress urinary incontinence episodes from the previous visit diary. 999999=population not analyzed. |                    |                    |                    |
| Units: UUI episodes<br>arithmetic mean<br>standard deviation   | 999999<br>± 999999 | 999999<br>± 999999 | 999999<br>± 999999 |
| Average number of urgency episodes over 24 hours in all OAB subjects   |                    |                    |                    |
| An urgency episode was defined as the "Need to Urinate Immediately" as indicated on the PVD. "Over 24 hours" corresponds to one Diary Day (i.e., time between when the subject got up for the day each   |                    |                    |                    |

|  |          |          |          |
|--|----------|----------|----------|
| morning and time the subject got up for the day the next morning as recorded in the PVD).<br>999999=population not analyzed.   |          |          |          |
| Units: urgency episodes  |          |          |          |
| arithmetic mean  | 8.13     | 8.11     | 7.92     |
| standard deviation   | ± 4.668  | ± 4.400  | ± 3.883  |
| Average number of total incontinence episodes over 24 hours in OAB Wet subjects  |          |          |          |
| Total incontinence was defined as having any reason for "Accidental Urine Leakage" and/or "Accidental Urine Leakage" checked, as indicated on the PVD. It is assumed that if the subject recorded a reason for leakage then the accidental urine leakage occurred. OAB Wet subjects were defined as those with an average of ≥8.0 micturitions per Diary Day; with an average of ≥1.0 UUI episodes per Diary Day; and, if stress urinary incontinence was present, with a total number of UUI episodes > the total number of stress urinary incontinence episodes from the previous visit diary.                   |          |          |          |
| Units: total incontinence episodes   |          |          |          |
| arithmetic mean  | 999999   | 999999   | 999999   |
| standard deviation   | ± 999999 | ± 999999 | ± 999999 |
| Coping Score from the OAB Questionnaire Long Form (OAB-q LF, 1-week recall) in all OAB subjects  |          |          |          |
| The OAB-q LF is a validated patient-reported outcome. 8 questions of the OAB-q LF ask subjects how well they have coped with their bladder symptoms during the previous week, as a measure of quality of life. Each question has a response ranging from "not coping" (=1) to "coping well" (=6). These questions make up the coping scale. The raw score (sum of question scores [ranging from 8 to 48]) is transformed to a unified score, ranging from 0 to 100. Higher scores correspond to a higher quality of life, and lower scores represent a lower quality of life. n=518, 524, 416.                     |          |          |          |
| Units: Units on a scale  |          |          |          |
| arithmetic mean  | 58.74    | 57.57    | 59.77    |
| standard deviation   | ± 27.140 | ± 28.090 | ± 26.399 |
| Average volume voided per micturition in all OAB subjects  |          |          |          |
| A micturition/void was defined as "Urinated in Toilet" as indicated on the PVD. The number of micturitions was defined as the number of times a subject voided in the toilet as indicated on the PVD. The average volume voided per micturition was calculated as the arithmetic mean of all voids for which a subject recorded the volume. 999999=population not analyzed. n=514, 524, 415 (only subjects with evaluable data were analyzed).   |          |          |          |
| Units: milliliters   |          |          |          |
| arithmetic mean  | 148.3    | 155.4    | 147.0    |
| standard deviation   | ± 60.67  | ± 63.07  | ± 60.79  |
| Health-related Quality of Life (HRQL) TS from the OAB-q LF (1-week recall) in all OAB subjects   |          |          |          |
| TS=total score. The OAB-q LF is a validated patient-reported outcome. The 25 questions comprising the subscales of the OAB-q LF ask subjects how much their symptoms have affected their life over the last week. Each question has a response ranging from "None of the time" (=1) to "All of the time" (=6). The raw score (sum of question scores for the 4 subscales [ranging from 25 to 150]) is transformed to a unified score, ranging from 0 to 100. Higher scores correspond to a higher quality of life, and lower scores represent a lower quality of life. n=518, 524, 416 (evaluable subjects).       |          |          |          |
| Units: Units on a scale  |          |          |          |
| arithmetic mean  | 63.74    | 62.71    | 64.53    |
| standard deviation   | ± 23.473 | ± 24.916 | ± 22.902 |
| Symptom Bother Score from the OAB-q LF (1-week recall) in all OAB subjects   |          |          |          |
| The OAB-q LF is a validated patient-reported outcome. The first 8 questions of the OAB-q LF ask subjects how much they were bothered by their bladder symptoms during the previous week. Each question has a response ranging from "Not at all" (=1) to "A very great deal" (=6). These questions make up the symptom bother scale. The raw score (sum of question scores [ranging from 8 to 48]) is transformed to a unified score, ranging from 0 to 100. Higher scores correspond to the symptoms having a larger bother, and lower scores represent a lower amount of bother due to symptoms. n=518, 524, 416. |          |          |          |
| Units: Units on a scale  |          |          |          |

|  |          |          |          |
|--|----------|----------|----------|
| arithmetic mean  | 50.07    | 49.68    | 48.01    |
| standard deviation   | ± 20.642 | ± 21.961 | ± 20.611 |
| Overall bladder symptoms based on PGI of Severity (PGI-Severity) in all OAB subjects   |          |          |          |
| The Patient Global Impression (PGI) questions are designed to assess a subject's overall impression of OAB. For the PGI-Severity score, subjects are asked to rate their OAB symptoms over the previous week with one of the following responses: 1 = none, 2 = mild, 3 = moderate, 4 = severe. 999999=population not analyzed. n=519, 525, 417 (only subjects with evaluable data were analyzed).   |          |          |          |
| Units: Units on a scale  |          |          |          |
| arithmetic mean  | 3.03     | 3.02     | 2.99     |
| standard deviation   | ± 0.645  | ± 0.619  | ± 0.639  |
| Overall control over bladder symptoms based on PGI of Control (PGI-Control) in all OAB subjects  |          |          |          |
| The PGI questions are designed to assess a subject's overall impression of OAB. For the PGI-Control score, subjects were asked to rate how much control they had over their OAB symptoms over the previous week with one of the following responses: 1 = complete control, 2 = a lot of control, 3 = some control, 4 = only a little control, 5 = no control. 999999=population not analyzed. n=519, 525, 417 (only subjects with evaluable data were analyzed). |          |          |          |
| Units: Units on a scale  |          |          |          |
| arithmetic mean  | 3.16     | 3.23     | 3.17     |
| standard deviation   | ± 0.964  | ± 0.911  | ± 0.934  |

|                               |                  |                         |                              |
|-------------------------------|------------------|-------------------------|------------------------------|
| <b>Reporting group values</b> | Placebo: OAB Wet | Vibegron 75 mg: OAB Wet | Tolterodine ER 4 mg: OAB Wet |
| Number of subjects            | 405              | 403                     | 319                          |
| Age categorical               |                  |                         |                              |
| Units:                        |                  |                         |                              |

|   |   |   |   |
|---|---|---|---|
| Age continuous  |   |   |   |
| Units: years  |   |   |   |
| arithmetic mean   |   |   |   |
| standard deviation  | ± | ± | ± |
| Gender categorical  |   |   |   |
| Units: Subjects   |   |   |   |
| Female  |   |   |   |
| Male  |   |   |   |
| Race/Ethnicity, Customized  |   |   |   |
| Units: Subjects   |   |   |   |
| American Indian or Alaska   |   |   |   |
| Asian   |   |   |   |
| Black or African American   |   |   |   |
| White   |   |   |   |
| Puerto Rican  |   |   |   |
| White and Black or African American   |   |   |   |
| Hispanic  |   |   |   |
| Filipino  |   |   |   |
| Moroccan  |   |   |   |
| Multiracial   |   |   |   |
| White, Black or African American  |   |   |   |
| Average number of micturitions per 24 hours in all overactive bladder (OAB) subjects                    |   |   |   |
| A micturition/void was defined as "Urinated in Toilet" as indicated on the Patient Voiding Diary (PVD). |   |   |   |

The number of micturitions was defined as the number of times a subject voided in the toilet as indicated on the PVD. The average daily number of micturitions was calculated using the daily entries in the PVD (which was to be completed prior to each study visit) as the total number of micturitions that occurred on a Complete Diary Day (CDD) divided by the number of CDDs in the PVD. 999999=population not analyzed.

|                     |          |          |          |
|---------------------|----------|----------|----------|
| Units: micturitions |          |          |          |
| arithmetic mean     | 999999   | 999999   | 999999   |
| standard deviation  | ± 999999 | ± 999999 | ± 999999 |

|   |  |  |  |
|---|--|--|--|
| Average number of urge urinary incontinence (UUI) episodes per 24 hours in OAB Wet subjects |  |  |  |
|---|--|--|--|

The number of UUI episodes was defined as the number of times a subject had checked "urge" as the main reason for the leakage in the PVD, regardless of whether more than one reason for leakage in addition to "urge" was checked. OAB Wet subjects were those subjects with an average of  $\geq 8.0$  micturitions per Diary Day (DD); with an average of  $\geq 1.0$  UUI episodes per DD; and, if stress urinary incontinence was present, with a total number of UUI episodes greater than the total number of stress urinary incontinence episodes from the previous visit diary. 999999=population not analyzed.

|                     |         |         |         |
|---------------------|---------|---------|---------|
| Units: UUI episodes |         |         |         |
| arithmetic mean     | 3.49    | 3.43    | 3.42    |
| standard deviation  | ± 3.053 | ± 2.894 | ± 2.592 |

|  |  |  |  |
|--|--|--|--|
| Average number of urgency episodes over 24 hours in all OAB subjects |  |  |  |
|--|--|--|--|

An urgency episode was defined as the "Need to Urinate Immediately" as indicated on the PVD. "Over 24 hours" corresponds to one Diary Day (i.e., time between when the subject got up for the day each morning and time the subject got up for the day the next morning as recorded in the PVD). 999999=population not analyzed.

|                         |          |          |          |
|-------------------------|----------|----------|----------|
| Units: urgency episodes |          |          |          |
| arithmetic mean         | 999999   | 999999   | 999999   |
| standard deviation      | ± 999999 | ± 999999 | ± 999999 |

|   |  |  |  |
|---|--|--|--|
| Average number of total incontinence episodes over 24 hours in OAB Wet subjects |  |  |  |
|---|--|--|--|

Total incontinence was defined as having any reason for "Accidental Urine Leakage" and/or "Accidental Urine Leakage" checked, as indicated on the PVD. It is assumed that if the subject recorded a reason for leakage then the accidental urine leakage occurred. OAB Wet subjects were defined as those with an average of  $\geq 8.0$  micturitions per Diary Day; with an average of  $\geq 1.0$  UUI episodes per Diary Day; and, if stress urinary incontinence was present, with a total number of UUI episodes > the total number of stress urinary incontinence episodes from the previous visit diary.

|                                    |         |         |         |
|------------------------------------|---------|---------|---------|
| Units: total incontinence episodes |         |         |         |
| arithmetic mean                    | 4.17    | 4.14    | 4.06    |
| standard deviation                 | ± 3.823 | ± 3.631 | ± 3.071 |

|   |  |  |  |
|---|--|--|--|
| Coping Score from the OAB Questionnaire Long Form (OAB-q LF, 1-week recall) in all OAB subjects |  |  |  |
|---|--|--|--|

The OAB-q LF is a validated patient-reported outcome. 8 questions of the OAB-q LF ask subjects how well they have coped with their bladder symptoms during the previous week, as a measure of quality of life. Each question has a response ranging from "not coping" (=1) to "coping well" (=6). These questions make up the coping scale. The raw score (sum of question scores [ranging from 8 to 48]) is transformed to a unified score, ranging from 0 to 100. Higher scores correspond to a higher quality of life, and lower scores represent a lower quality of life. n=518, 524, 416.

|                         |          |          |          |
|-------------------------|----------|----------|----------|
| Units: Units on a scale |          |          |          |
| arithmetic mean         | 999999   | 999999   | 999999   |
| standard deviation      | ± 999999 | ± 999999 | ± 999999 |

|   |  |  |  |
|---|--|--|--|
| Average volume voided per micturition in all OAB subjects |  |  |  |
|---|--|--|--|

A micturition/void was defined as "Urinated in Toilet" as indicated on the PVD. The number of micturitions was defined as the number of times a subject voided in the toilet as indicated on the PVD. The average volume voided per micturition was calculated as the arithmetic mean of all voids for which a subject recorded the volume. 999999=population not analyzed. n=514, 524, 415 (only subjects with evaluable data were analyzed).

|                    |  |  |  |
|--------------------|--|--|--|
| Units: milliliters |  |  |  |
|--------------------|--|--|--|

|  |          |          |          |
|--|----------|----------|----------|
| arithmetic mean  | 999999   | 999999   | 999999   |
| standard deviation   | ± 999999 | ± 999999 | ± 999999 |
| Health-related Quality of Life (HRQL) TS from the OAB-q LF (1-week recall) in all OAB subjects   |          |          |          |
| TS=total score. The OAB-q LF is a validated patient-reported outcome. The 25 questions comprising the subscales of the OAB-q LF ask subjects how much their symptoms have affected their life over the last week. Each question has a response ranging from "None of the time" (=1) to "All of the time" (=6). The raw score (sum of question scores for the 4 subscales [ranging from 25 to 150]) is transformed to a unified score, ranging from 0 to 100. Higher scores correspond to a higher quality of life, and lower scores represent a lower quality of life. n=518, 524, 416 (evaluable subjects).       |          |          |          |
| Units: Units on a scale  |          |          |          |
| arithmetic mean  | 999999   | 999999   | 999999   |
| standard deviation   | ± 999999 | ± 999999 | ± 999999 |
| Symptom Bother Score from the OAB-q LF (1-week recall) in all OAB subjects   |          |          |          |
| The OAB-q LF is a validated patient-reported outcome. The first 8 questions of the OAB-q LF ask subjects how much they were bothered by their bladder symptoms during the previous week. Each question has a response ranging from "Not at all" (=1) to "A very great deal" (=6). These questions make up the symptom bother scale. The raw score (sum of question scores [ranging from 8 to 48]) is transformed to a unified score, ranging from 0 to 100. Higher scores correspond to the symptoms having a larger bother, and lower scores represent a lower amount of bother due to symptoms. n=518, 524, 416. |          |          |          |
| Units: Units on a scale  |          |          |          |
| arithmetic mean  | 999999   | 999999   | 999999   |
| standard deviation   | ± 999999 | ± 999999 | ± 999999 |
| Overall bladder symptoms based on PGI of Severity (PGI-Severity) in all OAB subjects   |          |          |          |
| The Patient Global Impression (PGI) questions are designed to assess a subject's overall impression of OAB. For the PGI-Severity score, subjects are asked to rate their OAB symptoms over the previous week with one of the following responses: 1 = none, 2 = mild, 3 = moderate, 4 = severe. 999999=population not analyzed. n=519, 525, 417 (only subjects with evaluable data were analyzed).   |          |          |          |
| Units: Units on a scale  |          |          |          |
| arithmetic mean  | 999999   | 999999   | 999999   |
| standard deviation   | ± 999999 | ± 999999 | ± 999999 |
| Overall control over bladder symptoms based on PGI of Control (PGI-Control) in all OAB subjects  |          |          |          |
| The PGI questions are designed to assess a subject's overall impression of OAB. For the PGI-Control score, subjects were asked to rate how much control they had over their OAB symptoms over the previous week with one of the following responses: 1 = complete control, 2 = a lot of control, 3 = some control, 4 = only a little control, 5 = no control. 999999=population not analyzed. n=519, 525, 417 (only subjects with evaluable data were analyzed).   |          |          |          |
| Units: Units on a scale  |          |          |          |
| arithmetic mean  | 999999   | 999999   | 999999   |
| standard deviation   | ± 999999 | ± 999999 | ± 999999 |



## End points

### End points reporting groups

|  |  |
|--|--|
| Reporting group title  | Placebo                                |
| Reporting group description:   |  |
| Subjects received matching placebo, orally, once daily for 12 weeks.   |  |
| Reporting group title  | Vibegron 75 mg                         |
| Reporting group description:   |  |
| Subjects received vibegron 75 milligrams (mg), orally, once daily for 12 weeks.  |  |
| Reporting group title  | Tolterodine ER 4 mg                    |
| Reporting group description:   |  |
| Subjects received tolterodine ER 4 mg, orally, once daily for 12 weeks.  |  |
| Subject analysis set title   | Placebo: Full Analysis Set             |
| Subject analysis set type  | Full analysis                          |
| Subject analysis set description:  |  |
| Subjects received matching placebo, orally, once daily for 12 weeks. The Full Analysis Set is defined as all randomized OAB subjects who took at least 1 dose of double-blind study treatment and had at least 1 evaluable change from baseline micturition measurement.   |  |
| Subject analysis set title   | Vibegron 75 mg: Full Analysis Set      |
| Subject analysis set type  | Full analysis                          |
| Subject analysis set description:  |  |
| Subjects received vibegron 75 milligrams (mg), orally, once daily for 12 weeks. The Full Analysis Set is defined as all randomized OAB Subjects who took at least 1 dose of double-blind study treatment and had at least 1 evaluable change from baseline micturition measurement.  |  |
| Subject analysis set title   | Tolterodine ER 4 mg: Full Analysis Set |
| Subject analysis set type  | Full analysis                          |
| Subject analysis set description:  |  |
| Subjects received tolterodine extended release (ER) 4 mg, orally, once daily for 12 weeks. The Full Analysis Set is defined as all randomized OAB subjects who took at least 1 dose of double-blind study treatment and had at least 1 evaluable change from baseline micturition measurement.   |  |
| Subject analysis set title   | Placebo: OAB Wet                       |
| Subject analysis set type  | Full analysis                          |
| Subject analysis set description:  |  |
| Subjects who met the definition of OAB Wet at study entry (based on the PVD) received matching placebo, orally, once daily for 12 weeks. OAB Wet subjects were defined as those with an average of $\geq 8.0$ micturitions per Diary Day; with an average of $\geq 1.0$ UII episodes per Diary Day; and, if stress urinary incontinence was present, with a total number of UII episodes greater than the total number of stress urinary incontinence episodes from the previous visit diary. Analysis was conducted in members of the Full Analysis Set for Incontinence (FAS-I) Population, comprised of all randomized OAB Wet subjects who took at least 1 dose of double-blind study treatment and had at least 1 evaluable change from the Baseline UII measurement. |  |
| Subject analysis set title   | Vibegron 75 mg: OAB Wet                |
| Subject analysis set type  | Full analysis                          |
| Subject analysis set description:  |  |
| Subjects who met the definition of OAB Wet at study entry (based on the PVD) received vibegron 75 milligrams (mg), orally, once daily for 12 weeks. OAB Wet subjects were defined as those with an average of $\geq 8.0$ micturitions per Diary Day; with an average of $\geq 1.0$ UII episodes per Diary Day; and, if stress urinary incontinence was present, with a total number of UII episodes greater than the total number of stress urinary incontinence episodes from the previous visit diary. Analysis was conducted in members of the FAS-I Population, comprised of all randomized OAB Wet subjects who took at least 1 dose of double-blind study treatment and had at least 1 evaluable change from the Baseline UII measurement.                           |  |
| Subject analysis set title   | Tolterodine ER 4 mg: OAB Wet           |
| Subject analysis set type  | Full analysis                          |
| Subject analysis set description:  |  |
| Subjects who met the definition of OAB Wet at study entry (based on the PVD) received tolterodine  |  |

extended release (ER) 4 mg, orally, once daily for 12 weeks. OAB Wet subjects were defined as those with an average of  $\geq 8.0$  micturitions per Diary Day; with an average of  $\geq 1.0$  UUI episodes per Diary Day; and, if stress urinary incontinence was present, with a total number of UUI episodes greater than the total number of stress urinary incontinence episodes from the previous visit diary. Analysis was conducted in members of the FAS-I Population, comprised of all randomized OAB Wet subjects who took at least 1 dose of double-blind study treatment and had at least 1 evaluable change from the Baseline UUI measurement.

### Primary: Change from Baseline (CFB) at Week 12 in the average number of micturitions per 24 hours in all overactive bladder (OAB) subjects

|                 |   |
|-----------------|---|
| End point title | Change from Baseline (CFB) at Week 12 in the average number of micturitions per 24 hours in all overactive bladder (OAB) subjects |
|-----------------|---|

End point description:

A micturition/void is defined as "Urinated in Toilet" as indicated on the PVD. The number of micturitions is defined as the number of times a subject voided in the toilet as indicated on the PVD. The average daily number of micturitions was calculated using the daily entries in the PVD (which was to be completed prior to each study visit) as the total number of micturitions that occurred on a Complete Diary Day (CDD) divided by the number of CDDs in the PVD. CFB was calculated as the post-BL value minus the BL value. "Per 24 hours" corresponds to one Diary Day (i.e., time between when the subject got up for the day each morning and time the subject got up for the day the next morning as recorded in the PVD). Covariates included in the mixed model for repeated measures are study visit (Weeks 2, 4, 8, and 12), OAB type (wet/dry), sex, region (U.S./non-U.S.), BL number of micturitions, and treatment by study visit interaction. FAS=Full Analysis Set.

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

End point timeframe:

Baseline; Week 12

| End point values                    | Placebo: Full Analysis Set | Vibegron 75 mg: Full Analysis Set | Tolterodine ER 4 mg: Full Analysis Set |  |
|-------------------------------------|----------------------------|-----------------------------------|--|--|
| Subject group type                  | Subject analysis set       | Subject analysis set              | Subject analysis set                   |  |
| Number of subjects analysed         | 475 <sup>[1]</sup>         | 492 <sup>[2]</sup>                | 378 <sup>[3]</sup>                     |  |
| Units: micturitions                 |                            |                                   |  |  |
| least squares mean (standard error) | -1.3 ( $\pm$ 0.14)         | -1.8 ( $\pm$ 0.14)                | -1.6 ( $\pm$ 0.15)                     |  |

Notes:

[1] - FAS. Only subjects with evaluable data were analyzed.

[2] - FAS. Only subjects with evaluable data were analyzed.

[3] - FAS. Only subjects with evaluable data were analyzed.

### Statistical analyses

|                            |  |
|----------------------------|--|
| Statistical analysis title | LS Mean Difference: Vibegron 75 mg minus Placebo |
|----------------------------|--|

Statistical analysis description:

LS=least squares

|   |  |
|---|--|
| Comparison groups                       | Vibegron 75 mg: Full Analysis Set v Placebo: Full Analysis Set |
| Number of subjects included in analysis | 967  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | < 0.001 <sup>[4]</sup>   |
| Method                                  | Mixed Model for Repeated Measures (MMRM)                       |
| Parameter estimate                      | Least Squares Mean Difference                                  |
| Point estimate                          | -0.5   |

|                      |                            |
|----------------------|----------------------------|
| Confidence interval  |                            |
| level                | 95 %                       |
| sides                | 2-sided                    |
| lower limit          | -0.8                       |
| upper limit          | -0.2                       |
| Variability estimate | Standard error of the mean |
| Dispersion value     | 0.15                       |

Notes:

[4] - Hypothesis testing was performed for vibegron minus placebo.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | LS Mean Difference: Tolterodine ER minus Placebo                    |
| Comparison groups                       | Placebo: Full Analysis Set v Tolterodine ER 4 mg: Full Analysis Set |
| Number of subjects included in analysis | 853   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority   |
| P-value                                 | = 0.0988 <sup>[5]</sup>   |
| Method                                  | MMRM  |
| Parameter estimate                      | Least Squares Mean Difference                                       |
| Point estimate                          | -0.3  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -0.6  |
| upper limit                             | 0.1   |
| Variability estimate                    | Standard error of the mean  |
| Dispersion value                        | 0.16  |

Notes:

[5] - Comparisons between tolterodine ER and placebo are considered descriptive.

### **Primary: CFB at Week 12 in the average number of urge urinary incontinence (UUI) episodes per 24 hours in OAB Wet subjects**

|                 |   |
|-----------------|---|
| End point title | CFB at Week 12 in the average number of urge urinary incontinence (UUI) episodes per 24 hours in OAB Wet subjects |
|-----------------|---|

End point description:

The number of UUI episodes is defined as the number of times a subject had checked "urge" as the main reason for the leakage in the PVD, regardless of whether more than one reason for leakage in addition to "urge" was checked. The average daily number of UUI episodes was calculated using the daily entries in the PVD (which was to be completed prior to each study visit) as the total number of UUI episodes that occurred on a CDD divided by the number of CCDs in the PVD. CFB was calculated as the post-BL value minus the BL value. "Per 24 hours" corresponds to one Diary Day (i.e., time between when subject got up for the day each morning and time subject got up for the day the next morning as recorded in the PVD). Covariates included in the mixed model for repeated measures were study visit (Weeks 2, 4, 8, and 12), sex, region (U.S./non-U.S.), BL number of UUI episodes and treatment by study visit interaction. FAS-I=Full Analysis Set for Incontinence.

|                      |         |
|----------------------|---------|
| End point type       | Primary |
| End point timeframe: |         |
| Baseline; Week 12    |         |

| End point values                    | Placebo: OAB Wet     | Vibegron 75 mg: OAB Wet | Tolterodine ER 4 mg: OAB Wet |  |
|-------------------------------------|----------------------|-------------------------|------------------------------|--|
| Subject group type                  | Subject analysis set | Subject analysis set    | Subject analysis set         |  |
| Number of subjects analysed         | 372 <sup>[6]</sup>   | 383 <sup>[7]</sup>      | 286 <sup>[8]</sup>           |  |
| Units: UUI episodes                 |                      |                         |                              |  |
| least squares mean (standard error) | -1.4 (± 0.13)        | -2.0 (± 0.13)           | -1.8 (± 0.14)                |  |

Notes:

[6] - FAS-I. Only those subjects with evaluable data were analyzed.

[7] - FAS-I. Only those subjects with evaluable data were analyzed.

[8] - FAS-I. Only those subjects with evaluable data were analyzed.

## Statistical analyses

| Statistical analysis title              | LS Mean Difference: Vibegron 75 mg minus Placebo |
|---|--|
| Comparison groups                       | Placebo: OAB Wet v Vibegron 75 mg: OAB Wet       |
| Number of subjects included in analysis | 755  |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | superiority                                      |
| P-value                                 | < 0.0001 <sup>[9]</sup>                          |
| Method                                  | MMRM   |
| Parameter estimate                      | Least Squares Mean Difference                    |
| Point estimate                          | -0.6   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -0.9   |
| upper limit                             | -0.3   |
| Variability estimate                    | Standard error of the mean                       |
| Dispersion value                        | 0.14   |

Notes:

[9] - Hypothesis testing was performed for vibegron minus placebo.

| Statistical analysis title              | LS Mean Difference: Tolterodine ER minus Placebo |
|---|--|
| Comparison groups                       | Placebo: OAB Wet v Tolterodine ER 4 mg: OAB Wet  |
| Number of subjects included in analysis | 658  |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | superiority                                      |
| P-value                                 | = 0.0123 <sup>[10]</sup>                         |
| Method                                  | MMRM   |
| Parameter estimate                      | Least Squares Mean Difference                    |
| Point estimate                          | -0.4   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -0.7   |
| upper limit                             | -0.1   |
| Variability estimate                    | Standard error of the mean                       |
| Dispersion value                        | 0.15   |

Notes:

[10] - Comparisons between tolterodine ER and placebo are considered descriptive.

## Secondary: CFB at Week 12 in the average number of urgency episodes over 24 hours in all OAB subjects

|                 |  |
|-----------------|--|
| End point title | CFB at Week 12 in the average number of urgency episodes over 24 hours in all OAB subjects |
|-----------------|--|

### End point description:

An urgency episode is defined as the "Need to Urinate Immediately" as indicated on the PVD. CFB is calculated as the post-BL value minus the BL value. "Over 24 hours" corresponds to one Diary Day (i.e., time between when the subject got up for the day each morning and time the subject got up for the day the next morning as recorded in the PVD). Covariates included in the mixed model for repeated measures were study visit (Weeks 2, 4, 8, and 12), OAB type (wet/dry), sex, region (U.S./non-U.S.), BL number of urgency episodes, and treatment by study visit interaction.

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

### End point timeframe:

Baseline; Week 12

| End point values                    | Placebo: Full Analysis Set | Vibegron 75 mg: Full Analysis Set | Tolterodine ER 4 mg: Full Analysis Set |  |
|-------------------------------------|----------------------------|-----------------------------------|--|--|
| Subject group type                  | Subject analysis set       | Subject analysis set              | Subject analysis set                   |  |
| Number of subjects analysed         | 475 <sup>[11]</sup>        | 492 <sup>[12]</sup>               | 378 <sup>[13]</sup>                    |  |
| Units: urgency episodes             |                            |                                   |  |  |
| least squares mean (standard error) | -2.0 (± 0.19)              | -2.7 (± 0.19)                     | -2.5 (± 0.21)                          |  |

### Notes:

[11] - FAS. Only subjects with evaluable data were analyzed.

[12] - FAS. Only subjects with evaluable data were analyzed.

[13] - FAS. Only subjects with evaluable data were analyzed.

## Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | LS Mean Difference: Vibegron 75 mg minus Placebo               |
| Comparison groups                       | Placebo: Full Analysis Set v Vibegron 75 mg: Full Analysis Set |
| Number of subjects included in analysis | 967  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | = 0.002 <sup>[14]</sup>  |
| Method                                  | MMRM   |
| Parameter estimate                      | Least Squares Mean Difference                                  |
| Point estimate                          | -0.7   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -1.1   |
| upper limit                             | -0.2   |
| Variability estimate                    | Standard error of the mean                                     |
| Dispersion value                        | 0.22   |

### Notes:

[14] - Hypothesis testing was performed for vibegron minus placebo.

|                            |   |
|----------------------------|---|
| Statistical analysis title | LS Mean Difference: Tolterodine ER minus Placebo                    |
| Comparison groups          | Placebo: Full Analysis Set v Tolterodine ER 4 mg: Full Analysis Set |

|   |                               |
|---|-------------------------------|
| Number of subjects included in analysis | 853                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | superiority                   |
| P-value                                 | = 0.0648 <sup>[15]</sup>      |
| Method                                  | MMRM                          |
| Parameter estimate                      | Least Squares Mean Difference |
| Point estimate                          | -0.4                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -0.9                          |
| upper limit                             | 0                             |
| Variability estimate                    | Standard error of the mean    |
| Dispersion value                        | 0.23                          |

Notes:

[15] - Comparisons between tolterodine ER and placebo are considered descriptive.

### Secondary: Percentage of OAB Wet subjects with at least a 75% reduction from Baseline in UII episodes per 24 hours at Week 12

|                 |  |
|-----------------|--|
| End point title | Percentage of OAB Wet subjects with at least a 75% reduction from Baseline in UII episodes per 24 hours at Week 12 |
|-----------------|--|

End point description:

The number of UII episodes is defined as the number of times a subject had checked "urge" as the main reason for the leakage in the PVD, regardless of whether more than one reason for leakage in addition to "urge" was checked. The average daily number of UII episodes was calculated using the daily entries in the PVD (which was to be completed prior to each study visit) as the total number of UII episodes that occurred on a CDD divided by the number of CCDs in the PVD. CFB was calculated as the post-BL value minus the BL value. "Per 24 hours" corresponds to one Diary Day (i.e., time between when subject got up for the day each morning and time subject got up for the day the next morning as recorded in the PVD).

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

End point timeframe:

Baseline; Week 12

| End point values              | Placebo: OAB Wet     | Vibegron 75 mg: OAB Wet | Tolterodine ER 4 mg: OAB Wet |  |
|-------------------------------|----------------------|-------------------------|------------------------------|--|
| Subject group type            | Subject analysis set | Subject analysis set    | Subject analysis set         |  |
| Number of subjects analysed   | 405 <sup>[16]</sup>  | 403 <sup>[17]</sup>     | 319 <sup>[18]</sup>          |  |
| Units: percentage of subjects |                      |                         |                              |  |
| number (not applicable)       |                      |                         |                              |  |
| Unadjusted                    | 36.8                 | 52.4                    | 47.6                         |  |
| Adjusted for sex              | 32.8                 | 49.3                    | 42.2                         |  |

Notes:

[16] - FAS-I. The multiple imputation method was used for missing values.

[17] - FAS-I. The multiple imputation method was used for missing values.

[18] - FAS-I. The multiple imputation method was used for missing values.

### Statistical analyses

|                            |  |
|----------------------------|--|
| Statistical analysis title | Difference in Proportion: Vibegron 75 mg:Placebo |
| Comparison groups          | Placebo: OAB Wet v Vibegron 75 mg: OAB Wet       |

|   |                          |
|---|--------------------------|
| Number of subjects included in analysis | 808                      |
| Analysis specification                  | Pre-specified            |
| Analysis type                           | superiority              |
| P-value                                 | < 0.0001 <sup>[19]</sup> |
| Method                                  | Cochran-Mantel-Haenszel  |
| Parameter estimate                      | Difference in proportion |
| Point estimate                          | 16.5                     |
| Confidence interval                     |                          |
| level                                   | 95 %                     |
| sides                                   | 2-sided                  |
| lower limit                             | 9.7                      |
| upper limit                             | 23.4                     |

Notes:

[19] - The Cochran-Mantel-Haenszel risk difference estimate was stratified by sex (female/male), with weights proposed by Greenland and Robins.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Difference in Proportion: Tolterodine ER:Placebo |
| Comparison groups                       | Placebo: OAB Wet v Tolterodine ER 4 mg: OAB Wet  |
| Number of subjects included in analysis | 724  |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | superiority                                      |
| P-value                                 | = 0.012 <sup>[20]</sup>                          |
| Method                                  | Cochran-Mantel-Haenszel                          |
| Parameter estimate                      | Difference in proportion                         |
| Point estimate                          | 9.4  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 2.1  |
| upper limit                             | 16.7   |

Notes:

[20] - The Cochran-Mantel-Haenszel risk difference estimate was stratified by sex (female/male), with weights proposed by Greenland and Robins.

### **Secondary: Percentage of OAB Wet subjects with a 100% reduction from Baseline in UII episodes per 24 hours at Week 12**

|                 |  |
|-----------------|--|
| End point title | Percentage of OAB Wet subjects with a 100% reduction from Baseline in UII episodes per 24 hours at Week 12 |
|-----------------|--|

End point description:

The number of UII episodes is defined as the number of times a subject had checked "urge" as the main reason for the leakage in the PVD, regardless of whether more than one reason for leakage in addition to "urge" was checked. The average daily number of UII episodes was calculated using the daily entries in the PVD (which was to be completed prior to each study visit) as the total number of UII episodes that occurred on a CDD divided by the number of CCDs in the PVD. CFB was calculated as the post-BL value minus the BL value. "Per 24 hours" corresponds to one Diary Day (i.e., time between when subject got up for the day each morning and time subject got up for the day the next morning as recorded in the PVD).

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

End point timeframe:

Baseline; Week 12

| End point values              | Placebo: OAB Wet     | Vibegron 75 mg: OAB Wet | Tolterodine ER 4 mg: OAB Wet |  |
|-------------------------------|----------------------|-------------------------|------------------------------|--|
| Subject group type            | Subject analysis set | Subject analysis set    | Subject analysis set         |  |
| Number of subjects analysed   | 405 <sup>[21]</sup>  | 403 <sup>[22]</sup>     | 319 <sup>[23]</sup>          |  |
| Units: percentage of subjects |                      |                         |                              |  |
| number (not applicable)       |                      |                         |                              |  |
| Unadjusted                    | 22.5                 | 28.8                    | 26.6                         |  |
| Adjusted for sex              | 19.0                 | 25.3                    | 20.9                         |  |

Notes:

[21] - FAS-I. The multiple imputation method was used for missing values.

[22] - FAS-I. The multiple imputation method was used for missing values.

[23] - FAS-I. The multiple imputation method was used for missing values.

## Statistical analyses

| Statistical analysis title              | Difference in Proportion: Vibegron 75 mg:Placebo |
|---|--|
| Comparison groups                       | Placebo: OAB Wet v Vibegron 75 mg: OAB Wet       |
| Number of subjects included in analysis | 808  |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | superiority                                      |
| P-value                                 | = 0.036 <sup>[24]</sup>                          |
| Method                                  | Cochran-Mantel-Haenszel                          |
| Parameter estimate                      | Difference in proportion                         |
| Point estimate                          | 6.3  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 0.4  |
| upper limit                             | 12.1   |

Notes:

[24] - The Cochran-Mantel-Haenszel risk difference estimate was stratified by sex (female/male), with weights proposed by Greenland and Robins.

| Statistical analysis title              | Difference in Proportion: Tolterodine ER:Placebo |
|---|--|
| Comparison groups                       | Placebo: OAB Wet v Tolterodine ER 4 mg: OAB Wet  |
| Number of subjects included in analysis | 724  |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | superiority                                      |
| P-value                                 | = 0.5447 <sup>[25]</sup>                         |
| Method                                  | Cochran-Mantel-Haenszel                          |
| Parameter estimate                      | Difference in proportion                         |
| Point estimate                          | 1.9  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -4.1   |
| upper limit                             | 7.8  |

Notes:

[25] - The Cochran-Mantel-Haenszel risk difference estimate was stratified by sex (female/male), with weights proposed by Greenland and Robins.

## Secondary: Percentage of all OAB subjects with at least a 50% reduction from Baseline in urgency episodes per 24 hours at Week 12



|   |  |
|---|--|
| End point title   | Percentage of all OAB subjects with at least a 50% reduction from Baseline in urgency episodes per 24 hours at Week 12 |
| End point description:  |  |
| An urgency episode is defined as the "Need to Urinate Immediately" as indicated on the PVD. CFB is calculated as the post-BL value minus the BL value. "Per 24 hours" corresponds to one Diary Day (i.e., time between when the subject got up for the day each morning and time the subject got up for the day the next morning as recorded in the PVD). |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Baseline; Week 12   |  |

| End point values              | Placebo: Full Analysis Set | Vibegron 75 mg: Full Analysis Set | Tolterodine ER 4 mg: Full Analysis Set |  |
|-------------------------------|----------------------------|-----------------------------------|--|--|
| Subject group type            | Subject analysis set       | Subject analysis set              | Subject analysis set                   |  |
| Number of subjects analysed   | 520 <sup>[26]</sup>        | 526 <sup>[27]</sup>               | 417 <sup>[28]</sup>                    |  |
| Units: percentage of subjects |                            |                                   |  |  |
| number (not applicable)       |                            |                                   |  |  |
| Unadjusted                    | 38.3                       | 43.2                              | 41.2                                   |  |
| Adjusted for sex              | 32.8                       | 39.5                              | 36.4                                   |  |

Notes:

[26] - FAS. The multiple imputation method was used for missing values.

[27] - FAS. The multiple imputation method was used for missing values.

[28] - FAS. The multiple imputation method was used for missing values.

### Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Difference in Proportion: Vibegron 75 mg:Placebo               |
| Comparison groups                       | Placebo: Full Analysis Set v Vibegron 75 mg: Full Analysis Set |
| Number of subjects included in analysis | 1046   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | = 0.0235 <sup>[29]</sup>                                       |
| Method                                  | Cochran-Mantel-Haenszel  |
| Parameter estimate                      | Difference in proportion                                       |
| Point estimate                          | 6.8  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 0.9  |
| upper limit                             | 12.7   |

Notes:

[29] - The Cochran-Mantel-Haenszel risk difference estimate was stratified by sex and OAB type (wet/dry), with weights proposed by Greenland and Robins.

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | Difference in Proportion: Tolterodine ER:Placebo                    |
| Comparison groups                 | Placebo: Full Analysis Set v Tolterodine ER 4 mg: Full Analysis Set |

|   |                          |
|---|--------------------------|
| Number of subjects included in analysis | 937                      |
| Analysis specification                  | Pre-specified            |
| Analysis type                           | superiority              |
| P-value                                 | = 0.24 <sup>[30]</sup>   |
| Method                                  | Cochran-Mantel-Haenszel  |
| Parameter estimate                      | Difference in proportion |
| Point estimate                          | 3.7                      |
| Confidence interval                     |                          |
| level                                   | 95 %                     |
| sides                                   | 2-sided                  |
| lower limit                             | -2.5                     |
| upper limit                             | 10                       |

Notes:

[30] - The Cochran-Mantel-Haenszel risk difference estimate was stratified by sex and OAB type (wet/dry), with weights proposed by Greenland and Robins.

### Secondary: CFB at Week 12 in the average number of total incontinence episodes over 24 hours in OAB Wet subjects

|                 |   |
|-----------------|---|
| End point title | CFB at Week 12 in the average number of total incontinence episodes over 24 hours in OAB Wet subjects |
|-----------------|---|

End point description:

Total incontinence is defined as having any reason for "Accidental Urine Leakage" and/or "Accidental Urine Leakage" checked, as indicated on the PVD. It is assumed that if the subject recorded a reason for leakage then the accidental urine leakage occurred. CFB is calculated as the post-BL value minus the BL value. "Over 24 hours" corresponds to one Diary Day (i.e., time between when the subject got up for the day each morning and time the subject got up for the day the next morning as recorded in the PVD). Covariates included in the mixed model for repeated measures were study visit (Weeks 2, 4, 8, and 12), sex, region (U.S./non-U.S.), BL number of incontinence episodes, and treatment by study visit interaction.

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

End point timeframe:

Baseline; Week 12

| End point values                    | Placebo: OAB Wet     | Vibegron 75 mg: OAB Wet | Tolterodine ER 4 mg: OAB Wet |  |
|-------------------------------------|----------------------|-------------------------|------------------------------|--|
| Subject group type                  | Subject analysis set | Subject analysis set    | Subject analysis set         |  |
| Number of subjects analysed         | 372 <sup>[31]</sup>  | 383 <sup>[32]</sup>     | 286 <sup>[33]</sup>          |  |
| Units: total incontinence episodes  |                      |                         |                              |  |
| least squares mean (standard error) | -1.6 (± 0.15)        | -2.3 (± 0.15)           | -2.0 (± 0.16)                |  |

Notes:

[31] - FAS-I. Only subjects with evaluable data were analyzed.

[32] - FAS-I. Only subjects with evaluable data were analyzed.

[33] - FAS-I. Only subjects with evaluable data were analyzed.

### Statistical analyses

|                            |  |
|----------------------------|--|
| Statistical analysis title | LS Mean Difference: Vibegron 75 mg minus Placebo |
| Comparison groups          | Placebo: OAB Wet v Vibegron 75 mg: OAB Wet       |

|   |                               |
|---|-------------------------------|
| Number of subjects included in analysis | 755                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | superiority                   |
| P-value                                 | < 0.0001 <sup>[34]</sup>      |
| Method                                  | MMRM                          |
| Parameter estimate                      | Least Squares Mean Difference |
| Point estimate                          | -0.7                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -1                            |
| upper limit                             | -0.4                          |
| Variability estimate                    | Standard error of the mean    |
| Dispersion value                        | 0.16                          |

Notes:

[34] - Hypothesis testing was performed for vibegron minus placebo.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | LS Mean Difference: Tolterodine ER minus Placebo |
| Comparison groups                       | Placebo: OAB Wet v Tolterodine ER 4 mg: OAB Wet  |
| Number of subjects included in analysis | 658  |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | superiority                                      |
| P-value                                 | = 0.0074 <sup>[35]</sup>                         |
| Method                                  | MMRM   |
| Parameter estimate                      | Least Squares Mean Difference                    |
| Point estimate                          | -0.5   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -0.8   |
| upper limit                             | -0.1   |
| Variability estimate                    | Standard error of the mean                       |
| Dispersion value                        | 0.17   |

Notes:

[35] - Comparisons between tolterodine ER and placebo are considered descriptive.

### **Secondary: CFB at Week 12 in the Coping Score from the Overactive Bladder Questionnaire Long Form (OAB-q LF, 1-week recall) in all OAB subjects**

|                 |  |
|-----------------|--|
| End point title | CFB at Week 12 in the Coping Score from the Overactive Bladder Questionnaire Long Form (OAB-q LF, 1-week recall) in all OAB subjects |
|-----------------|--|

End point description:

The OAB-q LF is a validated patient-reported outcome. 8 questions of the OAB-q LF ask subjects how well they have coped with their bladder symptoms during the previous week, as a measure of quality of life (QoL). Each question has a response ranging from "not coping" (= 1) to "coping well" (= 6). These questions make up the coping scale. The raw score (sum of question scores [from 8 to 48]) is transformed to a unified score, from 0 to 100. Higher scores correspond to a higher QoL, and lower scores represent a lower QoL. CFB is calculated as the post-BL value minus the BL value. Covariates included in the MMRM were study visit (Weeks 2, 4, 8, and 12), sex, region (U.S./non-U.S.), OAB type (wet/dry), BL score, and treatment by study visit interaction. If < 50% of items were available, the subscore was regarded as missing; however, if ≥ 50% of items were available, the subscore included missing items imputed as the average of the remaining non-missing items for the subscore.

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

End point timeframe:

Baseline; Week 12

| End point values                    | Placebo: Full Analysis Set | Vibegron 75 mg: Full Analysis Set | Tolterodine ER 4 mg: Full Analysis Set |  |
|-------------------------------------|----------------------------|-----------------------------------|--|--|
| Subject group type                  | Subject analysis set       | Subject analysis set              | Subject analysis set                   |  |
| Number of subjects analysed         | 504 <sup>[36]</sup>        | 512 <sup>[37]</sup>               | 400 <sup>[38]</sup>                    |  |
| Units: units on a scale             |                            |                                   |  |  |
| least squares mean (standard error) | 12.9 ( $\pm$ 1.32)         | 16.5 ( $\pm$ 1.31)                | 16.0 ( $\pm$ 1.39)                     |  |

Notes:

[36] - FAS. Only subjects with evaluable data were analyzed.

[37] - FAS. Only subjects with evaluable data were analyzed.

[38] - FAS. Only subjects with evaluable data were analyzed.

### Statistical analyses

| Statistical analysis title              | LS Mean Difference: Vibegron 75 mg minus Placebo               |
|---|--|
| Comparison groups                       | Placebo: Full Analysis Set v Vibegron 75 mg: Full Analysis Set |
| Number of subjects included in analysis | 1016   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | = 0.0039 <sup>[39]</sup>                                       |
| Method                                  | MMRM   |
| Parameter estimate                      | Least Squares Mean Difference                                  |
| Point estimate                          | 3.6  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 1.2  |
| upper limit                             | 6  |
| Variability estimate                    | Standard error of the mean                                     |
| Dispersion value                        | 1.24   |

Notes:

[39] - Hypothesis testing was performed for vibegron minus placebo.

| Statistical analysis title              | LS Mean Difference: Tolterodine ER minus Placebo                    |
|---|---|
| Comparison groups                       | Placebo: Full Analysis Set v Tolterodine ER 4 mg: Full Analysis Set |
| Number of subjects included in analysis | 904   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority   |
| P-value                                 | = 0.021 <sup>[40]</sup>   |
| Method                                  | MMRM  |
| Parameter estimate                      | Least Squares Mean Difference                                       |
| Point estimate                          | 3.1   |

|                      |                            |
|----------------------|----------------------------|
| Confidence interval  |                            |
| level                | 95 %                       |
| sides                | 2-sided                    |
| lower limit          | 0.5                        |
| upper limit          | 5.7                        |
| Variability estimate | Standard error of the mean |
| Dispersion value     | 1.32                       |

Notes:

[40] - Comparisons between tolterodine ER and placebo are considered descriptive.

## Secondary: CFB at Week 12 in the average volume voided per micturition in all OAB subjects

|                 |   |
|-----------------|---|
| End point title | CFB at Week 12 in the average volume voided per micturition in all OAB subjects |
|-----------------|---|

End point description:

A micturition/void is defined as "Urinated in Toilet" as indicated on the PVD. The number of micturitions is defined as the number of times a subject voided in the toilet as indicated on the PVD. CFB is calculated as the post-BL value minus the BL value. Covariates included in the mixed model for repeated measures were study visit (Weeks 2, 4, 8, and 12), OAB type (wet/dry), sex, region (U.S./non-U.S.), BL volume (milliliters [mL]), and treatment by study visit interaction.

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

End point timeframe:

Baseline; Week 12

| End point values                    | Placebo: Full Analysis Set | Vibegron 75 mg: Full Analysis Set | Tolterodine ER 4 mg: Full Analysis Set |  |
|-------------------------------------|----------------------------|-----------------------------------|--|--|
| Subject group type                  | Subject analysis set       | Subject analysis set              | Subject analysis set                   |  |
| Number of subjects analysed         | 478 <sup>[41]</sup>        | 490 <sup>[42]</sup>               | 375 <sup>[43]</sup>                    |  |
| Units: mL                           |                            |                                   |  |  |
| least squares mean (standard error) | 2.2 (± 3.28)               | 23.5 (± 3.26)                     | 15.5 (± 3.52)                          |  |

Notes:

[41] - FAS. Only subjects with evaluable data were analyzed.

[42] - FAS. Only subjects with evaluable data were analyzed.

[43] - FAS. Only subjects with evaluable data were analyzed.

## Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | LS Mean Difference: Vibegron 75 mg minus Placebo               |
| Comparison groups                       | Placebo: Full Analysis Set v Vibegron 75 mg: Full Analysis Set |
| Number of subjects included in analysis | 968  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | < 0.0001 <sup>[44]</sup>                                       |
| Method                                  | MMRM   |
| Parameter estimate                      | Least Squares Mean Difference                                  |
| Point estimate                          | 21.2   |

|                      |                            |
|----------------------|----------------------------|
| Confidence interval  |                            |
| level                | 95 %                       |
| sides                | 2-sided                    |
| lower limit          | 14.3                       |
| upper limit          | 28.1                       |
| Variability estimate | Standard error of the mean |
| Dispersion value     | 3.52                       |

Notes:

[44] - Hypothesis testing was performed for vibegron minus placebo.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | LS Mean Difference: Tolterodine ER minus Placebo                    |
| Comparison groups                       | Placebo: Full Analysis Set v Tolterodine ER 4 mg: Full Analysis Set |
| Number of subjects included in analysis | 853   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority   |
| P-value                                 | < 0.001 <sup>[45]</sup>   |
| Method                                  | MMRM  |
| Parameter estimate                      | Least Squares Mean Difference                                       |
| Point estimate                          | 13.3  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 5.9   |
| upper limit                             | 20.7  |
| Variability estimate                    | Standard error of the mean  |
| Dispersion value                        | 3.76  |

Notes:

[45] - Comparisons between tolterodine ER and placebo are considered descriptive.

### **Secondary: CFB at Week 12 in the Health-related Quality of Life (HRQL) Total Score from the OAB-q LF (1-week recall) in all OAB subjects**

|                 |   |
|-----------------|---|
| End point title | CFB at Week 12 in the Health-related Quality of Life (HRQL) Total Score from the OAB-q LF (1-week recall) in all OAB subjects |
|-----------------|---|

End point description:

The OAB-q LF is a validated patient-reported outcome. The 25 questions comprising the Coping, Concern, Sleep and Social Interaction subscales of the OAB-q LF ask subjects how much their symptoms have affected their life over the last week. Each question has a response ranging from "None of the time" (= 1) to "All of the time" (= 6). The raw score (sum of question scores for the 4 subscales [ranging from 25 to 150]) is transformed to a unified score, ranging from 0 to 100. Higher scores correspond to a higher quality of life, and lower scores represent a lower quality of life. CFB is calculated as the post-BL value minus the BL value. Covariates included in the mixed model for repeated measures were study visit (Weeks 2, 4, 8, and 12), sex, region (U.S./non-U.S.), OAB type (wet/dry), BL score, and treatment by study visit interaction. If < 50% of items were available, the subscore (SS) was regarded as missing; if ≥ 50% of items were available, the SS included missing items for SS.

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

End point timeframe:

Baseline; Week 12

| End point values                    | Placebo: Full Analysis Set | Vibegron 75 mg: Full Analysis Set | Tolterodine ER 4 mg: Full Analysis Set |  |
|-------------------------------------|----------------------------|-----------------------------------|--|--|
| Subject group type                  | Subject analysis set       | Subject analysis set              | Subject analysis set                   |  |
| Number of subjects analysed         | 504 <sup>[46]</sup>        | 512 <sup>[47]</sup>               | 400 <sup>[48]</sup>                    |  |
| Units: units on a scale             |                            |                                   |  |  |
| least squares mean (standard error) | 10.8 (± 1.13)              | 14.6 (± 1.12)                     | 13.7 (± 1.19)                          |  |

Notes:

[46] - FAS. Only subjects with evaluable data were analyzed.

[47] - FAS. Only subjects with evaluable data were analyzed.

[48] - FAS. Only subjects with evaluable data were analyzed.

## Statistical analyses

| Statistical analysis title              | LS Mean Difference: Vibegron 75 mg minus Placebo               |
|---|--|
| Comparison groups                       | Placebo: Full Analysis Set v Vibegron 75 mg: Full Analysis Set |
| Number of subjects included in analysis | 1016   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | < 0.001 <sup>[49]</sup>  |
| Method                                  | MMRM   |
| Parameter estimate                      | Least Squares Mean Difference                                  |
| Point estimate                          | 3.8  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 1.7  |
| upper limit                             | 5.8  |
| Variability estimate                    | Standard error of the mean                                     |
| Dispersion value                        | 1.06   |

Notes:

[49] - Hypothesis testing was performed for vibegron minus placebo.

| Statistical analysis title              | LS Mean Difference: Tolterodine ER minus Placebo                    |
|---|---|
| Comparison groups                       | Placebo: Full Analysis Set v Tolterodine ER 4 mg: Full Analysis Set |
| Number of subjects included in analysis | 904   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority   |
| P-value                                 | = 0.0114  |
| Method                                  | MMRM  |
| Parameter estimate                      | Least Squares Mean Difference                                       |
| Point estimate                          | 2.9   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 0.6   |
| upper limit                             | 5.1   |
| Variability estimate                    | Standard error of the mean  |
| Dispersion value                        | 1.13  |

## Secondary: CFB at Week 12 in the Symptom Bother Score from the OAB-q LF (1-week recall) in all OAB subjects

|                 |  |
|-----------------|--|
| End point title | CFB at Week 12 in the Symptom Bother Score from the OAB-q LF (1-week recall) in all OAB subjects |
|-----------------|--|

### End point description:

The OAB-q LF is a validated patient-reported outcome. The first 8 questions of the OAB-q LF ask subjects how much they were bothered by their bladder symptoms during the previous week. Each question has a response ranging from "Not at all" (= 1) to "A very great deal" (= 6). These questions make up the symptom bother scale. The raw score (sum of question scores [from 8 to 48]) is transformed to a unified score, from 0 to 100. Higher scores correspond to the symptoms having a larger bother, and lower scores represent a lower amount of bother due to symptoms. CFB is calculated as the post-BL value minus the BL value. Covariates included in the MMRM were study visit (Weeks 2, 4, 8, and 12), sex, region (U.S./non-U.S.), OAB type (wet/dry), BL score, and treatment by study visit interaction. If < 50% of items were available, the SS was regarded as missing; if ≥ 50% of items were available, the SS included missing items imputed as the average of the remaining non-missing items for SS.

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

### End point timeframe:

Baseline; Week 12

| End point values                    | Placebo: Full Analysis Set | Vibegron 75 mg: Full Analysis Set | Tolterodine ER 4 mg: Full Analysis Set |  |
|-------------------------------------|----------------------------|-----------------------------------|--|--|
| Subject group type                  | Subject analysis set       | Subject analysis set              | Subject analysis set                   |  |
| Number of subjects analysed         | 504 <sup>[50]</sup>        | 512 <sup>[51]</sup>               | 400 <sup>[52]</sup>                    |  |
| Units: units on a scale             |                            |                                   |  |  |
| least squares mean (standard error) | -12.8 (± 1.25)             | -19.6 (± 1.24)                    | -17.4 (± 1.31)                         |  |

### Notes:

[50] - FAS. Only subjects with evaluable data were analyzed.

[51] - FAS. Only subjects with evaluable data were analyzed.

[52] - FAS. Only subjects with evaluable data were analyzed.

## Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | LS Mean Difference: Vibegron 75 mg minus Placebo               |
| Comparison groups                       | Placebo: Full Analysis Set v Vibegron 75 mg: Full Analysis Set |
| Number of subjects included in analysis | 1016   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | < 0.0001 <sup>[53]</sup>                                       |
| Method                                  | MMRM   |
| Parameter estimate                      | Least Squares Mean Difference                                  |
| Point estimate                          | -6.9   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -9.2   |
| upper limit                             | -4.6   |



|                      |                            |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value     | 1.17                       |

Notes:

[53] - Hypothesis testing was performed for vibegron minus placebo.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | LS Mean Difference: Tolterodine ER minus Placebo                    |
| Comparison groups                       | Placebo: Full Analysis Set v Tolterodine ER 4 mg: Full Analysis Set |
| Number of subjects included in analysis | 904   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority   |
| P-value                                 | < 0.001 <sup>[54]</sup>   |
| Method                                  | MMRM  |
| Parameter estimate                      | Least Squares Mean Difference                                       |
| Point estimate                          | -4.6  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -7.1  |
| upper limit                             | -2.2  |
| Variability estimate                    | Standard error of the mean  |
| Dispersion value                        | 1.25  |

Notes:

[54] - Comparisons between tolterodine ER and placebo are considered descriptive.

### Secondary: Percentage of all OAB subjects with an average number of micturitions < 8 per 24 hours at Week 12

|                 |   |
|-----------------|---|
| End point title | Percentage of all OAB subjects with an average number of micturitions < 8 per 24 hours at Week 12 |
|-----------------|---|

End point description:

A micturition/void is defined as "Urinated in Toilet" as indicated on the PVD. The number of micturitions is defined as the number of times a subject voided in the toilet as indicated on the PVD. A subject was defined as having an average of < 8 daily micturitions if the arithmetic mean of the number of micturitions per day in the PVD was less than 8 . "Per 24 hours" corresponds to one Diary Day (i.e., time between when the subject got up for the day each morning and time the subject got up for the day the next morning as recorded in the PVD).

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

End point timeframe:

Week 12

| End point values              | Placebo: Full Analysis Set | Vibegron 75 mg: Full Analysis Set | Tolterodine ER 4 mg: Full Analysis Set |  |
|-------------------------------|----------------------------|-----------------------------------|--|--|
| Subject group type            | Subject analysis set       | Subject analysis set              | Subject analysis set                   |  |
| Number of subjects analysed   | 520 <sup>[55]</sup>        | 526 <sup>[56]</sup>               | 417 <sup>[57]</sup>                    |  |
| Units: percentage of subjects |                            |                                   |  |  |
| number (not applicable)       |                            |                                   |  |  |
| Unadjusted                    | 28.7                       | 40.1                              | 35.0                                   |  |
| Adjusted for sex              | 24.8                       | 37.2                              | 31.6                                   |  |

Notes:

[55] - FAS

[56] - FAS

[57] - FAS

## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Difference in Proportion: Vibegron 75 mg:Placebo               |
| Comparison groups                       | Placebo: Full Analysis Set v Vibegron 75 mg: Full Analysis Set |
| Number of subjects included in analysis | 1046   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | < 0.0001 <sup>[58]</sup>                                       |
| Method                                  | Cochran-Mantel-Haenszel  |
| Parameter estimate                      | Difference in proportion                                       |
| Point estimate                          | 12.4   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 6.7  |
| upper limit                             | 18.1   |

Notes:

[58] - The Cochran-Mantel-Haenszel (CMH) risk difference estimate was stratified by OAB type (wet/dry) and sex (female/male), with weights proposed by Greenland and Robins.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference in Proportion: Tolterodine ER:Placebo                    |
| Comparison groups                       | Placebo: Full Analysis Set v Tolterodine ER 4 mg: Full Analysis Set |
| Number of subjects included in analysis | 937   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority   |
| P-value                                 | = 0.0236 <sup>[59]</sup>  |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Difference in proportion  |
| Point estimate                          | 6.9   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 0.9   |
| upper limit                             | 12.8  |

Notes:

[59] - The Cochran-Mantel-Haenszel (CMH) risk difference estimate was stratified by OAB type (wet/dry) and sex (female/male), with weights proposed by Greenland and Robins.

## Secondary: Percentage of OAB Wet subjects with at least a 50% reduction from Baseline in total incontinence episodes per 24 hours at Week 12

|                 |   |
|-----------------|---|
| End point title | Percentage of OAB Wet subjects with at least a 50% reduction from Baseline in total incontinence episodes per 24 hours at Week 12 |
|-----------------|---|

End point description:

Total incontinence is defined as having any reason for "Accidental Urine Leakage" and/or "Accidental Urine Leakage" checked, as indicated on the PVD. It is assumed that if the subject recorded a reason for leakage then the accidental urine leakage occurred. All events marked as having leakage, regardless of

cause, or where "Accidental Leakage" was checked, were used in the analysis. "Per 24 hours" corresponds to one Diary Day (i.e., time between when the subject got up for the day each morning and time the subject got up for the day the next morning as recorded in the PVD. The multiple imputation method was used for missing values.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline; Week 12    |           |

| End point values              | Placebo: OAB Wet     | Vibegron 75 mg: OAB Wet | Tolterodine ER 4 mg: OAB Wet |  |
|-------------------------------|----------------------|-------------------------|------------------------------|--|
| Subject group type            | Subject analysis set | Subject analysis set    | Subject analysis set         |  |
| Number of subjects analysed   | 405 <sup>[60]</sup>  | 403 <sup>[61]</sup>     | 319 <sup>[62]</sup>          |  |
| Units: percentage of subjects |                      |                         |                              |  |
| number (not applicable)       |                      |                         |                              |  |
| Unadjusted                    | 53.8                 | 64.0                    | 66.5                         |  |
| Adjusted for sex              | 49.9                 | 61.6                    | 61.5                         |  |

Notes:

[60] - FAS-I. Only subjects with evaluable data were analyzed.

[61] - FAS-I. Only subjects with evaluable data were analyzed.

[62] - FAS-I. Only subjects with evaluable data were analyzed.

## Statistical analyses

| Statistical analysis title              | Difference in Proportion: Vibegron 75 mg:Placebo |
|---|--|
| Comparison groups                       | Vibegron 75 mg: OAB Wet v Placebo: OAB Wet       |
| Number of subjects included in analysis | 808  |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | superiority                                      |
| P-value                                 | < 0.001 <sup>[63]</sup>                          |
| Method                                  | Cochran-Mantel-Haenszel                          |
| Parameter estimate                      | Difference in proportion                         |
| Point estimate                          | 11.7   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 4.7  |
| upper limit                             | 18.6   |

Notes:

[63] - The Cochran-Mantel-Haenszel risk difference estimate was stratified by sex (female/male), with weights proposed by Greenland and Robins.

| Statistical analysis title              | Difference in Proportion: Tolterodine ER:Placebo |
|---|--|
| Comparison groups                       | Placebo: OAB Wet v Tolterodine ER 4 mg: OAB Wet  |
| Number of subjects included in analysis | 724  |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | superiority                                      |
| P-value                                 | = 0.0022 <sup>[64]</sup>                         |
| Method                                  | Cochran-Mantel-Haenszel                          |
| Parameter estimate                      | Difference in proportion                         |
| Point estimate                          | 11.5   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 4.2     |
| upper limit         | 18.9    |

Notes:

[64] - The Cochran-Mantel-Haenszel risk difference estimate was stratified by sex (female/male), with weights proposed by Greenland and Robins.

### Secondary: CFB at Week 12 in overall bladder symptoms based on Patient Global Impression of Severity (PGI-Severity) in all OAB subjects

|                 |  |
|-----------------|--|
| End point title | CFB at Week 12 in overall bladder symptoms based on Patient Global Impression of Severity (PGI-Severity) in all OAB subjects |
|-----------------|--|

End point description:

The Patient Global Impression (PGI) questions are designed to assess a subject's overall impression of OAB. For the PGI-Severity score, subjects are asked to rate their OAB symptoms over the previous week with one of the following responses: 1 = none, 2 = mild, 3 = moderate, 4 = severe. CFB is calculated as the post-BL value minus the BL value. Covariates included in the mixed model for repeated measures were study visit (Weeks 2, 4, 8, and 12), OAB type (wet/dry), sex, region (U.S./non-U.S.), BL score, and treatment by study visit interaction.

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

End point timeframe:

Baseline; Week 12

| End point values                    | Placebo: Full Analysis Set | Vibegron 75 mg: Full Analysis Set | Tolterodine ER 4 mg: Full Analysis Set |  |
|-------------------------------------|----------------------------|-----------------------------------|--|--|
| Subject group type                  | Subject analysis set       | Subject analysis set              | Subject analysis set                   |  |
| Number of subjects analysed         | 484 <sup>[65]</sup>        | 494 <sup>[66]</sup>               | 382 <sup>[67]</sup>                    |  |
| Units: units on a scale             |                            |                                   |  |  |
| least squares mean (standard error) | -0.5 (± 0.04)              | -0.8 (± 0.04)                     | -0.7 (± 0.04)                          |  |

Notes:

[65] - FAS. Only subjects with evaluable data were analyzed.

[66] - FAS. Only subjects with evaluable data were analyzed.

[67] - FAS. Only subjects with evaluable data were analyzed.

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | LS Mean Difference: Vibegron 75 mg minus Placebo               |
| Comparison groups                       | Placebo: Full Analysis Set v Vibegron 75 mg: Full Analysis Set |
| Number of subjects included in analysis | 978  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | < 0.0001 <sup>[68]</sup>                                       |
| Method                                  | MMRM   |
| Parameter estimate                      | Least Squares Mean Difference                                  |
| Point estimate                          | -0.2   |

|                      |                            |
|----------------------|----------------------------|
| Confidence interval  |                            |
| level                | 95 %                       |
| sides                | 2-sided                    |
| lower limit          | -0.3                       |
| upper limit          | -0.1                       |
| Variability estimate | Standard error of the mean |
| Dispersion value     | 0.04                       |

Notes:

[68] - Hypothesis testing was performed for vibegron minus placebo.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | LS Mean Difference: Tolterodine ER minus Placebo                    |
| Comparison groups                       | Placebo: Full Analysis Set v Tolterodine ER 4 mg: Full Analysis Set |
| Number of subjects included in analysis | 866   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority   |
| P-value                                 | = 0.0055 <sup>[69]</sup>  |
| Method                                  | MMRM  |
| Parameter estimate                      | Least Squares Mean Difference                                       |
| Point estimate                          | -0.1  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -0.2  |
| upper limit                             | 0   |
| Variability estimate                    | Standard error of the mean  |
| Dispersion value                        | 0.05  |

Notes:

[69] - Hypothesis testing was performed for vibegron minus placebo.

### **Secondary: CFB at Week 12 in overall control over bladder symptoms based on Patient Global Impression of Control (PGI-Control) in all OAB subjects**

|                 |   |
|-----------------|---|
| End point title | CFB at Week 12 in overall control over bladder symptoms based on Patient Global Impression of Control (PGI-Control) in all OAB subjects |
|-----------------|---|

End point description:

The Patient Global Impression (PGI) questions are designed to assess a subject's overall impression of OAB. For the PGI-Control score, subjects were asked to rate how much control they had over their OAB symptoms over the previous week with one of the following responses: 1 = complete control, 2 = a lot of control, 3 = some control, 4 = only a little control, 5 = no control. CFB is calculated as the post-BL value minus the BL value. Covariates included in the mixed model for repeated measures were study visit (Weeks 2, 4, 8, and 12), OAB type (wet/dry), sex, region (U.S./non-U.S.), BL score, and treatment by study visit interaction.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline; Week 12    |           |

| End point values                    | Placebo: Full Analysis Set | Vibegron 75 mg: Full Analysis Set | Tolterodine ER 4 mg: Full Analysis Set |  |
|-------------------------------------|----------------------------|-----------------------------------|--|--|
| Subject group type                  | Subject analysis set       | Subject analysis set              | Subject analysis set                   |  |
| Number of subjects analysed         | 484 <sup>[70]</sup>        | 494 <sup>[71]</sup>               | 382 <sup>[72]</sup>                    |  |
| Units: units on a scale             |                            |                                   |  |  |
| least squares mean (standard error) | -0.7 (± 0.05)              | -1.0 (± 0.05)                     | -0.9 (± 0.05)                          |  |

Notes:

[70] - FAS. Only subjects with evaluable data were analyzed.

[71] - FAS. Only subjects with evaluable data were analyzed.

[72] - FAS. Only subjects with evaluable data were analyzed.

## Statistical analyses

| Statistical analysis title              | LS Mean Difference: Vibegron 75 mg minus Placebo               |
|---|--|
| Comparison groups                       | Placebo: Full Analysis Set v Vibegron 75 mg: Full Analysis Set |
| Number of subjects included in analysis | 978  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | < 0.0001 <sup>[73]</sup>                                       |
| Method                                  | MMRM   |
| Parameter estimate                      | Least Squares Mean Difference                                  |
| Point estimate                          | -0.3   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -0.4   |
| upper limit                             | -0.2   |
| Variability estimate                    | Standard error of the mean                                     |
| Dispersion value                        | 0.05   |

Notes:

[73] - Hypothesis testing was performed for vibegron minus placebo.

| Statistical analysis title              | LS Mean Difference: Tolterodine ER minus Placebo                    |
|---|---|
| Comparison groups                       | Placebo: Full Analysis Set v Tolterodine ER 4 mg: Full Analysis Set |
| Number of subjects included in analysis | 866   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority   |
| P-value                                 | < 0.001 <sup>[74]</sup>   |
| Method                                  | MMRM  |
| Parameter estimate                      | Least Squares Mean Difference                                       |
| Point estimate                          | -0.2  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -0.3  |
| upper limit                             | -0.1  |
| Variability estimate                    | Standard error of the mean  |
| Dispersion value                        | 0.06  |

---

Notes:

[74] - Comparisons between tolterodine ER and placebo are considered descriptive.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

from the time the subject provided informed consent to participate in the study at the Screening Visit until completion of the Follow-up Visit (up to Day 113 or Early Withdrawal plus 28 days)

Adverse event reporting additional description:

Treatment-emergent adverse events were collected in members of the Safety Set, comprised of all subjects who received at least 1 dose of study treatment. Subjects were included in the treatment group corresponding to the study treatment they actually received for the analysis of safety data.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | Vibegron 75 mg |
|-----------------------|----------------|

Reporting group description:

Subjects received vibegron 75 milligrams (mg), orally, once daily for 12 weeks.

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects received matching placebo, orally, once daily for 12 weeks.

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Tolterodine ER 4 mg |
|-----------------------|---------------------|

Reporting group description:

Subjects received tolterodine extended release (ER) 4 mg, orally, once daily for 12 weeks.

| Serious adverse events  | Vibegron 75 mg  | Placebo         | Tolterodine ER 4 mg |
|---|-----------------|-----------------|---------------------|
| Total subjects affected by serious adverse events                   |                 |                 |                     |
| subjects affected / exposed   | 8 / 545 (1.47%) | 6 / 540 (1.11%) | 10 / 430 (2.33%)    |
| number of deaths (all causes)                                       | 0               | 0               | 1                   |
| number of deaths resulting from adverse events                      | 0               | 0               | 0                   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                 |                     |
| Cholangiocarcinoma  |                 |                 |                     |
| subjects affected / exposed   | 0 / 545 (0.00%) | 1 / 540 (0.19%) | 0 / 430 (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               |
| Colorectal adenocarcinoma   |                 |                 |                     |
| subjects affected / exposed   | 1 / 545 (0.18%) | 0 / 540 (0.00%) | 0 / 430 (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               |
| Ovarian adenoma   |                 |                 |                     |



|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed                          | 0 / 545 (0.00%) | 0 / 540 (0.00%) | 1 / 430 (0.23%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Prostate cancer                                      |                 |                 |                 |
| subjects affected / exposed                          | 0 / 545 (0.00%) | 0 / 540 (0.00%) | 1 / 430 (0.23%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Vascular disorders                                   |                 |                 |                 |
| Hypotension  |                 |                 |                 |
| subjects affected / exposed                          | 0 / 545 (0.00%) | 1 / 540 (0.19%) | 0 / 430 (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 |                 |                 |                 |
| Chest pain   |                 |                 |                 |
| subjects affected / exposed                          | 0 / 545 (0.00%) | 1 / 540 (0.19%) | 0 / 430 (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           |
| Non-cardiac chest pain                               |                 |                 |                 |
| subjects affected / exposed                          | 1 / 545 (0.18%) | 0 / 540 (0.00%) | 0 / 430 (0.00%) |
| occurrences causally related to treatment / all      | 1 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders      |                 |                 |                 |
| Dyspnoea   |                 |                 |                 |
| subjects affected / exposed                          | 0 / 545 (0.00%) | 0 / 540 (0.00%) | 1 / 430 (0.23%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Pleural effusion                                     |                 |                 |                 |
| subjects affected / exposed                          | 1 / 545 (0.18%) | 0 / 540 (0.00%) | 0 / 430 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Pneumonia aspiration                                 |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 545 (0.00%) | 0 / 540 (0.00%) | 1 / 430 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Psychiatric disorders                           |                 |                 |                 |
| Depression                                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 0 / 540 (0.00%) | 1 / 430 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Panic attack                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 0 / 540 (0.00%) | 1 / 430 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Investigations                                  |                 |                 |                 |
| Ejection fraction decreased                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 1 / 540 (0.19%) | 0 / 430 (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           |
| Injury, poisoning and procedural complications  |                 |                 |                 |
| Post procedural complication                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 0 / 540 (0.00%) | 1 / 430 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Rib fracture                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 1 / 540 (0.19%) | 0 / 430 (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                               |                 |                 |                 |
| Aortic valve incompetence                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 1 / 540 (0.19%) | 0 / 430 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Atrial fibrillation                             |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 545 (0.18%) | 0 / 540 (0.00%) | 0 / 430 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac failure congestive                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 545 (0.18%) | 0 / 540 (0.00%) | 0 / 430 (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           |
| Coronary artery stenosis                        |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 1 / 540 (0.19%) | 0 / 430 (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                        |                 |                 |                 |
| Cerebrovascular accident                        |                 |                 |                 |
| subjects affected / exposed                     | 1 / 545 (0.18%) | 0 / 540 (0.00%) | 1 / 430 (0.23%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| Encephalopathy                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 0 / 540 (0.00%) | 1 / 430 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Loss of consciousness                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 0 / 540 (0.00%) | 1 / 430 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Syncope   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 0 / 540 (0.00%) | 1 / 430 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Ear and labyrinth disorders                     |                 |                 |                 |
| Vertigo positional                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 0 / 540 (0.00%) | 1 / 430 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Abdominal pain                                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 545 (0.18%) | 0 / 540 (0.00%) | 0 / 430 (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           |
| Appendix disorder                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 545 (0.18%) | 0 / 540 (0.00%) | 0 / 430 (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           |
| Colitis   |                 |                 |                 |
| subjects affected / exposed                     | 1 / 545 (0.18%) | 0 / 540 (0.00%) | 0 / 430 (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           |
| Rectal haemorrhage                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 1 / 540 (0.19%) | 0 / 430 (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           |
| Hepatobiliary disorders                         |                 |                 |                 |
| Cholelithiasis                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 1 / 540 (0.19%) | 0 / 430 (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 |                 |                 |                 |
| Muscular weakness                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 0 / 540 (0.00%) | 1 / 430 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| Pneumonia                                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 545 (0.18%) | 1 / 540 (0.19%) | 0 / 430 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Sepsis  |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 545 (0.00%) | 0 / 540 (0.00%) | 1 / 430 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| Urinary tract infection                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 0 / 540 (0.00%) | 1 / 430 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| Metabolism and nutrition disorders              |                 |                 |                 |
| Dehydration                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 1 / 540 (0.19%) | 0 / 430 (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           |
| Lactic acidosis                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 545 (0.00%) | 1 / 540 (0.19%) | 0 / 430 (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 %

| <b>Non-serious adverse events</b>                     | Vibegron 75 mg   | Placebo          | Tolterodine ER 4 mg |
|---|------------------|------------------|---------------------|
| Total subjects affected by non-serious adverse events |                  |                  |                     |
| subjects affected / exposed                           | 36 / 545 (6.61%) | 38 / 540 (7.04%) | 50 / 430 (11.63%)   |
| Gastrointestinal disorders                            |                  |                  |                     |
| Dry mouth   |                  |                  |                     |
| subjects affected / exposed                           | 9 / 545 (1.65%)  | 5 / 540 (0.93%)  | 28 / 430 (6.51%)    |
| occurrences (all)                                     | 9                | 5                | 29                  |
| Infections and infestations                           |                  |                  |                     |
| Urinary tract infection                               |                  |                  |                     |
| subjects affected / exposed                           | 27 / 545 (4.95%) | 33 / 540 (6.11%) | 24 / 430 (5.58%)    |
| occurrences (all)                                     | 32               | 36               | 28                  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 05 October 2017  | <ul style="list-style-type: none"><li>- Changes were made to description of contraception requirements and methods for female subject.</li><li>- Plan to use a paper diary as backup was added.</li></ul>  |
| 01 November 2017 | <ul style="list-style-type: none"><li>- Inclusion and exclusion criterion were updated.</li><li>- A note that paper diaries may be used was added.</li><li>- Clarification that pelvic examinations may be part of the physical examination and clarification that urinalysis was to be performed if there was a positive dipstick result was made.</li><li>- Follicle-stimulating hormone was removed from clinical laboratory test performed.</li><li>- The timing for collection of paper diaries (if used) was added.</li><li>- References to the Week 2 time point as a visit were reworded to clarify that a study visit does not occur at Week 2.</li><li>- "Tablet" or "capsule" descriptors were added.</li><li>- Wording was added to indicate the study treatment should be swallowed whole.</li><li>- Wording was added to require a witnessed dose at the clinic at Run-In and Baseline Visits.</li><li>- Pharmacokinetic (PK) sub-study language was changed.</li><li>- Dispense study medication was language was combined.</li><li>- Clarified that tablet/capsule count was to be recorded in the interactive voice or web response system rather than case report form.</li><li>- Added adverse events suggestive of cystitis or urinary tract infection and moved liver test values to end of list.</li></ul> |
| 30 January 2018  | <ul style="list-style-type: none"><li>- Addition of exploratory efficacy endpoints</li><li>- Change of 5% in response efficacy endpoint</li><li>- Change in statistical analysis from Last Observation Carried Forward to multiple imputation; subgroup analyses to include primary mixed model for repeated measure analysis model with a subgroup by treatment interaction term.</li><li>- Updated Schedule of Activities and visit events</li><li>- Updated language around timing of data collection for adverse events (AEs) and serious adverse events.</li><li>- Changed days of screening compliance</li><li>- Replaced "discontinued" with "interrupted"</li><li>- Removed study medication rechallenge in subjects with a grade 3 or higher drug-related AE reported</li><li>- Updated Patient Voiding Diary and Urine Volume Collection instructions, training, and description</li><li>- Updated instructions on Reminders for Diary Collection</li><li>- Updated Electronic Diary instructions and training</li><li>- Deletion of data collection of food/meal intake prior to PK sampling</li><li>- Updated Major Adverse Cardiac and Cerebrovascular Events language to match clinical adjudication committee Charter</li><li>- Addition of time frame around pregnancy and infant outcome</li></ul>              |
| 12 February 2018 | Minor typographical/formatting errors were corrected.  |

|                  |  |
|------------------|--|
| 15 November 2018 | <ul style="list-style-type: none"> <li>- The key secondary efficacy endpoints were reordered, and key/other secondary efficacy endpoints were added and removed.</li> <li>- Exploratory endpoints were reordered and analysis timepoints were updated for some endpoints.</li> <li>- Exploratory endpoints were added and removed.</li> <li>- Removed language indicating that AEs from time of informed consent to first dose of study treatment should be recorded as medical history.</li> <li>- One objective/hypothesis was added, four key secondary objectives/hypotheses were deleted, and the objectives/hypotheses were reordered and renumbered accordingly.</li> </ul> |
|------------------|--|

Notes:

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## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported