



Clinical trial results:

A Phase IIb Randomized, Placebo- and Active Comparator (Tolterodine)-Controlled, 2-Part Clinical Study of the Efficacy and Safety of MK-4618 in Patients with Overactive Bladder

A 52-week Extension to: A Phase IIb Randomized, Placebo- and Active Comparator (Tolterodine)-Controlled, 2-Part Clinical Study of the Efficacy and Safety of MK-4618 in Patients with Overactive Bladder

Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2010-022121-15 |
| Trial protocol | SE DE GB DK AT NO PL IT |
| Global end of trial date | 10 October 2013 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v2 (current) |
| This version publication date | 15 July 2016 |
| First version publication date | 19 April 2015 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 4618-008 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01314872 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Merck Sharp & Dohme Corp. |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033 |
| Public contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |
| Scientific contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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 | 10 October 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 22 October 2012 |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 October 2013 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

(1.) To investigate a dose-related reduction in average number of daily micturitions of vibegron compared with placebo at Week 8 in participants with Overactive Bladder (OAB). (2.) To assess the safety and tolerability of treatment with the selected vibegron (MK-4618) doses either alone or dosed concomitantly with tolterodine ER.

The primary hypothesis of the base study is that administration of vibegron demonstrates a dose-related reduction, compared with placebo, in average number of daily micturitions in participants with OAB after 8 weeks of treatment.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 31 March 2011 |
| 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 | Norway: 75 |
| Country: Number of subjects enrolled | Poland: 38 |
| Country: Number of subjects enrolled | Sweden: 47 |
| Country: Number of subjects enrolled | United Kingdom: 67 |
| Country: Number of subjects enrolled | Austria: 9 |
| Country: Number of subjects enrolled | Denmark: 47 |
| Country: Number of subjects enrolled | Germany: 104 |
| Country: Number of subjects enrolled | Italy: 4 |
| Country: Number of subjects enrolled | United States: 525 |
| Country: Number of subjects enrolled | Australia: 1 |
| Country: Number of subjects enrolled | Canada: 20 |
| Country: Number of subjects enrolled | Japan: 288 |
| Country: Number of subjects enrolled | Korea, Republic of: 38 |

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Mexico: 3 |
| Country: Number of subjects enrolled | New Zealand: 20 |
| Country: Number of subjects enrolled | Peru: 35 |
| Country: Number of subjects enrolled | Puerto Rico: 5 |
| Country: Number of subjects enrolled | Russian Federation: 15 |
| Country: Number of subjects enrolled | South Africa: 54 |
| Worldwide total number of subjects | 1395 |
| EEA total number of subjects | 391 |

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) | 982 |
| From 65 to 84 years | 413 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This was a 2-Part, randomized, double blind placebo- and active-controlled, parallel-group study of vibegron in men and women with OAB. Participants enrolled in Part 1 were not eligible to participate in Part 2. Participants who completed Part 1 or Part 2 were eligible to enroll in an optional 1-year safety extension.

Period 1

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

Arms

| | |
|------------------------------|-----------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Part 1: placebo |

Arm description:

Participants received two placebo matching vibegron tablets and one placebo matching tolterodine extended release (ER) capsule, taken orally each morning, for 8 weeks.

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

Dosage and administration details:

Participants received placebo matching vibegron tablets, taken orally each morning.

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

Dosage and administration details:

Participants received a placebo matching tolterodine ER capsule, taken orally each morning.

| | |
|------------------|-----------------------|
| Arm title | Part 1: vibegron 3 mg |
|------------------|-----------------------|

Arm description:

Participants received one vibegron 3 mg tablet, one placebo matching vibegron tablet, and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | vibegron |
| Investigational medicinal product code | |
| Other name | MK-4618 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received vibegron tablets at dosages of 3 mg, 15 mg, 50 mg, or 100 mg depending on their vibegron Arm assignment, taken orally each morning.

| | |
|---|------------------------------|
| Investigational medicinal product name | placebo matching tolterodine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Other use |
| Dosage and administration details: | |
| Participants received a placebo matching tolterodine ER capsule, taken orally each morning. | |
| Investigational medicinal product name | placebo matching vibegron |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Participants received placebo matching vibegron tablets, taken orally each morning. | |
| Arm title | Part 1: vibegron 15 mg |
| Arm description: | |
| Participants received one vibegron 15 mg tablet, one placebo matching vibegron tablet, and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks. | |
| Arm type | Experimental |
| Investigational medicinal product name | vibegron |
| Investigational medicinal product code | |
| Other name | MK-4618 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Participants received vibegron tablets at dosages of 3 mg, 15 mg, 50 mg, or 100 mg depending on their vibegron Arm assignment, taken orally each morning. | |
| Investigational medicinal product name | placebo matching tolterodine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Participants received a placebo matching tolterodine ER capsule, taken orally each morning. | |
| Investigational medicinal product name | placebo matching vibegron |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Participants received placebo matching vibegron tablets, taken orally each morning. | |
| Arm title | Part 1: vibegron 50 mg |
| Arm description: | |
| Participants received one vibegron 50 mg tablet, one placebo matching vibegron tablet, and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks. | |
| Arm type | Experimental |
| Investigational medicinal product name | vibegron |
| Investigational medicinal product code | |
| Other name | 4618 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:
Participants received vibegron tablets at dosages of 3 mg, 15 mg, 50 mg, or 100 mg depending on their vibegron Arm assignment, taken orally each morning.

| | |
|--|---------------------------|
| Investigational medicinal product name | placebo matching vibegron |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:
Participants received placebo matching vibegron tablets, taken orally each morning.

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

Dosage and administration details:
Participants received a placebo matching tolterodine ER capsule, taken orally each morning.

| | |
|------------------|-------------------------|
| Arm title | Part 1: vibegron 100 mg |
|------------------|-------------------------|

Arm description:
Participants received two vibegron 50 mg tablets and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks.

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | vibegron |
| Investigational medicinal product code | |
| Other name | MK-4618 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:
Participants received vibegron tablets at dosages of 3 mg, 15 mg, 50 mg, or 100 mg depending on their vibegron Arm assignment, taken orally each morning.

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

Dosage and administration details:
Participants received a placebo matching tolterodine ER capsule, taken orally each morning.

| | |
|------------------|-----------------------------|
| Arm title | Part 1: tolterodine ER 4 mg |
|------------------|-----------------------------|

Arm description:
Participants received one tolterodine ER 4 mg capsule and two placebo matching vibegron tablets, taken orally each morning, for 8 weeks.

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

Dosage and administration details:
Participants received one tolterodine ER 4 mg capsule, taken orally once a day.

| | |
|--|---------------------------|
| Investigational medicinal product name | placebo matching vibegron |
| Investigational medicinal product code | |
| Other name | |

| | |
|--------------------------|----------|
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received placebo matching vibegron tablets, taken orally each morning.

| | |
|------------------|---|
| Arm title | Part 1: vibegron 50 mg + tolterodine ER 4 mg/vibegron 50 mg |
|------------------|---|

Arm description:

Participants received one vibegron 50 mg tablet and one placebo matching vibegron tablet, taken orally each morning, for 8 weeks. They also received one tolterodine ER 4 mg capsule for the first 4 weeks and one placebo matching tolterodine ER capsule for the second 4 weeks, both taken orally each morning.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | vibegron |
| Investigational medicinal product code | |
| Other name | MK-4618 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received vibegron tablets at dosages of 3 mg, 15 mg, 50 mg, or 100 mg depending on their vibegron Arm assignment, taken orally each morning.

| | |
|--|---------------------------|
| Investigational medicinal product name | placebo matching vibegron |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

participants received placebo matching vibegron tablets, taken orally each morning.

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

Dosage and administration details:

Participants received a placebo matching tolterodine ER capsule, taken orally each morning.

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

Dosage and administration details:

Participants received one tolterodine ER 4 mg capsule, taken orally each morning.

| | |
|------------------|-----------------|
| Arm title | Part 2: placebo |
|------------------|-----------------|

Arm description:

Participants received two placebo matching vibegron tablets and one placebo matching tolterodine ER capsule, taken orally each morning, for 4 weeks.

| | |
|--|------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | placebo matching tolterodine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received a placebo matching tolterodine ER capsule, taken orally each morning.

| | |
|---|---|
| Investigational medicinal product name | placebo matching vibegron |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Participants received placebo matching vibegron tablets, taken orally each morning. | |
| Arm title | Part 2: vibegron 100 mg |
| Arm description: | |
| Participants received two vibegron 50 mg tablets and one placebo matching tolterodine ER capsule, taken orally each morning, for 4 weeks. | |
| Arm type | Experimental |
| Investigational medicinal product name | placebo matching tolterodine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Participants received a placebo matching tolterodine ER capsule, taken orally each morning. | |
| Investigational medicinal product name | vibegron |
| Investigational medicinal product code | |
| Other name | MK-4618 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Participants received vibegron tablets at dosages of 3 mg, 15 mg, 50 mg, or 100 mg depending on their vibegron Arm assignment, taken orally each morning. | |
| Arm title | Part 2: tolterodine ER 4 mg |
| Arm description: | |
| Participants received one tolterodine ER 4 mg capsule and two placebo matching vibegron tablets, taken orally each morning, for 4 weeks. | |
| Arm type | Active comparator |
| Investigational medicinal product name | placebo matching vibegron |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Participants received placebo matching vibegron tablets, taken orally each morning. | |
| Investigational medicinal product name | tolterodine ER |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Participants received one tolterodine ER 4 mg capsule, taken orally once a day. | |
| Arm title | Part 2: vibegron 100 mg + tolterodine ER 4 mg |
| Arm description: | |
| Participants received two vibegron 50 mg tablets and one tolterodine ER 4 mg capsule, taken orally each morning, for 4 weeks. | |
| Arm type | Experimental |

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

Dosage and administration details:

Participants received one tolterodine ER 4 mg capsule, taken orally once a day.

| | |
|--|----------|
| Investigational medicinal product name | vibegron |
| Investigational medicinal product code | |
| Other name | MK-4618 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received vibegron tablets at dosages of 3 mg, 15 mg, 50 mg, or 100 mg depending on their vibegron Arm assignment, taken orally each morning.

| Number of subjects in period 1 | Part 1: placebo | Part 1: vibegron 3 mg | Part 1: vibegron 15 mg |
|---------------------------------------|-----------------|-----------------------|------------------------|
| Started | 141 | 144 | 134 |
| Completed | 131 | 138 | 128 |
| Not completed | 10 | 6 | 6 |
| Consent withdrawn by subject | 3 | 1 | - |
| Physician decision | - | 1 | - |
| Adverse event, non-fatal | 4 | 2 | 3 |
| Lost to follow-up | - | 1 | 2 |
| Lack of efficacy | 1 | - | - |
| Protocol deviation | 2 | 1 | 1 |

| Number of subjects in period 1 | Part 1: vibegron 50 mg | Part 1: vibegron 100 mg | Part 1: tolterodine ER 4 mg |
|---------------------------------------|------------------------|-------------------------|-----------------------------|
| Started | 150 | 149 | 135 |
| Completed | 143 | 142 | 128 |
| Not completed | 7 | 7 | 7 |
| Consent withdrawn by subject | 2 | 3 | 1 |
| Physician decision | 1 | - | - |
| Adverse event, non-fatal | 2 | 2 | 4 |
| Lost to follow-up | 2 | 1 | 1 |
| Lack of efficacy | - | - | 1 |
| Protocol deviation | - | 1 | - |

| Number of subjects in period 1 | Part 1: vibegron 50 mg + tolterodine ER 4 mg/vibegron 50 mg | Part 2: placebo | Part 2: vibegron 100 mg |
|---------------------------------------|---|-----------------|-------------------------|
| Started | 134 | 64 | 112 |
| Completed | 126 | 57 | 106 |
| Not completed | 8 | 7 | 6 |

| | | | |
|------------------------------|---|---|---|
| Consent withdrawn by subject | 3 | 2 | 2 |
| Physician decision | - | - | - |
| Adverse event, non-fatal | 4 | 2 | 3 |
| Lost to follow-up | 1 | 1 | 1 |
| Lack of efficacy | - | 2 | - |
| Protocol deviation | - | - | - |

| Number of subjects in period 1 | Part 2: tolterodine ER 4 mg | Part 2: vibegron 100 mg + tolterodine ER 4 mg |
|--------------------------------|-----------------------------|---|
| | | |
| Started | 122 | 110 |
| Completed | 118 | 107 |
| Not completed | 4 | 3 |
| Consent withdrawn by subject | 2 | 1 |
| Physician decision | 1 | - |
| Adverse event, non-fatal | - | 1 |
| Lost to follow-up | - | - |
| Lack of efficacy | - | - |
| Protocol deviation | 1 | 1 |

Period 2

| | |
|------------------------------|-----------------------------|
| Period 2 title | Extension Study |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|---------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Extension Study: vibegron 50 mg |

Arm description:

Participants in Base Study/Part 1 who received vibegron 50 mg continued their treatment in the Extension Study. In addition, participants in Base Study/Part 1 who received vibegron 3 mg received vibegron 50 mg in the Extension Study. Also, participants in Base Study/Part 1 who received vibegron 50 mg + tolterodine ER for 4 weeks, followed by vibegron 50 mg alone for 4 weeks, remained on vibegron 50 mg in the Extension Study. In the extension, participants received one vibegron 50 mg tablet, one placebo matching vibegron tablet, and one placebo matching tolterodine ER capsule, taken orally each morning, for 52 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:

Participants were randomized to receive vibegron tablets at dosages of 3 mg, 15 mg, 50 mg, or 100 mg, taken orally each morning.

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

Dosage and administration details:

Participants received a placebo matching tolterodine ER capsule, taken orally each morning.

| | |
|--|---------------------------|
| Investigational medicinal product name | placebo matching vibegron |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received placebo matching vibegron tablets, taken orally each morning.

| | |
|------------------|----------------------------------|
| Arm title | Extension Study: vibegron 100 mg |
|------------------|----------------------------------|

Arm description:

Participants in Base Study/Part 1 or Part 2 who received vibegron 100 mg continued their treatment in the Extension Study. In addition, participants in Base Study/Part 1 who received vibegron 15 mg received vibegron 100 mg in the Extension Study. In the extension, participants received two vibegron 50 mg tablets and one placebo matching tolterodine ER capsule, taken orally each morning, for 52 weeks.

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

Dosage and administration details:

Participants received a placebo matching tolterodine ER capsule, taken orally each morning.

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

Dosage and administration details:

Participants received vibegron tablets at dosages of 3 mg, 15 mg, 50 mg, or 100 mg, taken orally each morning.

| | |
|------------------|--------------------------------------|
| Arm title | Extension Study: tolterodine ER 4 mg |
|------------------|--------------------------------------|

Arm description:

Participants in Base Study/Part 1 or Part 2 who received tolterodine ER 4 mg continued their treatment in the Extension Study. In addition, participants in Base Study/Part 1 who received placebo also received tolterodine ER 4 mg in the Extension Study. In the extension, participants received one tolterodine ER 4 mg capsule and two placebo matching vibegron tablets, taken orally each morning, for 52 weeks.

| | |
|--|---------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | placebo matching vibegron |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received placebo matching vibegron tablets, taken orally each morning.

| | |
|---|--|
| Investigational medicinal product name | tolterodine ER |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Participants received one tolterodine ER 4 mg capsule, taken orally each morning. | |
| Arm title | Extension Study: vibegron 100 mg + tolterodine ER 4 mg |

Arm description:

Participants in Base Study/Part 1 who received vibegron 100 mg + tolterodine ER 4 mg continued their treatment in the Extension Study. In addition, participants in Base Study/Part 2 who received placebo were assigned to the vibegron 100 mg + tolterodine ER 4 mg arm in the Extension Study. In the extension, participants received two vibegron 50 mg tablets and one tolterodine ER 4 mg capsule, taken orally each morning, for 52 weeks.

| | |
|--|----------------|
| Arm type | Experimental |
| Investigational medicinal product name | tolterodine ER |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received one tolterodine ER 4 mg capsule, taken orally once a day.

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

Dosage and administration details:

Participants received vibegron tablets at dosages of 3 mg, 15 mg, 50 mg, or 100 mg, taken orally each morning.

| Number of subjects in period 2^[1] | Extension Study: vibegron 50 mg | Extension Study: vibegron 100 mg | Extension Study: tolterodine ER 4 mg |
|---|---------------------------------|----------------------------------|--------------------------------------|
| Started | 223 | 248 | 240 |
| Completed | 175 | 188 | 187 |
| Not completed | 48 | 60 | 53 |
| Consent withdrawn by subject | 14 | 17 | 12 |
| Adverse event, non-fatal | 13 | 16 | 24 |
| Pregnancy | - | - | - |
| Non-compliance with study drug | 3 | 3 | 1 |
| Study terminated by sponsor | 2 | 2 | 3 |
| Lost to follow-up | 6 | 7 | 2 |
| Lack of efficacy | 7 | 12 | 9 |
| Protocol deviation | 3 | 3 | 2 |

| | |
|---|------------------------------------|
| Number of subjects in period 2^[1] | Extension Study: vibegron 100 mg + |
|---|------------------------------------|

| | tolterodine ER 4 mg |
|--------------------------------|---------------------|
| Started | 134 |
| Completed | 110 |
| Not completed | 24 |
| Consent withdrawn by subject | 4 |
| Adverse event, non-fatal | 9 |
| Pregnancy | 1 |
| Non-compliance with study drug | 2 |
| Study terminated by sponsor | - |
| Lost to follow-up | 6 |
| Lack of efficacy | 2 |
| Protocol deviation | - |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Participants who completed Part 1 or Part 2 of the Base Study were eligible to enroll in an optional 1-year safety extension.

Baseline characteristics

Reporting groups

| | |
|--|---|
| Reporting group title | Part 1: placebo |
| Reporting group description: Participants received two placebo matching vibegron tablets and one placebo matching tolterodine extended release (ER) capsule, taken orally each morning, for 8 weeks. | |
| Reporting group title | Part 1: vibegron 3 mg |
| Reporting group description: Participants received one vibegron 3 mg tablet, one placebo matching vibegron tablet, and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks. | |
| Reporting group title | Part 1: vibegron 15 mg |
| Reporting group description: Participants received one vibegron 15 mg tablet, one placebo matching vibegron tablet, and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks. | |
| Reporting group title | Part 1: vibegron 50 mg |
| Reporting group description: Participants received one vibegron 50 mg tablet, one placebo matching vibegron tablet, and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks. | |
| Reporting group title | Part 1: vibegron 100 mg |
| Reporting group description: Participants received two vibegron 50 mg tablets and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks. | |
| Reporting group title | Part 1: tolterodine ER 4 mg |
| Reporting group description: Participants received one tolterodine ER 4 mg capsule and two placebo matching vibegron tablets, taken orally each morning, for 8 weeks. | |
| Reporting group title | Part 1: vibegron 50 mg + tolterodine ER 4 mg/vibegron 50 mg |
| Reporting group description: Participants received one vibegron 50 mg tablet and one placebo matching vibegron tablet, taken orally each morning, for 8 weeks. They also received one tolterodine ER 4 mg capsule for the first 4 weeks and one placebo matching tolterodine ER capsule for the second 4 weeks, both taken orally each morning. | |
| Reporting group title | Part 2: placebo |
| Reporting group description: Participants received two placebo matching vibegron tablets and one placebo matching tolterodine ER capsule, taken orally each morning, for 4 weeks. | |
| Reporting group title | Part 2: vibegron 100 mg |
| Reporting group description: Participants received two vibegron 50 mg tablets and one placebo matching tolterodine ER capsule, taken orally each morning, for 4 weeks. | |
| Reporting group title | Part 2: tolterodine ER 4 mg |
| Reporting group description: Participants received one tolterodine ER 4 mg capsule and two placebo matching vibegron tablets, taken orally each morning, for 4 weeks. | |
| Reporting group title | Part 2: vibegron 100 mg + tolterodine ER 4 mg |
| Reporting group description: Participants received two vibegron 50 mg tablets and one tolterodine ER 4 mg capsule, taken orally each morning, for 4 weeks. | |

| Reporting group values | Part 1: placebo | Part 1: vibegron 3 mg | Part 1: vibegron 15 mg |
|------------------------|-----------------|-----------------------|------------------------|
| Number of subjects | 141 | 144 | 134 |

| | | | |
|---|-------------|---------------|---------------|
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | 58.6 ± 9 | 59.4 ± 8.7 | 58.6 ± 8.1 |
| Gender categorical Units: Subjects | | | |
| Female | 128 | 131 | 125 |
| Male | 13 | 13 | 9 |

| | | | |
|------------------------------------|------------------------|-------------------------|-----------------------------|
| Reporting group values | Part 1: vibegron 50 mg | Part 1: vibegron 100 mg | Part 1: tolterodine ER 4 mg |
| Number of subjects | 150 | 149 | 135 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|---------------|---------------|---------------|
| Age continuous Units: years arithmetic mean standard deviation | 60.3 ± 8.7 | 60.3 ± 8.3 | 59.1 ± 8.1 |
| Gender categorical Units: Subjects | | | |
| Female | 129 | 135 | 121 |
| Male | 21 | 14 | 14 |

| | | | |
|------------------------------------|---|-----------------|-------------------------|
| Reporting group values | Part 1: vibegron 50 mg + tolterodine ER 4 mg/vibegron 50 mg | Part 2: placebo | Part 2: vibegron 100 mg |
| Number of subjects | 134 | 64 | 112 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|---------------|----------------|----------------|
| Age continuous Units: years arithmetic mean standard deviation | 59.4 ± 8.5 | 56.3 ± 10.6 | 57.2 ± 10.1 |
| Gender categorical Units: Subjects | | | |
| Female | 119 | 57 | 101 |
| Male | 15 | 7 | 11 |

| | | | |
|------------------------------------|-----------------------------|---|-------|
| Reporting group values | Part 2: tolterodine ER 4 mg | Part 2: vibegron 100 mg + tolterodine ER 4 mg | Total |
| Number of subjects | 122 | 110 | 1395 |
| Age categorical Units: Subjects | | | |

| | | | |
|--------------------|--------|--------|------|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 57.9 | 55.5 | |
| standard deviation | ± 10.9 | ± 11.7 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 110 | 95 | 1251 |
| Male | 12 | 15 | 144 |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Part 1: placebo |
| Reporting group description: Participants received two placebo matching vibegron tablets and one placebo matching tolterodine extended release (ER) capsule, taken orally each morning, for 8 weeks. | |
| Reporting group title | Part 1: vibegron 3 mg |
| Reporting group description: Participants received one vibegron 3 mg tablet, one placebo matching vibegron tablet, and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks. | |
| Reporting group title | Part 1: vibegron 15 mg |
| Reporting group description: Participants received one vibegron 15 mg tablet, one placebo matching vibegron tablet, and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks. | |
| Reporting group title | Part 1: vibegron 50 mg |
| Reporting group description: Participants received one vibegron 50 mg tablet, one placebo matching vibegron tablet, and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks. | |
| Reporting group title | Part 1: vibegron 100 mg |
| Reporting group description: Participants received two vibegron 50 mg tablets and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks. | |
| Reporting group title | Part 1: tolterodine ER 4 mg |
| Reporting group description: Participants received one tolterodine ER 4 mg capsule and two placebo matching vibegron tablets, taken orally each morning, for 8 weeks. | |
| Reporting group title | Part 1: vibegron 50 mg + tolterodine ER 4 mg/vibegron 50 mg |
| Reporting group description: Participants received one vibegron 50 mg tablet and one placebo matching vibegron tablet, taken orally each morning, for 8 weeks. They also received one tolterodine ER 4 mg capsule for the first 4 weeks and one placebo matching tolterodine ER capsule for the second 4 weeks, both taken orally each morning. | |
| Reporting group title | Part 2: placebo |
| Reporting group description: Participants received two placebo matching vibegron tablets and one placebo matching tolterodine ER capsule, taken orally each morning, for 4 weeks. | |
| Reporting group title | Part 2: vibegron 100 mg |
| Reporting group description: Participants received two vibegron 50 mg tablets and one placebo matching tolterodine ER capsule, taken orally each morning, for 4 weeks. | |
| Reporting group title | Part 2: tolterodine ER 4 mg |
| Reporting group description: Participants received one tolterodine ER 4 mg capsule and two placebo matching vibegron tablets, taken orally each morning, for 4 weeks. | |
| Reporting group title | Part 2: vibegron 100 mg + tolterodine ER 4 mg |
| Reporting group description: Participants received two vibegron 50 mg tablets and one tolterodine ER 4 mg capsule, taken orally each morning, for 4 weeks. | |
| Reporting group title | Extension Study: vibegron 50 mg |
| Reporting group description: Participants in Base Study/Part 1 who received vibegron 50 mg continued their treatment in the Extension Study. In addition, participants in Base Study/Part 1 who received vibegron 3 mg received vibegron 50 mg in the Extension Study. Also, participants in Base Study/Part 1 who received vibegron 50 mg + tolterodine ER for 4 weeks, followed by vibegron 50 mg alone for 4 weeks, remained on vibegron 50 mg in the Extension Study. In the extension, participants received one vibegron 50 mg tablet, one placebo matching vibegron tablet, and one placebo matching tolterodine ER capsule, taken | |

orally each morning, for 52 weeks.

| | |
|-----------------------|----------------------------------|
| Reporting group title | Extension Study: vibegron 100 mg |
|-----------------------|----------------------------------|

Reporting group description:

Participants in Base Study/Part 1 or Part 2 who received vibegron 100 mg continued their treatment in the Extension Study. In addition, participants in Base Study/Part 1 who received vibegron 15 mg received vibegron 100 mg in the Extension Study. In the extension, participants received two vibegron 50 mg tablets and one placebo matching tolterodine ER capsule, taken orally each morning, for 52 weeks.

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Extension Study: tolterodine ER 4 mg |
|-----------------------|--------------------------------------|

Reporting group description:

Participants in Base Study/Part 1 or Part 2 who received tolterodine ER 4 mg continued their treatment in the Extension Study. In addition, participants in Base Study/Part 1 who received placebo also received tolterodine ER 4 mg in the Extension Study. In the extension, participants received one tolterodine ER 4 mg capsule and two placebo matching vibegron tablets, taken orally each morning, for 52 weeks.

| | |
|-----------------------|--|
| Reporting group title | Extension Study: vibegron 100 mg + tolterodine ER 4 mg |
|-----------------------|--|

Reporting group description:

Participants in Base Study/Part 1 who received vibegron 100 mg + tolterodine ER 4 mg continued their treatment in the Extension Study. In addition, participants in Base Study/Part 2 who received placebo were assigned to the vibegron 100 mg + tolterodine ER 4 mg arm in the Extension Study. In the extension, participants received two vibegron 50 mg tablets and one tolterodine ER 4 mg capsule, taken orally each morning, for 52 weeks.

Primary: Base Study/Part 1: Change from Baseline in Average Daily Number of Micturitions at Week 8

| | |
|-----------------|--|
| End point title | Base Study/Part 1: Change from Baseline in Average Daily Number of Micturitions at Week 8 ^[1] |
|-----------------|--|

End point description:

Participants were required to keep a voiding diary, recording the occurrence of each micturition. The average daily number of micturitions was calculated as the total number of micturitions that occurred over a week (4 to 10 days) during the Base Study, divided by the total number of days of voiding kept in the participant's diary. Baseline was defined as the average daily number of daily micturitions that occurred during the week of placebo run-in prior to Week 0 visit. This endpoint was based on the full analysis set population, which included all randomized participants who received at least one dose of study treatment and have either baseline data or at least one post-randomization observation for the analysis endpoint.

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

End point timeframe:

Baseline and Week 8

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Participants in this treatment group took MK-4618 50 mg + tolterodine ER 4 mg for the first 4 weeks and MK-4618 50 mg in the later 4 weeks. This treatment group was not statistically analyzed.

| End point values | Part 1: placebo | Part 1: vibegron 3 mg | Part 1: vibegron 15 mg | Part 1: vibegron 50 mg |
|--|-----------------------|------------------------|------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 141 | 144 | 132 | 148 |
| Units: Average Daily Number of Micturitions | | | | |
| least squares mean (confidence interval 95%) | -1.16 (-1.5 to -0.82) | -1.62 (-1.95 to -1.29) | -1.61 (-1.96 to -1.27) | -1.8 (-2.13 to -1.47) |

| End point values | Part 1: vibegron 100 mg | Part 1: tolterodine ER 4 mg | Part 1: vibegron 50 mg + tolterodine ER 4 mg/vibegron 50 mg | |
|--|-------------------------------|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 148 | 134 | 134 | |
| Units: Average Daily Number of Micturitions | | | | |
| least squares mean (confidence interval 95%) | -2.07 (-2.4 to -1.74) | -1.71 (-2.05 to -1.36) | -2.05 (-2.4 to -1.7) | |

Statistical analyses

| Statistical analysis title | Difference in Least Squares (LS) Means |
|---|---|
| Statistical analysis description: | |
| Difference in LS Means: vibegron 3 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: vibegron 3 mg |
| Number of subjects included in analysis | 285 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.056 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS means |
| Point estimate | -0.46 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.92 |
| upper limit | 0.01 |

| Statistical analysis title | Difference in LS Means |
|--|--|
| Statistical analysis description: | |
| Difference in LS Means: vibegron 15 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: vibegron 15 mg |
| Number of subjects included in analysis | 273 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.064 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.45 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.93 |
| upper limit | 0.03 |

| | |
|--|--|
| Statistical analysis title | Difference in LS Means |
| Statistical analysis description: | |
| Difference in LS Means: vibegron 50 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: vibegron 50 mg |
| Number of subjects included in analysis | 289 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.007 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.11 |
| upper limit | -0.18 |

| | |
|---|---|
| Statistical analysis title | Difference in LS Means |
| Statistical analysis description: | |
| Difference in LS Means: vibegron 100 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: vibegron 100 mg |
| Number of subjects included in analysis | 289 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.91 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.37 |
| upper limit | -0.44 |

| | |
|---|---|
| Statistical analysis title | Difference in LS Means |
| Statistical analysis description: | |
| Difference in LS Means: tolterodine ER 4 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: tolterodine ER 4 mg |

| | |
|---|--|
| Number of subjects included in analysis | 275 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.026 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.54 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.02 |
| upper limit | -0.07 |

Primary: Base Study/Part 1 + Part 2: Number of Participants Who Experienced an Adverse Event (AE)

| | |
|-----------------|---|
| End point title | Base Study/Part 1 + Part 2: Number of Participants Who Experienced an Adverse Event (AE) ^[2] |
|-----------------|---|

End point description:

An AE is defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a study drug, whether or not it is considered related to the study drug. This endpoint was based on the all participants as treated population, which consisted of all randomized participants who received at least one dose of study treatment. Participants were included in the treatment group corresponding to the study treatment they actually received.

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

End point timeframe:

Part 1: up to 8 weeks; Part 2: up to 4 weeks. The time frame was an additional 2 weeks for participants not continuing to the Extension Study.

Notes:

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

Justification: No statistical analysis was conducted for Base Study/Part 1 + Part 2: Number of Participants Who Experienced an Adverse Event (AE).

| End point values | Part 1: placebo | Part 1: vibegron 3 mg | Part 1: vibegron 15 mg | Part 1: vibegron 50 mg |
|-----------------------------|-----------------|-----------------------|------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 141 | 144 | 134 | 148 |
| Units: Participants | 66 | 55 | 70 | 62 |

| End point values | Part 1: vibegron 100 mg | Part 1: tolterodine ER 4 mg | Part 1: vibegron 50 mg + tolterodine ER 4 mg/vibegron 50 mg | Part 2: placebo |
|-----------------------------|-------------------------|-----------------------------|---|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 149 | 135 | 134 | 64 |
| Units: Participants | 70 | 68 | 69 | 22 |

| End point values | Part 2: vibegron 100 mg | Part 2: tolterodine ER 4 mg | Part 2: vibegron 100 mg + tolterodine ER 4 mg | |
|-----------------------------|-------------------------------|-----------------------------------|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 112 | 122 | 110 | |
| Units: Participants | 37 | 48 | 40 | |

Statistical analyses

No statistical analyses for this end point

Primary: Base Study/Part 1 + Part 2: Number of Participants Who Had Study Medication Withdrawn Due to an AE

| | |
|-----------------|---|
| End point title | Base Study/Part 1 + Part 2: Number of Participants Who Had Study Medication Withdrawn Due to an AE ^[3] |
|-----------------|---|

End point description:

An AE is defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a study drug, whether or not it is considered related to the study drug. This endpoint was based on the all participants as treated population, which consisted of all randomized participants who received at least one dose of study treatment. Participants were included in the treatment group corresponding to the study treatment they actually received.

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

End point timeframe:

Part 1: up to 8 weeks; Part 2: up to 4 weeks

Notes:

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

Justification: No statistical analysis was conducted for Base Study/Part 1 + Part 2: Number of Participants Who Had Study Medication Withdrawn Due to an AE.

| End point values | Part 1: placebo | Part 1: vibegron 3 mg | Part 1: vibegron 15 mg | Part 1: vibegron 50 mg |
|-----------------------------|-----------------|--------------------------|------------------------------|------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 141 | 144 | 134 | 148 |
| Units: Participants | 3 | 3 | 4 | 2 |

| End point values | Part 1: vibegron 100 mg | Part 1: tolterodine ER 4 mg | Part 1: vibegron 50 mg + tolterodine ER 4 mg/vibegron 50 mg | Part 2: placebo |
|-----------------------------|-------------------------------|-----------------------------------|--|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 149 | 135 | 134 | 64 |
| Units: Participants | 2 | 4 | 3 | 2 |

| End point values | Part 2: vibegron 100 mg | Part 2: tolterodine ER 4 mg | Part 2: vibegron 100 mg + tolterodine ER 4 mg | |
|-----------------------------|-------------------------------|-----------------------------------|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 112 | 122 | 110 | |
| Units: Participants | 4 | 0 | 2 | |

Statistical analyses

No statistical analyses for this end point

Primary: Extension Study: Number of Participants Who Experienced an AE

| | |
|-----------------|--|
| End point title | Extension Study: Number of Participants Who Experienced an AE ^[4] |
|-----------------|--|

End point description:

An AE is defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a study drug, whether or not it is considered related to the study drug. This endpoint was based on the all participants as treated population, which consisted of all randomized participants who received at least one dose of study treatment. Participants were included in the treatment group corresponding to the study treatment they actually received.

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

End point timeframe:

Up to Week 54 of the Extension Study

Notes:

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

Justification: No statistical analysis was conducted for Extension Study: Number of Participants Who Experienced an AE.

| End point values | Extension Study: vibegron 50 mg | Extension Study: vibegron 100 mg | Extension Study: tolterodine ER 4 mg | Extension Study: vibegron 100 mg + tolterodine ER 4 mg |
|-----------------------------|--|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 223 | 248 | 240 | 134 |
| Units: Participants | 134 | 157 | 158 | 82 |

Statistical analyses

No statistical analyses for this end point

Primary: Extension Study: Number of Participants Who Had Study Medication Withdrawn Due to an AE

| | |
|-----------------|---|
| End point title | Extension Study: Number of Participants Who Had Study |
|-----------------|---|

End point description:

An AE is defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a study drug, whether or not it is considered related to the study drug. This endpoint was based on the all participants as treated population, which consisted of all randomized participants who received at least one dose of study treatment. Participants were included in the treatment group corresponding to the study treatment they actually received.

End point type

Primary

End point timeframe:

Up to Week 52 of the Extension Study

Notes:

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

Justification: No statistical analysis was conducted for Extension Study: Number of Participants Who Had Study Medication Withdrawn Due to an AE.

| End point values | Extension Study: vibegron 50 mg | Extension Study: vibegron 100 mg | Extension Study: tolterodine ER 4 mg | Extension Study: vibegron 100 mg + tolterodine ER 4 mg |
|-----------------------------|------------------------------------|-------------------------------------|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 223 | 248 | 240 | 134 |
| Units: Participants | 11 | 14 | 24 | 7 |

Statistical analyses

No statistical analyses for this end point

Secondary: Base Study/Part 1: Change from Baseline in Average Daily Number of Urge Incontinence Episodes at Week 8

End point title

Base Study/Part 1: Change from Baseline in Average Daily Number of Urge Incontinence Episodes at Week 8^[6]

End point description:

Participants were required to keep a voiding diary, recording the occurrence of each urge incontinence episode. The average daily number of urge incontinence episodes was calculated as the total number of times a participant experienced such an episode over a week (4 to 10 days) during the Base Study, divided by the total number of days of voiding kept in the participant's diary. This endpoint was based on the full analysis set population, which included all randomized participants who received at least one dose of study treatment and have either baseline data or at least one post-randomization observation for the analysis endpoint. This outcome measure included OAB Wet (OAB with urinary urgency incontinence) participants only. Baseline was defined as the average daily number of urge incontinence episodes that occurred during the week of placebo run-in prior to Week 0 visit.

End point type

Secondary

End point timeframe:

Baseline and Week 8

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Participants in this treatment group took MK-4618 50 mg + tolterodine ER 4 mg for the first 4 weeks and MK-4618 50 mg in the later 4 weeks. This treatment group was not statistically analyzed.

| End point values | Part 1: placebo | Part 1: vibegron 3 mg | Part 1: vibegron 15 mg | Part 1: vibegron 50 mg |
|--|------------------------|------------------------|------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 118 | 113 | 111 | 121 |
| Units: Number of Urge Incontinence Episodes | | | | |
| least squares mean (confidence interval 95%) | -1.24 (-1.52 to -0.95) | -1.52 (-1.81 to -1.23) | -1.81 (-2.1 to 1.51) | -1.95 (-2.23 to -1.67) |

| End point values | Part 1: vibegron 100 mg | Part 1: tolterodine ER 4 mg | Part 1: vibegron 50 mg + tolterodine ER 4 mg/vibegron 50 mg | |
|--|-------------------------|-----------------------------|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 122 | 100 | 111 | |
| Units: Number of Urge Incontinence Episodes | | | | |
| least squares mean (confidence interval 95%) | -1.95 (-2.23 to -1.67) | -1.69 (-2 to -1.38) | -1.71 (-2.01 to -1.42) | |

Statistical analyses

| Statistical analysis title | Difference in LS Means |
|--|---|
| Statistical analysis description: Difference in LS Means: vibegron 3 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: vibegron 3 mg |
| Number of subjects included in analysis | 231 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.167 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.28 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.68 |
| upper limit | 0.12 |

| Statistical analysis title | Difference in LS Means |
|---|--|
| Statistical analysis description: Difference in LS Means: vibegron 15 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: vibegron 15 mg |

| | |
|---|--|
| Number of subjects included in analysis | 229 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.005 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.97 |
| upper limit | -0.17 |

| | |
|--|--|
| Statistical analysis title | Difference in LS Means |
| Statistical analysis description: | |
| Difference in LS Means: vibegron 50 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: vibegron 50 mg |
| Number of subjects included in analysis | 239 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.11 |
| upper limit | -0.33 |

| | |
|---|---|
| Statistical analysis title | Difference in LS Means |
| Statistical analysis description: | |
| Difference in LS Means: vibegron 100 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: vibegron 100 mg |
| Number of subjects included in analysis | 240 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | -0.32 |

| | |
|--|---|
| Statistical analysis title | Difference in LS Means |
| Statistical analysis description: Difference in LS Means: tolterodine ER 4 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: tolterodine ER 4 mg |
| Number of subjects included in analysis | 218 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.03 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.46 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.87 |
| upper limit | -0.04 |

Secondary: Base Study/Part 1: Change from Baseline in Average Daily Number of Total Incontinence Episodes at Week 8

| | |
|--|---|
| End point title | Base Study/Part 1: Change from Baseline in Average Daily Number of Total Incontinence Episodes at Week 8 ^[7] |
| End point description: Participants were required to keep a voiding diary, recording the occurrence of each total incontinence episode. The average daily number of total incontinence episodes was calculated as the total number of times a participant experienced such an episode over a week (4 to 10 days) during the Base Study, divided by the total number of days of voiding kept in the participant's diary. This endpoint was based on the full analysis set population, which included all randomized participants who received at least one dose of study treatment and have either baseline data or at least one post-randomization observation for the analysis endpoint. This outcome measure included OAB Wet participants only. Baseline was defined as the average daily number of total incontinence episodes that occurred during the week of placebo run-in prior to Week 0 visit. | |
| End point type | Secondary |
| End point timeframe: Baseline and Week 8 | |

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Participants in this treatment group took MK-4618 50 mg + tolterodine ER 4 mg for the first 4 weeks and MK-4618 50 mg in the later 4 weeks. This treatment group was not statistically analyzed.

| End point values | Part 1: placebo | Part 1: vibegron 3 mg | Part 1: vibegron 15 mg | Part 1: vibegron 50 mg |
|--|------------------------|------------------------|------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 118 | 113 | 111 | 121 |
| Units: Incontinence Episodes | | | | |
| least squares mean (confidence interval 95%) | -1.52 (-1.84 to -1.21) | -1.71 (-2.02 to -1.39) | -2.01 (-2.33 to -1.69) | -2.13 (-2.43 to -1.82) |

| End point values | Part 1: vibegron 100 mg | Part 1: tolterodine ER 4 mg | Part 1: vibegron 50 mg + tolterodine ER 4 mg/vibegron 50 mg | |
|--|-------------------------------|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 122 | 100 | 111 | |
| Units: Incontinence Episodes | | | | |
| least squares mean (confidence interval 95%) | -2.11 (-2.41 to -1.8) | -1.86 (-2.2 to -1.52) | -2 (-2.32 to -1.68) | |

Statistical analyses

| Statistical analysis title | Difference in LS Means |
|--|---|
| Statistical analysis description: Difference in LS Means: vibegron 3 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: vibegron 3 mg |
| Number of subjects included in analysis | 231 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.401 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.18 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.61 |
| upper limit | 0.25 |

| Statistical analysis title | Difference in LS Means |
|---|--|
| Statistical analysis description: Difference in LS Means: vibegron 15 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: vibegron 15 mg |
| Number of subjects included in analysis | 229 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.029 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.48 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.91 |
| upper limit | -0.05 |

| | |
|--|--|
| Statistical analysis title | Difference in LS Means |
| Statistical analysis description: | |
| Difference in LS Means: vibegron 50 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: vibegron 50 mg |
| Number of subjects included in analysis | 239 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.005 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.02 |
| upper limit | -0.18 |

| | |
|---|---|
| Statistical analysis title | Difference in LS Means |
| Statistical analysis description: | |
| Difference in LS Means: vibegron 100 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: vibegron 100 mg |
| Number of subjects included in analysis | 240 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.007 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.58 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.01 |
| upper limit | -0.16 |

| | |
|---|---|
| Statistical analysis title | Difference in LS Means |
| Statistical analysis description: | |
| Difference in LS Means: tolterodine ER 4 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: tolterodine ER 4 mg |

| | |
|---|--|
| Number of subjects included in analysis | 218 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.14 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.34 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.78 |
| upper limit | 0.11 |

Secondary: Base Study/Part 1: Change from Baseline in Average Daily Number of Strong Urge Episodes at Week 8

| | |
|-----------------|--|
| End point title | Base Study/Part 1: Change from Baseline in Average Daily Number of Strong Urge Episodes at Week 8 ^[8] |
|-----------------|--|

End point description:

Participants were required to keep a voiding diary, recording the occurrence of each strong urge episode. The average daily number of strong urge episodes was calculated as the total number of times a participant experienced such an episode over a week (4 to 10 days) during the Base Study, divided by the total number of days of voiding kept in the participant's diary. Baseline was defined as the average daily number of strong urge episodes that occurred during the week of placebo run-in prior to Week 0 visit. This endpoint was based on the full analysis set population, which included all randomized participants who received at least one dose of study treatment and have either baseline data or at least one post-randomization observation for the analysis endpoint.

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

End point timeframe:

Baseline and Week 8

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Participants in this treatment group took MK-4618 50 mg + tolterodine ER 4 mg for the first 4 weeks and MK-4618 50 mg in the later 4 weeks. This treatment group was not statistically analyzed.

| End point values | Part 1: placebo | Part 1: vibegron 3 mg | Part 1: vibegron 15 mg | Part 1: vibegron 50 mg |
|--|------------------------|-----------------------|------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 141 | 144 | 132 | 148 |
| Units: Strong Urge Episodes | | | | |
| least squares mean (confidence interval 95%) | -1.59 (-2.07 to -1.11) | -1.77 (-2.24 to -1.3) | -2.27 (-2.76 to -1.78) | -2.36 (-2.82 to -1.89) |

| End point values | Part 1: vibegron 100 mg | Part 1: tolterodine ER 4 mg | Part 1: vibegron 50 mg + tolterodine ER 4 mg/vibegron 50 mg | |
|------------------|-------------------------|-----------------------------|---|--|
|------------------|-------------------------|-----------------------------|---|--|

| | | | | |
|--|-----------------------|------------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 148 | 134 | 134 | |
| Units: Strong Urge Episodes | | | | |
| least squares mean (confidence interval 95%) | -2.83 (-3.3 to -2.37) | -2.53 (-3.03 to -2.04) | -2.73 (-3.22 to -2.24) | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Difference in LS Means |
| Statistical analysis description: | |
| Difference in LS Means: vibegron 3 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: vibegron 3 mg |
| Number of subjects included in analysis | 285 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.598 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.18 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.84 |
| upper limit | 0.49 |

| | |
|--|--|
| Statistical analysis title | Difference in LS Means |
| Statistical analysis description: | |
| Difference in LS Means: vibegron 15 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: vibegron 15 mg |
| Number of subjects included in analysis | 273 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.052 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.67 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.35 |
| upper limit | 0.01 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Difference in LS Means |
|-----------------------------------|------------------------|

| | |
|--|--|
| Statistical analysis description: | |
| Difference in LS Means: vibegron 50 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: vibegron 50 mg |
| Number of subjects included in analysis | 289 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.024 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.43 |
| upper limit | -0.1 |

| | |
|---|---|
| Statistical analysis title | Difference in LS Means |
| Statistical analysis description: | |
| Difference in LS Means: vibegron 100 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: vibegron 100 mg |
| Number of subjects included in analysis | 289 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -1.24 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.9 |
| upper limit | -0.58 |

| | |
|---|---|
| Statistical analysis title | Difference in LS Means |
| Statistical analysis description: | |
| Difference in LS Means: tolterodine ER 4 mg vs. placebo at Week 8 | |
| Comparison groups | Part 1: placebo v Part 1: tolterodine ER 4 mg |
| Number of subjects included in analysis | 275 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.007 |
| Method | Constrained Longitudinal Data Analysis |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.94 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.62 |
| upper limit | -0.26 |

Secondary: Extension Study: Change From Baseline in Average Daily Number of Micturitions at Week 52

| | |
|-----------------|--|
| End point title | Extension Study: Change From Baseline in Average Daily Number of Micturitions at Week 52 |
|-----------------|--|

End point description:

Participants were required to keep a voiding diary, recording the daily occurrence of each micturition. The average daily number of micturitions was calculated as the total number of recorded micturitions that occurred during the 52-week Extension Study, divided by the total number of days of voiding kept in the participant's diary. Baseline was defined as the value at Week 0 of the Base Study. This endpoint was based on the full analysis set population, which included all randomized participants who received at least one dose of study treatment and have either baseline data or at least one post-randomization observation for the analysis endpoint.

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

End point timeframe:

Baseline and Week 52 of Extension Study

| End point values | Extension Study: vibegron 50 mg | Extension Study: vibegron 100 mg | Extension Study: tolterodine ER 4 mg | Extension Study: vibegron 100 mg + tolterodine ER 4 mg |
|--|---------------------------------|----------------------------------|--------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 223 | 246 | 240 | 134 |
| Units: Average Daily Number of Micturitions | | | | |
| least squares mean (confidence interval 95%) | -2.53 (-2.87 to -2.2) | -2.77 (-3.08 to -2.45) | -2.15 (-2.47 to -1.83) | -3.25 (-3.67 to -2.83) |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Difference in LS Means |
|----------------------------|------------------------|

Statistical analysis description:

Difference in LS Means: vibegron 100 mg + tolterodine ER 4 mg vs. vibegron 100 mg at Week 52

| | |
|-------------------|---|
| Comparison groups | Extension Study: vibegron 100 mg v Extension Study: vibegron 100 mg + tolterodine ER 4 mg |
|-------------------|---|

| | |
|---|------------------------|
| Number of subjects included in analysis | 380 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.49 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 0.03 |

| | |
|--|---|
| Statistical analysis title | Difference in LS Means |
| Statistical analysis description: | |
| Difference in LS Means: vibegron 100 mg + tolterodine ER 4 mg vs. tolterodine ER 4 mg at Week 52 | |
| Comparison groups | Extension Study: tolterodine ER 4 mg v Extension Study: vibegron 100 mg + tolterodine ER 4 mg |
| Number of subjects included in analysis | 374 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in LS Means |
| Point estimate | -1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.62 |
| upper limit | -0.58 |

Secondary: Extension Study: Change from Baseline in Average Daily Number of Urge Incontinence Episodes at Week 52

| | |
|--|--|
| End point title | Extension Study: Change from Baseline in Average Daily Number of Urge Incontinence Episodes at Week 52 |
| End point description: | |
| Participants were required to keep a voiding diary, recording the occurrence of each urge incontinence episode. The average daily number of urge incontinence episodes was calculated as the total number of times a participant experienced such an episode during 52-week Extension Study, divided by the total number of days of voiding kept in the participant's diary. This endpoint was based on the full analysis set population, which included all randomized participants who received at least one dose of study treatment and have either baseline data or at least one post-randomization observation for the analysis endpoint. This outcome measure included OAB Wet participants only. Baseline was defined as the value at Week 0 of the Base Study. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 52 of Extension Study | |

| End point values | Extension Study: vibegron 50 mg | Extension Study: vibegron 100 mg | Extension Study: tolterodine ER 4 mg | Extension Study: vibegron 100 mg + tolterodine ER 4 mg |
|--|------------------------------------|-------------------------------------|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 179 | 200 | 189 | 112 |
| Units: Avg Daily No of Urge Incontinence Eps | | | | |
| least squares mean (confidence interval 95%) | -2.43 (-2.72 to -2.14) | -2.15 (-2.43 to -1.87) | -2.23 (-2.51 to -1.94) | -2.44 (-2.79 to -2.09) |

Statistical analyses

| Statistical analysis title | Difference in LS Means |
|--|---|
| Statistical analysis description: | |
| Difference in LS Means: vibegron 100 mg + tolterodine ER 4 mg vs. vibegron 100 mg at Week 52 | |
| Comparison groups | Extension Study: vibegron 100 mg v Extension Study: vibegron 100 mg + tolterodine ER 4 mg |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.29 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.71 |
| upper limit | 0.13 |

| Statistical analysis title | Difference in LS Means |
|---|---|
| Comparison groups | Extension Study: vibegron 100 mg + tolterodine ER 4 mg v Extension Study: tolterodine ER 4 mg |
| Number of subjects included in analysis | 301 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.21 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.64 |
| upper limit | 0.21 |

Secondary: Extension Study: Change from Baseline in Average Daily Number of Total Incontinence Episodes at Week 52

| | |
|--|---|
| End point title | Extension Study: Change from Baseline in Average Daily Number of Total Incontinence Episodes at Week 52 |
| End point description: | |
| Participants were required to keep a voiding diary, recording the occurrence of each total incontinence episode. The average daily number of total incontinence episodes was calculated as the total number of times a participant experienced such an episode during 52-week Extension Study, divided by the total number of days of voiding kept in the participant's diary. This endpoint was based on the full analysis set population, which included all randomized participants who received at least one dose of study treatment and have either baseline data or at least one post-randomization observation for the analysis endpoint. This outcome measure included OAB Wet participants only. Baseline was defined as the value at Week 0 of the Base Study. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 52 of Extension Study | |

| End point values | Extension Study: vibegron 50 mg | Extension Study: vibegron 100 mg | Extension Study: tolterodine ER 4 mg | Extension Study: vibegron 100 mg + tolterodine ER 4 mg |
|---|---------------------------------|----------------------------------|--------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 179 | 200 | 189 | 112 |
| Units: Avg Daily No of Total Incontinence Eps | | | | |
| least squares mean (confidence interval 95%) | -2.7 (-3.03 to -2.36) | -2.42 (-2.74 to -2.09) | -2.5 (-2.83 to -2.17) | -2.48 (-2.89 to -2.07) |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Difference in LS Means |
| Comparison groups | Extension Study: vibegron 100 mg + tolterodine ER 4 mg v Extension Study: tolterodine ER 4 mg |
| Number of subjects included in analysis | 301 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in LS Means |
| Point estimate | 0.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.48 |
| upper limit | 0.51 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Difference in LS Means |
| Comparison groups | Extension Study: vibegron 100 mg + tolterodine ER 4 mg v Extension Study: vibegron 100 mg |

| | |
|---|------------------------|
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.07 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.56 |
| upper limit | 0.43 |

Secondary: Extension Study: Change From Baseline in Average Daily Number of Strong Urge Episodes at Week 52

| | |
|---|--|
| End point title | Extension Study: Change From Baseline in Average Daily Number of Strong Urge Episodes at Week 52 |
| End point description: | |
| Participants were required to keep a voiding diary, recording the occurrence of each strong urge episode. The average daily number of strong urge episodes was calculated as the total number of times a participant experienced such an episode during 52-week Extension Study, divided by the total number of days of voiding kept in the participant's diary. Baseline was defined as the value at Week 0 of the Base Study. This endpoint was based on the full analysis set population, which included all randomized participants who received at least one dose of study treatment and have either baseline data or at least one post-randomization observation for the analysis endpoint. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 52 of Extension Study | |

| End point values | Extension Study: vibegron 50 mg | Extension Study: vibegron 100 mg | Extension Study: tolterodine ER 4 mg | Extension Study: vibegron 100 mg + tolterodine ER 4 mg |
|---|---------------------------------|----------------------------------|--------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 223 | 246 | 240 | 134 |
| Units: Avg Daily Number of Strong Urge Episodes | | | | |
| least squares mean (confidence interval 95%) | -3.11 (-3.55 to -2.67) | -3.42 (-3.84 to -3) | -2.94 (-3.36 to -2.52) | -4.18 (-4.74 to -3.63) |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Difference in LS Means |
| Comparison groups | Extension Study: vibegron 100 mg + tolterodine ER 4 mg v Extension Study: vibegron 100 mg |

| | |
|---|------------------------|
| Number of subjects included in analysis | 380 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.45 |
| upper limit | -0.08 |

| | |
|---|--|
| Statistical analysis title | Difference in LS Means |
| Comparison groups | Extension Study: vibegron 100 mg + tolterodine ER 4 mg v Extension Study: tolterodine ER 4 mg |
| Number of subjects included in analysis | 374 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in LS Means |
| Point estimate | -1.24 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.93 |
| upper limit | -0.56 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Base Study/Part 1: up to 8 weeks; Base Study/Part 2: up to 4 weeks (time frame was additional 2 weeks for Parts 1 and 2 participants not continuing to Extension Study); Extension Study: up to 54 weeks (including 2 week follow-up).

Adverse event reporting additional description:

All participants as treated population consisted of all randomized participants who received at least one dose of study treatment. Participants were included in treatment group corresponding to study treatment they actually received. Two randomized participants who were not treated were excluded from Part 1: vibegron 50 mg arm.

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

Dictionary used

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

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

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | Part 1: placebo |
|-----------------------|-----------------|

Reporting group description:

Participants received two placebo matching vibegron tablets and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks.

| | |
|-----------------------|-----------------------|
| Reporting group title | Part 1: vibegron 3 mg |
|-----------------------|-----------------------|

Reporting group description:

Participants received one vibegron 3 mg tablet, one placebo matching vibegron tablet, and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks.

| | |
|-----------------------|------------------------|
| Reporting group title | Part 1: vibegron 15 mg |
|-----------------------|------------------------|

Reporting group description:

Participants received one vibegron 15 mg tablet, one placebo matching vibegron tablet, and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks.

| | |
|-----------------------|------------------------|
| Reporting group title | Part 1: vibegron 50 mg |
|-----------------------|------------------------|

Reporting group description:

Participants received one vibegron 50 mg tablet, one placebo matching vibegron tablet, and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks.

| | |
|-----------------------|-------------------------|
| Reporting group title | Part 1: vibegron 100 mg |
|-----------------------|-------------------------|

Reporting group description:

Participants received two vibegron 50 mg tablets and one placebo matching tolterodine ER capsule, taken orally each morning, for 8 weeks.

| | |
|-----------------------|-----------------------------|
| Reporting group title | Part 1: tolterodine ER 4 mg |
|-----------------------|-----------------------------|

Reporting group description:

Participants received one tolterodine ER 4 mg capsule and two placebo matching vibegron tablets, taken orally each morning, for 8 weeks.

| | |
|-----------------------|---|
| Reporting group title | Part 1: vibegron 50 mg + tolterodine ER 4 mg/vibegron 50 mg |
|-----------------------|---|

Reporting group description:

Participants received one vibegron 50 mg tablet and one placebo matching vibegron tablet, taken orally each morning, for 8 weeks. They also received one tolterodine ER 4 mg capsule for the first 4 weeks and one placebo matching tolterodine ER capsule for the second 4 weeks, both taken orally each morning.

| | |
|-----------------------|-----------------|
| Reporting group title | Part 2: placebo |
|-----------------------|-----------------|

Reporting group description:

Participants received two placebo matching vibegron tablets and one placebo matching tolterodine ER capsule, taken orally each morning, for 4 weeks.

| | |
|-----------------------|---|
| Reporting group title | Part 2: vibegron 100 mg + tolterodine ER 4 mg |
|-----------------------|---|

Reporting group description:

Participants received two vibegron 50 mg tablets and one tolterodine ER 4 mg capsule, taken orally each morning, for 4 weeks.

| | |
|-----------------------|-----------------------------|
| Reporting group title | Part 2: tolterodine ER 4 mg |
|-----------------------|-----------------------------|

Reporting group description:

Participants received one tolterodine ER 4 mg capsule and two placebo matching vibegron tablets, taken orally each morning, for 4 weeks.

| | |
|-----------------------|-------------------------|
| Reporting group title | Part 2: vibegron 100 mg |
|-----------------------|-------------------------|

Reporting group description:

Participants received two vibegron 50 mg tablets and one placebo matching tolterodine ER capsule, taken orally each morning, for 4 weeks.

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Extension Study: tolterodine ER 4 mg |
|-----------------------|--------------------------------------|

Reporting group description:

Participants received one tolterodine ER 4 mg capsule and two placebo matching vibegron tablets, taken orally each morning, for 52 weeks.

| | |
|-----------------------|----------------------------------|
| Reporting group title | Extension Study: vibegron 100 mg |
|-----------------------|----------------------------------|

Reporting group description:

Participants received two vibegron 50 mg tablets and one placebo matching tolterodine ER capsule, taken orally each morning, for 52 weeks.

| | |
|-----------------------|---------------------------------|
| Reporting group title | Extension Study: vibegron 50 mg |
|-----------------------|---------------------------------|

Reporting group description:

Participants received one vibegron 50 mg tablet, one placebo matching vibegron tablet, and one placebo matching tolterodine ER capsule, taken orally each morning, for 52 weeks.

| | |
|-----------------------|--|
| Reporting group title | Extension Study: vibegron 100 mg + tolterodine ER 4 mg |
|-----------------------|--|

Reporting group description:

Participants received two vibegron 50 mg tablets and one tolterodine ER 4 mg capsule, taken orally each morning, for 52 weeks.

| Serious adverse events | Part 1: placebo | Part 1: vibegron 3 mg | Part 1: vibegron 15 mg |
|---|-----------------|-----------------------|------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 141 (1.42%) | 1 / 144 (0.69%) | 0 / 134 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung adenocarcinoma stage IV | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 1 / 144 (0.69%) | 0 / 134 (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 |
| Ovarian cancer | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-----------------|-----------------|-----------------|
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 141 (0.71%) | 0 / 144 (0.00%) | 0 / 134 (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 |
| General disorders and administration site conditions | | | |
| Device dislocation | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 1 / 141 (0.71%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Contusion | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incisional hernia | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple fractures | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Multiple injuries | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle rupture | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Overdose | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Atrial septal defect | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Autoimmune thrombocytopenia | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus paralytic | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle haemorrhage | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Periarthritis | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Borrelia infection | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tracheobronchitis | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 141 (0.00%) | 0 / 144 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Part 1: vibegron 50 mg | Part 1: vibegron 100 mg | Part 1: tolterodine ER 4 mg |
|---|------------------------|-------------------------|-----------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 148 (0.68%) | 0 / 149 (0.00%) | 1 / 135 (0.74%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung adenocarcinoma stage IV | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian cancer | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Device dislocation | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 1 / 148 (0.68%) | 0 / 149 (0.00%) | 0 / 135 (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 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Contusion | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot fracture | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incisional hernia | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple fractures | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple injuries | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle rupture | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Overdose | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wrist fracture | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Atrial septal defect | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 1 / 135 (0.74%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Autoimmune thrombocytopenia | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus paralytic | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hepatotoxicity | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle haemorrhage | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Periarthritis | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Borrelia infection | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Cellulitis | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tracheobronchitis | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 149 (0.00%) | 0 / 135 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Part 1: vibegron 50 mg + tolterodine ER 4 mg/vibegron 50 mg | Part 2: placebo | Part 2: vibegron 100 mg + tolterodine ER 4 mg |
|---|---|-----------------|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 134 (0.75%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung adenocarcinoma stage IV | | | |

| | | | |
|--|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian cancer | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Device dislocation | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Contusion | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incisional hernia | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|----------------|-----------------|
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple fractures | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple injuries | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle rupture | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Overdose | | | |
| subjects affected / exposed | 1 / 134 (0.75%) | 0 / 64 (0.00%) | 0 / 110 (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 |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Atrial septal defect | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|----------------|-----------------|
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Autoimmune thrombocytopenia | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain lower | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus paralytic | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|----------------|-----------------|
| Muscle haemorrhage | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Periarthritis | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Borrelia infection | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tracheobronchitis | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| Dehydration | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 134 (0.00%) | 0 / 64 (0.00%) | 0 / 110 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Part 2: tolterodine ER 4 mg | Part 2: vibegron 100 mg | Extension Study: tolterodine ER 4 mg |
|---|-----------------------------|-------------------------|--------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 122 (1.64%) | 0 / 112 (0.00%) | 18 / 240 (7.50%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung adenocarcinoma stage IV | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian cancer | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| 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 | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Device dislocation | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| 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 | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Contusion | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot fracture | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 112 (0.00%) | 0 / 240 (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 |
| Incisional hernia | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple fractures | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple injuries | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle rupture | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Overdose | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Atrial septal defect | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Dizziness | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 112 (0.00%) | 0 / 240 (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 |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Autoimmune thrombocytopenia | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| 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 lower | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 112 (0.00%) | 0 / 240 (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 |
| Ileus | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus paralytic | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle haemorrhage | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Periarthritis | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| 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 | | | |
| Appendicitis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Borrelia infection | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 2 / 240 (0.83%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tracheobronchitis | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 0 / 240 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 112 (0.00%) | 1 / 240 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Extension Study: vibegron 100 mg | Extension Study: vibegron 50 mg | Extension Study: vibegron 100 mg + tolterodine ER 4 mg |
|--|-------------------------------------|------------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 8 / 248 (3.23%) | 14 / 223 (6.28%) | 1 / 134 (0.75%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from | 0 | 0 | 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast cancer | | | |
| subjects affected / exposed | 1 / 248 (0.40%) | 0 / 223 (0.00%) | 0 / 134 (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 |
| Lung adenocarcinoma stage IV | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian cancer | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Device dislocation | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 1 / 223 (0.45%) | 0 / 134 (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 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 1 / 248 (0.40%) | 0 / 223 (0.00%) | 0 / 134 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Contusion | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 1 / 223 (0.45%) | 0 / 134 (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 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incisional hernia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 248 (0.00%) | 1 / 223 (0.45%) | 0 / 134 (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 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple fractures | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 1 / 223 (0.45%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple injuries | | | |
| subjects affected / exposed | 1 / 248 (0.40%) | 0 / 223 (0.00%) | 0 / 134 (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 |
| Muscle rupture | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Overdose | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 1 / 223 (0.45%) | 0 / 134 (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 |
| Congenital, familial and genetic disorders | | | |
| Atrial septal defect | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 248 (0.40%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 248 (0.40%) | 0 / 223 (0.00%) | 0 / 134 (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 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 1 / 248 (0.40%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 2 / 223 (0.90%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 1 / 223 (0.45%) | 0 / 134 (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 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 1 / 223 (0.45%) | 0 / 134 (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 |

| | | | |
|--|-----------------|-----------------|-----------------|
| Autoimmune thrombocytopenia subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain lower subjects affected / exposed | 1 / 248 (0.40%) | 0 / 223 (0.00%) | 0 / 134 (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 |
| Gastroesophageal reflux disease subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus subjects affected / exposed | 0 / 248 (0.00%) | 1 / 223 (0.45%) | 0 / 134 (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 |
| Ileus paralytic subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute subjects affected / exposed | 1 / 248 (0.40%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hepatotoxicity subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 248 (0.00%) | 1 / 223 (0.45%) | 0 / 134 (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 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 1 / 223 (0.45%) | 0 / 134 (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 |
| Muscle haemorrhage | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 1 / 223 (0.45%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 2 / 223 (0.90%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Periarthritis | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Borrelia infection | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 1 / 134 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tracheobronchitis | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 1 / 223 (0.45%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 248 (0.00%) | 0 / 223 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | Part 1: placebo | Part 1: vibegron 3 mg | Part 1: vibegron 15 mg |
|---|-------------------|-----------------------|------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 32 / 141 (22.70%) | 21 / 144 (14.58%) | 27 / 134 (20.15%) |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 2 / 141 (1.42%) | 3 / 144 (2.08%) | 6 / 134 (4.48%) |
| occurrences (all) | 2 | 3 | 6 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 7 / 141 (4.96%) | 3 / 144 (2.08%) | 6 / 134 (4.48%) |
| occurrences (all) | 8 | 3 | 6 |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 3 / 141 (2.13%) | 5 / 144 (3.47%) | 6 / 134 (4.48%) |
| occurrences (all) | 4 | 5 | 6 |
| Dry mouth | | | |

| | | | |
|---|------------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 2 / 141 (1.42%) 2 | 5 / 144 (3.47%) 5 | 6 / 134 (4.48%) 6 |
| Diarrhoea subjects affected / exposed occurrences (all) | 5 / 141 (3.55%) 6 | 4 / 144 (2.78%) 4 | 2 / 134 (1.49%) 2 |
| Infections and infestations | | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 14 / 141 (9.93%) 15 | 3 / 144 (2.08%) 3 | 7 / 134 (5.22%) 8 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 2 / 141 (1.42%) 2 | 2 / 144 (1.39%) 3 | 1 / 134 (0.75%) 1 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 5 / 141 (3.55%) 5 | 5 / 144 (3.47%) 5 | 5 / 134 (3.73%) 5 |

| Non-serious adverse events | Part 1: vibegron 50 mg | Part 1: vibegron 100 mg | Part 1: tolterodine ER 4 mg |
|--|------------------------|-------------------------|-----------------------------|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 30 / 148 (20.27%) | 33 / 149 (22.15%) | 33 / 135 (24.44%) |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose subjects affected / exposed occurrences (all) | 4 / 148 (2.70%) 5 | 11 / 149 (7.38%) 11 | 5 / 135 (3.70%) 5 |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 6 / 148 (4.05%) 8 | 10 / 149 (6.71%) 13 | 4 / 135 (2.96%) 4 |
| Gastrointestinal disorders | | | |
| Constipation subjects affected / exposed occurrences (all) | 6 / 148 (4.05%) 6 | 1 / 149 (0.67%) 1 | 4 / 135 (2.96%) 4 |
| Dry mouth subjects affected / exposed occurrences (all) | 7 / 148 (4.73%) 8 | 3 / 149 (2.01%) 3 | 14 / 135 (10.37%) 14 |
| Diarrhoea | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 148 (0.68%) 1 | 5 / 149 (3.36%) 5 | 7 / 135 (5.19%) 8 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 8 / 148 (5.41%) | 6 / 149 (4.03%) | 3 / 135 (2.22%) |
| occurrences (all) | 9 | 6 | 3 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 3 / 149 (2.01%) | 2 / 135 (1.48%) |
| occurrences (all) | 0 | 3 | 2 |
| Urinary tract infection | | | |
| subjects affected / exposed | 8 / 148 (5.41%) | 6 / 149 (4.03%) | 4 / 135 (2.96%) |
| occurrences (all) | 8 | 6 | 5 |

| Non-serious adverse events | Part 1: vibegron 50 mg + tolterodine ER 4 mg/vibegron 50 mg | Part 2: placebo | Part 2: vibegron 100 mg + tolterodine ER 4 mg |
|---|---|-----------------|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 27 / 134 (20.15%) | 6 / 64 (9.38%) | 20 / 110 (18.18%) |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 2 / 134 (1.49%) | 0 / 64 (0.00%) | 1 / 110 (0.91%) |
| occurrences (all) | 2 | 0 | 1 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 6 / 134 (4.48%) | 2 / 64 (3.13%) | 7 / 110 (6.36%) |
| occurrences (all) | 7 | 4 | 7 |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 6 / 134 (4.48%) | 2 / 64 (3.13%) | 4 / 110 (3.64%) |
| occurrences (all) | 6 | 2 | 4 |
| Dry mouth | | | |
| subjects affected / exposed | 11 / 134 (8.21%) | 4 / 64 (6.25%) | 13 / 110 (11.82%) |
| occurrences (all) | 11 | 4 | 14 |
| Diarrhoea | | | |
| subjects affected / exposed | 6 / 134 (4.48%) | 0 / 64 (0.00%) | 1 / 110 (0.91%) |
| occurrences (all) | 6 | 0 | 1 |
| Infections and infestations | | | |

| | | | |
|---|----------------------|---------------------|----------------------|
| Nasopharyngitis subjects affected / exposed occurrences (all) | 3 / 134 (2.24%) 4 | 0 / 64 (0.00%) 0 | 2 / 110 (1.82%) 2 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 1 / 134 (0.75%) 1 | 0 / 64 (0.00%) 0 | 0 / 110 (0.00%) 0 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 7 / 134 (5.22%) 8 | 2 / 64 (3.13%) 2 | 5 / 110 (4.55%) 5 |

| Non-serious adverse events | Part 2: tolterodine ER 4 mg | Part 2: vibegron 100 mg | Extension Study: tolterodine ER 4 mg |
|--|--|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 21 / 122 (17.21%) | 5 / 112 (4.46%) | 70 / 240 (29.17%) |
| Injury, poisoning and procedural complications Accidental overdose subjects affected / exposed occurrences (all) | 1 / 122 (0.82%) 1 | 0 / 112 (0.00%) 0 | 1 / 240 (0.42%) 2 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 5 / 122 (4.10%) 6 | 2 / 112 (1.79%) 2 | 6 / 240 (2.50%) 7 |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Dry mouth subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) | 1 / 122 (0.82%) 1 8 / 122 (6.56%) 8 2 / 122 (1.64%) 2 | 1 / 112 (0.89%) 1 1 / 112 (0.89%) 1 0 / 112 (0.00%) 0 | 9 / 240 (3.75%) 9 18 / 240 (7.50%) 18 10 / 240 (4.17%) 10 |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection | 1 / 122 (0.82%) 1 | 4 / 112 (3.57%) 4 | 20 / 240 (8.33%) 25 |

| | | | |
|-----------------------------|-----------------|-----------------|-------------------|
| subjects affected / exposed | 1 / 122 (0.82%) | 1 / 112 (0.89%) | 10 / 240 (4.17%) |
| occurrences (all) | 1 | 1 | 10 |
| Urinary tract infection | | | |
| subjects affected / exposed | 8 / 122 (6.56%) | 2 / 112 (1.79%) | 27 / 240 (11.25%) |
| occurrences (all) | 8 | 2 | 44 |

| Non-serious adverse events | Extension Study: vibegron 100 mg | Extension Study: vibegron 50 mg | Extension Study: vibegron 100 mg + tolterodine ER 4 mg |
|---|-------------------------------------|------------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 73 / 248 (29.44%) | 59 / 223 (26.46%) | 38 / 134 (28.36%) |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 4 / 248 (1.61%) | 7 / 223 (3.14%) | 1 / 134 (0.75%) |
| occurrences (all) | 4 | 8 | 1 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 4 / 248 (1.61%) | 13 / 223 (5.83%) | 5 / 134 (3.73%) |
| occurrences (all) | 4 | 13 | 5 |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 7 / 248 (2.82%) | 2 / 223 (0.90%) | 9 / 134 (6.72%) |
| occurrences (all) | 7 | 2 | 9 |
| Dry mouth | | | |
| subjects affected / exposed | 8 / 248 (3.23%) | 8 / 223 (3.59%) | 6 / 134 (4.48%) |
| occurrences (all) | 8 | 8 | 6 |
| Diarrhoea | | | |
| subjects affected / exposed | 9 / 248 (3.63%) | 9 / 223 (4.04%) | 2 / 134 (1.49%) |
| occurrences (all) | 10 | 9 | 4 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 24 / 248 (9.68%) | 12 / 223 (5.38%) | 15 / 134 (11.19%) |
| occurrences (all) | 30 | 18 | 19 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 14 / 248 (5.65%) | 9 / 223 (4.04%) | 9 / 134 (6.72%) |
| occurrences (all) | 14 | 9 | 9 |
| Urinary tract infection | | | |

| | | | |
|-----------------------------|------------------|-------------------|-----------------|
| subjects affected / exposed | 22 / 248 (8.87%) | 27 / 223 (12.11%) | 8 / 134 (5.97%) |
| occurrences (all) | 33 | 42 | 8 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 31 March 2011 | Extension Study, Amendment 008-10. The primary reason for this amendment was to add the 12-month safety and efficacy extension to the base study 008-00. Patients completing the base had the opportunity to receive an additional 1 year of treatment if they participated in the extension. |
| 16 May 2012 | Extension Study, Amendment 008-11. The primary reason for this amendment was to update the extension study protocol with the dose of vibegron 100 mg that patients enrolled in Part 2 of the base study who completed it would receive in the extension. Vibegron 100 mg was updated as the monotherapy dose and the dose to be administered concomitantly with tolterodine ER 4 mg. The protocol previously had indicated "X" mg. |
| 16 May 2012 | Base Study, Amendment 008-02. The primary reasons for this amendment were as follows: 1) To allow for the inclusion of women of childbearing potential, expanding the age range from 40-75 to 18-75. 2) To update the base protocol with the dose of vibegron for Part 2 of the base study. Vibegron 100 mg was selected as the monotherapy dose and the dose to be administered concomitantly with tolterodine ER 4 mg. The protocol previously had indicated "X" mg. 3) To remove the exclusion criteria that had prohibited use of beta-adrenergic blocking agents (beta blockers), calcium channel blockers, direct acting vasodilators, angiotensin converting enzyme (ACE) inhibitors, and angiotensin II receptor antagonists. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported