



## Clinical trial results:

### A Study Evaluating the Efficacy and Safety of BOTOX® and Solifenacin in Patients with Overactive Bladder and Urinary Incontinence

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2012-003255-11 |
| Trial protocol           | GB DE CZ BE PL |
| Global end of trial date | 27 March 2015  |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 01 June 2016 |
| First version publication date | 01 June 2016 |

#### Trial information

##### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | 191622-125 |
|-----------------------|------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01767519 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Allergan Limited  |
| Sponsor organisation address | Allergan Limited Marlow International The Parkway, Marlow, United Kingdom, SL7 1YL                    |
| Public contact               | Allergan Limited EU Regulatory Dept, Allergan Limited, 44 1628 494444, ml-eu_reg_affairs@allergan.com |
| Scientific contact           | Allergan Limited EU Regulatory Dept, Allergan Limited, 44 1628 494444, ml-eu_reg_affairs@allergan.com |

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 25 September 2015 |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 30 September 2014 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 27 March 2015     |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy and safety of intradetrusor BOTOX 100 U compared to placebo in patients with overactive bladder (OAB) and urinary incontinence whose symptoms had not been adequately managed with anticholinergic therapy and were solifenacin-naïve.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 25 March 2013 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Belgium: 2         |
| Country: Number of subjects enrolled | Canada: 13         |
| Country: Number of subjects enrolled | Czech Republic: 49 |
| Country: Number of subjects enrolled | United Kingdom: 5  |
| Country: Number of subjects enrolled | Germany: 25        |
| Country: Number of subjects enrolled | Poland: 96         |
| Country: Number of subjects enrolled | United States: 166 |
| Worldwide total number of subjects   | 356                |
| EEA total number of subjects         | 177                |

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)      | 190 |
| From 65 to 84 years       | 160 |
| 85 years and over         | 6   |

## Subject disposition

### Recruitment

Recruitment details:

Participant Flow is for Treatment cycle 1, which is the double-blind portion of the study and includes the primary timepoint.

### Pre-assignment

Screening details:

Patients were screened up to 28 days prior to randomization on Day 1.

### Period 1

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

### Arms

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

Arm description:

Treatment Cycle 1: BOTOX injected at Day 1 with one solifenacin placebo capsule taken orally once daily for up to 24 weeks. After a minimum of 12 weeks, patients could request/qualify for a second BOTOX injection.

|  |  |
|--|--|
| Arm type                               | Experimental                               |
| Investigational medicinal product name | BOTOX®                                     |
| Investigational medicinal product code |  |
| Other name                             | onabotulinumtoxinA, botulinum toxin Type A |
| Pharmaceutical forms                   | Injection                                  |
| Routes of administration               | Intramuscular use                          |

Dosage and administration details:

Treatment Cycle 1: BOTOX injected at Day 1 with one solifenacin placebo capsule taken orally once daily for up to 24 weeks. After a minimum of 12 weeks, patients could request/qualify for a second BOTOX injection.

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | solifenacin |
|------------------|-------------|

Arm description:

Treatment Cycle 1: Oral solifenacin taken once daily starting at Day 1 for up to 24 weeks with intradetrusor injection of BOTOX placebo on Day 1. After a minimum of 12 weeks, patients could request/qualify for a BOTOX injection.

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

Dosage and administration details:

Treatment Cycle 1: Oral solifenacin taken once daily starting at Day 1 for up to 24 weeks with intradetrusor injection of BOTOX placebo on Day 1. After a minimum of 12 weeks, patients could request/qualify for a BOTOX injection.

|                  |         |
|------------------|---------|
| <b>Arm title</b> | placebo |
|------------------|---------|

Arm description:

Treatment Cycle 1: One solifenacin placebo capsule taken orally once daily starting at Day 1 for up to 24 weeks with an intradetrusor injection of BOTOX placebo at Day 1. After a minimum of 12 weeks,

patients could request/qualify for a BOTOX injection.

|  |                   |
|--|-------------------|
| Arm type                               | Placebo           |
| Investigational medicinal product name | placebo           |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Treatment Cycle 1: One solifenacin placebo capsule taken orally once daily starting at Day 1 for up to 24 weeks with an intradetrusor injection of BOTOX placebo at Day 1. After a minimum of 12 weeks, patients could request/qualify for a BOTOX injection.

| <b>Number of subjects in period 1</b> | <b>BOTOX®</b> | <b>solifenacin</b> | <b>placebo</b> |
|---------------------------------------|---------------|--------------------|----------------|
| Started                               | 145           | 151                | 60             |
| Completed                             | 131           | 138                | 55             |
| Not completed                         | 14            | 13                 | 5              |
| Other Reasons                         | 4             | 4                  | 2              |
| Adverse event, non-fatal              | 5             | 5                  | 1              |
| Personal Reasons                      | 1             | -                  | -              |
| Lost to follow-up                     | 3             | 1                  | 2              |
| Lack of efficacy                      | 1             | -                  | -              |
| Protocol deviation                    | -             | 3                  | -              |

## Baseline characteristics

### Reporting groups

|   |             |
|---|-------------|
| Reporting group title   | BOTOX®      |
| Reporting group description:  |             |
| Treatment Cycle 1: BOTOX injected at Day 1 with one solifenacin placebo capsule taken orally once daily for up to 24 weeks. After a minimum of 12 weeks, patients could request/qualify for a second BOTOX injection.   |             |
| Reporting group title   | solifenacin |
| Reporting group description:  |             |
| Treatment Cycle 1: Oral solifenacin taken once daily starting at Day 1 for up to 24 weeks with intradetrusor injection of BOTOX placebo on Day 1. After a minimum of 12 weeks, patients could request/qualify for a BOTOX injection.                          |             |
| Reporting group title   | placebo     |
| Reporting group description:  |             |
| Treatment Cycle 1: One solifenacin placebo capsule taken orally once daily starting at Day 1 for up to 24 weeks with an intradetrusor injection of BOTOX placebo at Day 1. After a minimum of 12 weeks, patients could request/qualify for a BOTOX injection. |             |

| Reporting group values                     | BOTOX®  | solifenacin | placebo |
|--|---------|-------------|---------|
| Number of subjects                         | 145     | 151         | 60      |
| Age categorical<br>Units: Subjects         |         |             |         |
| Adults (18-64 years)                       | 77      | 79          | 34      |
| From 65-84 years                           | 67      | 69          | 24      |
| 85 years and over                          | 1       | 3           | 2       |
| Age continuous<br>Units: years             |         |             |         |
| arithmetic mean                            | 61.4    | 62.9        | 61.2    |
| standard deviation                         | ± 12.82 | ± 11.79     | ± 12.19 |
| Gender, Male/Female<br>Units: Participants |         |             |         |
| Male                                       | 22      | 17          | 9       |
| Female                                     | 123     | 134         | 51      |
| Age, Customized<br>Units: Subjects         |         |             |         |
| <65 years                                  | 77      | 79          | 34      |
| ≥65 years                                  | 68      | 72          | 26      |

| Reporting group values             | Total |  |  |
|------------------------------------|-------|--|--|
| Number of subjects                 | 356   |  |  |
| Age categorical<br>Units: Subjects |       |  |  |
| Adults (18-64 years)               | 190   |  |  |
| From 65-84 years                   | 160   |  |  |
| 85 years and over                  | 6     |  |  |
| Age continuous<br>Units: years     |       |  |  |
| arithmetic mean                    |       |  |  |
| standard deviation                 | -     |  |  |

|  |     |  |  |
|--|-----|--|--|
| Gender, Male/Female<br>Units: Participants |     |  |  |
| Male                                       | 48  |  |  |
| Female                                     | 308 |  |  |
| Age, Customized<br>Units: Subjects         |     |  |  |
| <65 years                                  | 190 |  |  |
| ≥65 years                                  | 166 |  |  |

## End points

### End points reporting groups

|   |             |
|---|-------------|
| Reporting group title   | BOTOX®      |
| Reporting group description:<br>Treatment Cycle 1: BOTOX injected at Day 1 with one solifenacin placebo capsule taken orally once daily for up to 24 weeks. After a minimum of 12 weeks, patients could request/qualify for a second BOTOX injection.   |             |
| Reporting group title   | solifenacin |
| Reporting group description:<br>Treatment Cycle 1: Oral solifenacin taken once daily starting at Day 1 for up to 24 weeks with intradetrusor injection of BOTOX placebo on Day 1. After a minimum of 12 weeks, patients could request/qualify for a BOTOX injection.                          |             |
| Reporting group title   | placebo     |
| Reporting group description:<br>Treatment Cycle 1: One solifenacin placebo capsule taken orally once daily starting at Day 1 for up to 24 weeks with an intradetrusor injection of BOTOX placebo at Day 1. After a minimum of 12 weeks, patients could request/qualify for a BOTOX injection. |             |

### Primary: Change from Study Baseline in Number of Episodes of Urinary Incontinence in Treatment Cycle 1

|   |  |
|---|--|
| End point title   | Change from Study Baseline in Number of Episodes of Urinary Incontinence in Treatment Cycle 1 <sup>[1]</sup> |
| End point description:<br>Urinary incontinence is defined as involuntary loss of urine as recorded in a patient bladder diary in the 3 consecutive days prior to the study visit in Treatment Cycle 1. The number of incontinence episodes are averaged daily during this period. A negative number change from baseline indicates an improvement and a positive number change from baseline indicates a worsening. |  |
| End point type  | Primary  |
| End point timeframe:<br>Study Baseline, Week 12   |  |

Notes:

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

Justification: No Statistical Analysis is reported for this outcome measure

| End point values                      | BOTOX®          | solifenacin     | placebo         |  |
|---------------------------------------|-----------------|-----------------|-----------------|--|
| Subject group type                    | Reporting group | Reporting group | Reporting group |  |
| Number of subjects analysed           | 145             | 151             | 60              |  |
| Units: Incontinence Episodes          |                 |                 |                 |  |
| arithmetic mean (standard deviation)  |                 |                 |                 |  |
| Study Baseline                        | 4.86 (± 3.206)  | 5.23 (± 3.333)  | 4.38 (± 2.485)  |  |
| Change from Study Baseline at Week 12 | -3.1 (± 2.799)  | -2.66 (± 3.059) | -0.98 (± 2.417) |  |

### Statistical analyses

No statistical analyses for this end point



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**Primary: Percentage of Patients with 100% Reduction in Incontinence Episodes in Treatment Cycle 1**

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|                 |   |
|-----------------|---|
| End point title | Percentage of Patients with 100% Reduction in Incontinence Episodes in Treatment Cycle 1 <sup>[2]</sup> |
|-----------------|---|

End point description:

Urinary incontinence is defined as involuntary loss of urine as recorded in a patient bladder diary in the 3 consecutive days prior to the study visit in Treatment Cycle 1. The number of incontinence episodes are averaged daily during this period and compared to baseline to determine 100% reduction in episodes.

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

End point timeframe:

Study Baseline, Week 12

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 is reported for this outcome measure

| End point values              | BOTOX®          | solifenacin     | placebo         |  |
|-------------------------------|-----------------|-----------------|-----------------|--|
| Subject group type            | Reporting group | Reporting group | Reporting group |  |
| Number of subjects analysed   | 145             | 151             | 60              |  |
| Units: Percentage of Patients |                 |                 |                 |  |
| number (not applicable)       | 33.8            | 24.5            | 11.7            |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Percentage of Patients with a Positive Response on the Single-Item Treatment Benefit Scale During Treatment Cycle 1**

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|                 |   |
|-----------------|---|
| End point title | Percentage of Patients with a Positive Response on the Single-Item Treatment Benefit Scale During Treatment Cycle 1 |
|-----------------|---|

End point description:

A positive treatment response on the Treatment Benefit Scale is a score of either 1 or 2, representing 'greatly improved' or 'improved.'

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

End point timeframe:

Week 12

| End point values              | BOTOX®              | solifenacin       | placebo             |  |
|-------------------------------|---------------------|-------------------|---------------------|--|
| Subject group type            | Reporting group     | Reporting group   | Reporting group     |  |
| Number of subjects analysed   | 145                 | 151               | 60                  |  |
| Units: Percentage of Patients |                     |                   |                     |  |
| number (confidence interval)  | 71.3 (62.9 to 78.7) | 74 (66.1 to 80.9) | 44.8 (31.7 to 58.5) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Study Baseline in the Number of Micturition Episodes in Treatment Cycle 1

|   |   |
|---|---|
| End point title   | Change from Study Baseline in the Number of Micturition Episodes in Treatment Cycle 1 |
| End point description:<br>The number of micturition episodes (the number of times a patient urinates into the toilet) in Treatment Cycle 1 was recorded by the patient in a bladder diary during 3 consecutive days in the week prior to the visit. A negative number change from baseline indicates an improvement and a positive number change from baseline indicates a worsening. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Study Baseline, Week 12   |   |

| End point values                                   | BOTOX®          | solifenacin     | placebo         |  |
|--|-----------------|-----------------|-----------------|--|
| Subject group type                                 | Reporting group | Reporting group | Reporting group |  |
| Number of subjects analysed                        | 145             | 151             | 60              |  |
| Units: Micturition Episodes                        |                 |                 |                 |  |
| arithmetic mean (standard deviation)               |                 |                 |                 |  |
| Study Baseline                                     | 10.74 (± 2.52)  | 10.4 (± 2.665)  | 10.18 (± 2.491) |  |
| Change from Study Baseline at Wk 12 (N=135,144,57) | -2.4 (± 2.827)  | -2.03 (± 2.833) | -0.87 (± 2.413) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Study Baseline in the Number of Nocturia Episodes in Treatment Cycle 1

|   |  |
|---|--|
| End point title   | Change from Study Baseline in the Number of Nocturia Episodes in Treatment Cycle 1 |
| End point description:<br>Nocturia episodes are measured over a 3 day diary prior to each visit in Treatment Cycle 1. A nocturia episode is a void (urinating into the toilet) that interrupts one's sleep. A negative number change from baseline indicates an improvement and a positive number change from baseline indicates a worsening. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Study Baseline, Week 12   |  |

| End point values                                      | BOTOX®          | solifenacin     | placebo         |  |
|---|-----------------|-----------------|-----------------|--|
| Subject group type                                    | Reporting group | Reporting group | Reporting group |  |
| Number of subjects analysed                           | 145             | 151             | 60              |  |
| Units: Nocturia Episodes                              |                 |                 |                 |  |
| arithmetic mean (standard deviation)                  |                 |                 |                 |  |
| Study Baseline  | 2.03 (± 1.159)  | 2.04 (± 1.083)  | 1.98 (± 0.937)  |  |
| Change from Study Baseline at Wk 12<br>(N=135,144,57) | -0.54 (± 1.195) | -0.49 (± 1.133) | -0.23 (± 1.091) |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Study Baseline in the Role Limitations Domain on the King's Health Questionnaire in Treatment Cycle 1

|                 |   |
|-----------------|---|
| End point title | Change from Study Baseline in the Role Limitations Domain on the King's Health Questionnaire in Treatment Cycle 1 |
|-----------------|---|

End point description:

The King's Health Questionnaire is a disease-specific questionnaire that measures the quality of life of patients with urinary incontinence. The questionnaire consists of 7 domains, including the role limitations domain. Domain scores range from 0 to 100, with a lower score indicating a preferable health status. A negative number change from baseline indicates an improvement and a positive number change from baseline indicates a worsening.

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

End point timeframe:

Study Baseline, Week 12

| End point values                                      | BOTOX®           | solifenacin       | placebo           |  |
|---|------------------|-------------------|-------------------|--|
| Subject group type                                    | Reporting group  | Reporting group   | Reporting group   |  |
| Number of subjects analysed                           | 145              | 150               | 59                |  |
| Units: Scores on a Scale                              |                  |                   |                   |  |
| arithmetic mean (standard deviation)                  |                  |                   |                   |  |
| Study Baseline  | 76.09 (± 24.281) | 72.11 (± 26.581)  | 81.36 (± 20.781)  |  |
| Change from Study Baseline at Wk 12<br>(N=135,145,57) | -30 (± 33.259)   | -23.79 (± 31.899) | -17.25 (± 29.033) |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Study Baseline in the Social Limitations Domain on the King's Health Questionnaire in Treatment Cycle 1

|                 |   |
|-----------------|---|
| End point title | Change from Study Baseline in the Social Limitations Domain on the King's Health Questionnaire in Treatment Cycle 1 |
|-----------------|---|

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**End point description:**

The King's Health Questionnaire is a disease-specific questionnaire that measures the quality of life of patients with urinary incontinence. The questionnaire consists of 7 domains, including the social limitations domain. Domain scores range from 0 to 100, with a lower score indicating a preferable health status. A negative number change from baseline indicates an improvement and a positive number change from baseline indicates a worsening.

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

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**End point timeframe:**

Study Baseline, Week 12

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| End point values                                   | BOTOX®            | solifenacin      | placebo          |  |
|--|-------------------|------------------|------------------|--|
| Subject group type                                 | Reporting group   | Reporting group  | Reporting group  |  |
| Number of subjects analysed                        | 145               | 150              | 59               |  |
| Units: Scores on a Scale                           |                   |                  |                  |  |
| arithmetic mean (standard deviation)               |                   |                  |                  |  |
| Study Baseline                                     | 59.66 (± 21.442)  | 56.22 (± 22.708) | 62.57 (± 22.551) |  |
| Change from Study Baseline at Wk 12 (N=135,145,57) | -13.46 (± 21.906) | -12.7 (± 21.361) | -7.6 (± 21.667)  |  |

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**Statistical analyses**

No statistical analyses for this end point

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## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from signing the informed consent to the end of study.

Adverse event reporting additional description:

The safety population includes all patients who received at least 1 dose of study medication. The safety population is used to assess adverse events and serious adverse events. Adverse events and serious adverse events are displayed for the placebo-controlled treatment Cycle 1.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 18.0 |
|--------------------|------|

### Reporting groups

|                       |        |
|-----------------------|--------|
| Reporting group title | BOTOX® |
|-----------------------|--------|

Reporting group description:

Treatment Cycle 1: BOTOX injected at Day 1 with one solifenacin placebo capsule taken orally once daily for up to 24 weeks. After a minimum of 12 weeks, patients could request/qualify for a second BOTOX injection.

|                       |         |
|-----------------------|---------|
| Reporting group title | placebo |
|-----------------------|---------|

Reporting group description:

Treatment Cycle 1: One solifenacin placebo capsule taken orally once daily starting at Day 1 for up to 24 weeks with an intradetrusor injection of BOTOX placebo at Day 1. After a minimum of 12 weeks, patients could request/qualify for a BOTOX injection.

|                       |             |
|-----------------------|-------------|
| Reporting group title | solifenacin |
|-----------------------|-------------|

Reporting group description:

Treatment Cycle 1: Oral solifenacin taken once daily starting at Day 1 for up to 24 weeks with intradetrusor injection of BOTOX placebo on Day 1. After a minimum of 12 weeks, patients could request/qualify for a BOTOX injection.

| Serious adverse events  | BOTOX®          | placebo        | solifenacin     |
|---|-----------------|----------------|-----------------|
| Total subjects affected by serious adverse events                   |                 |                |                 |
| subjects affected / exposed   | 6 / 145 (4.14%) | 2 / 60 (3.33%) | 6 / 147 (4.08%) |
| 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   | 1 / 145 (0.69%) | 0 / 60 (0.00%) | 1 / 147 (0.68%) |
| occurrences causally related to treatment / all                     | 0 / 1           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0          | 0 / 0           |
| Injury, poisoning and procedural complications                      |                 |                |                 |
| Limb traumatic amputation   |                 |                |                 |

|   |                                     |                |                 |
|---|-------------------------------------|----------------|-----------------|
| subjects affected / exposed                     | 1 / 145 (0.69%)                     | 0 / 60 (0.00%) | 0 / 147 (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                               |                                     |                |                 |
| Angina pectoris                                 |                                     |                |                 |
| subjects affected / exposed                     | 1 / 145 (0.69%)                     | 0 / 60 (0.00%) | 0 / 147 (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           |
| Bradycardia                                     |                                     |                |                 |
| subjects affected / exposed                     | 1 / 145 (0.69%)                     | 0 / 60 (0.00%) | 0 / 147 (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 / 145 (0.69%)                     | 0 / 60 (0.00%) | 0 / 147 (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                        |                                     |                |                 |
| Migraine  |                                     |                |                 |
| alternative assessment type: Non-systematic     |                                     |                |                 |
| subjects affected / exposed                     | 1 / 145 (0.69%)                     | 0 / 60 (0.00%) | 0 / 147 (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           |
| Dizziness                                       |                                     |                |                 |
| alternative assessment type: Non-systematic     |                                     |                |                 |
| subjects affected / exposed                     | 0 / 145 (0.00%)                     | 1 / 60 (1.67%) | 0 / 147 (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           |
| Reproductive system and breast disorders        |                                     |                |                 |
| Endometrial hyperplasia                         |                                     |                |                 |
|   | Additional description: FEMALE ONLY |                |                 |
| subjects affected / exposed                     | 0 / 145 (0.00%)                     | 0 / 60 (0.00%) | 1 / 147 (0.68%) |
| occurrences causally related to treatment / all | 0 / 0                               | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0                               | 0 / 0          | 0 / 0           |
| Hepatobiliary disorders                         |                                     |                |                 |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| Cholelithiasis                                  |                 |                |                 |
| subjects affected / exposed                     | 0 / 145 (0.00%) | 0 / 60 (0.00%) | 1 / 147 (0.68%) |
| 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   |                 |                |                 |
| alternative assessment type: Non-systematic     |                 |                |                 |
| subjects affected / exposed                     | 1 / 145 (0.69%) | 0 / 60 (0.00%) | 0 / 147 (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           |
| Polysubstance dependence                        |                 |                |                 |
| subjects affected / exposed                     | 0 / 145 (0.00%) | 0 / 60 (0.00%) | 1 / 147 (0.68%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Renal and urinary disorders                     |                 |                |                 |
| Haematuria                                      |                 |                |                 |
| subjects affected / exposed                     | 0 / 145 (0.00%) | 1 / 60 (1.67%) | 0 / 147 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Musculoskeletal and connective tissue disorders |                 |                |                 |
| Osteoarthritis                                  |                 |                |                 |
| alternative assessment type: Non-systematic     |                 |                |                 |
| subjects affected / exposed                     | 0 / 145 (0.00%) | 0 / 60 (0.00%) | 2 / 147 (1.36%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 2           |
| 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                            | BOTOX®            | placebo          | solifenacin       |
|---|-------------------|------------------|-------------------|
| Total subjects affected by non-serious adverse events |                   |                  |                   |
| subjects affected / exposed                           | 95 / 145 (65.52%) | 27 / 60 (45.00%) | 78 / 147 (53.06%) |
| Investigations  |                   |                  |                   |
| Residual urine volume                                 |                   |                  |                   |
| subjects affected / exposed                           | 10 / 145 (6.90%)  | 1 / 60 (1.67%)   | 0 / 147 (0.00%)   |
| occurrences (all)                                     | 10                | 1                | 0                 |

|   |   |  |   |
|---|---|--|---|
| Gastrointestinal disorders<br>Dry mouth<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)  | 4 / 145 (2.76%)<br>4  | 0 / 60 (0.00%)<br>0  | 12 / 147 (8.16%)<br>12  |
| Renal and urinary disorders<br>Urinary retention<br>subjects affected / exposed<br>occurrences (all)<br><br>Dysuria<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)  | 10 / 145 (6.90%)<br>12<br><br>6 / 145 (4.14%)<br>6                                | 0 / 60 (0.00%)<br>0<br><br>2 / 60 (3.33%)<br>2                             | 1 / 147 (0.68%)<br>2<br><br>8 / 147 (5.44%)<br>11                                 |
| Infections and infestations<br>Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)<br><br>Bacteriuria<br>subjects affected / exposed<br>occurrences (all)<br><br>Nasopharyngitis<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all) | 37 / 145 (25.52%)<br>53<br><br>11 / 145 (7.59%)<br>15<br><br>2 / 145 (1.38%)<br>2 | 6 / 60 (10.00%)<br>7<br><br>3 / 60 (5.00%)<br>3<br><br>3 / 60 (5.00%)<br>3 | 15 / 147 (10.20%)<br>19<br><br>14 / 147 (9.52%)<br>15<br><br>2 / 147 (1.36%)<br>2 |



## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported