



Clinical trial results:

Long-term Extension Study of BOTOX® in the Treatment of Urinary Incontinence Due to Neurogenic Detrusor Overactivity in Patients 5 to 17 Years of Age

Summary

| | |
|--------------------------|----------------------|
| EudraCT number | 2012-004898-30 |
| Trial protocol | BE CZ AT IT DE PL FR |
| Global end of trial date | 03 October 2019 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 19 April 2020 |
| First version publication date | 19 April 2020 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | 191622-121 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01852058 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Allergan plc |
| Sponsor organisation address | 1st Floor, Marlow International, The Parkway, Marlow Buckinghamshire, United Kingdom, SL7 1YL |
| Public contact | Clinical Trials Registry Team, Allergan plc, 001 8772778566, IR-CTRegistration@allergan.com |
| Scientific contact | Therapeutic Area, Head, Allergan plc, 001 862-261-7000, IR- CTRegistration@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? | Yes |

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 03 October 2019 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 03 October 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial is to evaluate the long-term safety and efficacy of onabotulinumtoxinA (botulinum toxin Type A; BOTOX®) for the treatment of urinary incontinence due to neurogenic detrusor overactivity in participants who successfully completed Study 191622-120 (NCT01852045).

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 | 11 January 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Belgium: 13 |
| Country: Number of subjects enrolled | Czech Republic: 5 |
| Country: Number of subjects enrolled | France: 11 |
| Country: Number of subjects enrolled | Italy: 5 |
| Country: Number of subjects enrolled | Poland: 22 |
| Country: Number of subjects enrolled | Canada: 2 |
| Country: Number of subjects enrolled | Turkey: 2 |
| Country: Number of subjects enrolled | United States: 35 |
| Worldwide total number of subjects | 95 |
| EEA total number of subjects | 56 |

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) | 47 |
| Adolescents (12-17 years) | 48 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants who successfully completed Study 191622-120 (NCT01852045) were enrolled in this study and were followed for up to an additional 60 weeks.

Pre-assignment

Screening details:

Data from the participant's participation in this extension Study 191622-121 (121) were integrated with the corresponding participant's data from the preceding Study 191622-120 (120).

Period 1

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

Arms

| | |
|------------------------------|-------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | OnabotulinumtoxinA 50 U |

Arm description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | OnabotulinumtoxinA |
| Investigational medicinal product code | |
| Other name | BOTOX® botulinum toxin Type A |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

OnabotulinumtoxinA injected into the detrusor wall. Treatments were administered as needed with a minimum of a 12-week interval between doses.

| | |
|------------------|--------------------------|
| Arm title | OnabotulinumtoxinA 100 U |
|------------------|--------------------------|

Arm description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|--|-----------------------------------|
| Arm type | Experimental |
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| Investigational medicinal product code | |
| Other name | BOTOX® botulinum toxin Type A |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

OnabotulinumtoxinA injected into the detrusor wall. Treatments were administered as needed with a minimum of a 12-week interval between doses.

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| Investigational medicinal product code | |
| Other name | BOTOX® botulinum toxin Type A |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

OnabotulinumtoxinA injected into the detrusor wall. Treatments were administered as needed with a minimum of a 12-week interval between doses.

| Number of subjects in period 1 | OnabotulinumtoxinA 50 U | OnabotulinumtoxinA 100 U | OnabotulinumtoxinA 200 U |
|---------------------------------------|----------------------------|-----------------------------|-----------------------------|
| Started | 31 | 39 | 25 |
| Completed | 22 | 36 | 17 |
| Not completed | 9 | 3 | 8 |
| Adverse event, non-fatal | 1 | - | - |
| Protocol Deviation | 1 | - | - |
| Withdrawal by Subject | 3 | 1 | 1 |
| Lost to follow-up | 2 | - | - |
| Reason not Specified | 1 | 2 | 6 |
| Lack of efficacy | 1 | - | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------------------|
| Reporting group title | OnabotulinumtoxinA 50 U |
|-----------------------|-------------------------|

Reporting group description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|-----------------------|--------------------------|
| Reporting group title | OnabotulinumtoxinA 100 U |
|-----------------------|--------------------------|

Reporting group description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|-----------------------|--------------------------|
| Reporting group title | OnabotulinumtoxinA 200 U |
|-----------------------|--------------------------|

Reporting group description:

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| Reporting group values | OnabotulinumtoxinA 50 U | OnabotulinumtoxinA 100 U | OnabotulinumtoxinA 200 U |
|---|----------------------------|-----------------------------|-----------------------------|
| Number of subjects | 31 | 39 | 25 |
| Age categorical Units: Subjects | | | |
| Children (2-11 years) | 15 | 22 | 10 |
| Adolescents (12-17 years) | 16 | 17 | 15 |
| Age Continuous Units: years | | | |
| arithmetic mean | 11.7 | 10.8 | 11.7 |
| standard deviation | ± 3.49 | ± 3.36 | ± 3.22 |
| Sex: Female, Male Units: participants | | | |
| Female | 17 | 14 | 13 |
| Male | 14 | 25 | 12 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| White | 22 | 28 | 18 |
| Black or African American | 6 | 3 | 2 |
| Asian | 1 | 2 | 0 |
| Hispanic | 1 | 3 | 3 |
| Other | 1 | 3 | 2 |

| Reporting group values | Total | | |
|------------------------------------|-------|--|--|
| Number of subjects | 95 | | |
| Age categorical Units: Subjects | | | |
| Children (2-11 years) | 47 | | |

| | | | |
|---------------------------|----|--|--|
| Adolescents (12-17 years) | 48 | | |
|---------------------------|----|--|--|

| | | | |
|---|----|--|--|
| Age Continuous Units: years arithmetic mean standard deviation | - | | |
| Sex: Female, Male Units: participants | | | |
| Female | 44 | | |
| Male | 51 | | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| White | 68 | | |
| Black or African American | 11 | | |
| Asian | 3 | | |
| Hispanic | 7 | | |
| Other | 6 | | |

End points

End points reporting groups

| | |
|---|--------------------------|
| Reporting group title | OnabotulinumtoxinA 50 U |
| Reporting group description: Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg). | |
| Reporting group title | OnabotulinumtoxinA 100 U |
| Reporting group description: Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg). | |
| Reporting group title | OnabotulinumtoxinA 200 U |
| Reporting group description: Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg). | |
| Subject analysis set title | OnabotulinumtoxinA 50 U |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg). | |
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| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg). | |
| Subject analysis set title | OnabotulinumtoxinA 200 U |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg). | |
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Subject analysis set description:

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| | |
|----------------------------|--------------------------|
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| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
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| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|----------------------------|---|
| Subject analysis set title | OnabotulinumtoxinA 50 U (Treatment Cycle 1) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 1. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|----------------------------|--|
| Subject analysis set title | OnabotulinumtoxinA 100 U (Treatment Cycle 1) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 1. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|----------------------------|--|
| Subject analysis set title | OnabotulinumtoxinA 200 U (Treatment Cycle 1) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 1. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|----------------------------|---|
| Subject analysis set title | OnabotulinumtoxinA 50 U (Treatment Cycle 2) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 2. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|----------------------------|--|
| Subject analysis set title | OnabotulinumtoxinA 100 U (Treatment Cycle 2) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 2. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|----------------------------|--|
| Subject analysis set title | OnabotulinumtoxinA 200 U (Treatment Cycle 2) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 2. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|----------------------------|---|
| Subject analysis set title | OnabotulinumtoxinA 50 U (Treatment Cycle 3) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 3. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|----------------------------|--|
| Subject analysis set title | OnabotulinumtoxinA 100 U (Treatment Cycle 3) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 3. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|----------------------------|--|
| Subject analysis set title | OnabotulinumtoxinA 200 U (Treatment Cycle 3) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 3. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|----------------------------|---|
| Subject analysis set title | OnabotulinumtoxinA 50 U (Treatment Cycle 4) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 4. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|----------------------------|--|
| Subject analysis set title | OnabotulinumtoxinA 100 U (Treatment Cycle 4) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 4. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|----------------------------|--|
| Subject analysis set title | OnabotulinumtoxinA 200 U (Treatment Cycle 4) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 4. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Primary: Change From Study Baseline in the Daily Normalized Daytime Average Number of Urinary Incontinence Episodes in Treatment Cycle 1

| | |
|-----------------|--|
| End point title | Change From Study Baseline in the Daily Normalized Daytime Average Number of Urinary Incontinence Episodes in Treatment Cycle 1 ^[1] |
|-----------------|--|

End point description:

Urinary incontinence was defined as involuntary loss of urine as recorded by the participant in a bladder diary during 2 consecutive days in the week prior to the study visit (normalized to a 12 hour daytime period). Daytime is defined as the time between waking up to start the day and going to bed to sleep for the night. The number of daily daytime incontinence episodes were averaged during the 2-day period. A negative change from Baseline indicates improvement. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into the extension study who received at least 1 BOTOX treatment over the course of the total evaluation period, starting from their first treatment in Study 120. 'n' is the number of participants with evaluable data at the given time point.

| | |
|---|---------|
| End point type | Primary |
| End point timeframe: | |
| Study Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 1 | |
| 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: Statistical analyses were not available | |

| End point values | Onabotulinumt oxinA 50 U (Treatment Cycle 1) | Onabotulinumt oxinA 100 U (Treatment Cycle 1) | Onabotulinumt oxinA 200 U (Treatment Cycle 1) | |
|--|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 31 | 39 | 25 | |
| Units: urinary incontinence episodes per day | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n= 31, 39, 25) | 2.66 (± 0.876) | 2.97 (± 1.135) | 3.99 (± 5.492) | |
| Change from Baseline to Week 6 (n= 30, 36, 23) | -1.19 (± 1.156) | -1.39 (± 1.585) | -2.19 (± 5.738) | |

Statistical analyses

No statistical analyses for this end point

Primary: Change From Study Baseline in the Daily Normalized Daytime Average Number of Urinary Incontinence Episodes in Treatment Cycle 2

| | |
|-----------------|--|
| End point title | Change From Study Baseline in the Daily Normalized Daytime Average Number of Urinary Incontinence Episodes in Treatment Cycle 2 ^[2] |
|-----------------|--|

End point description:

Urinary incontinence was defined as involuntary loss of urine as recorded by the participant in a bladder diary during 2 consecutive days in the week prior to the study visit (normalized to a 12 hour daytime period). Daytime is defined as the time between waking up to start the day and going to bed to sleep for the night. The number of daily daytime incontinence episodes were averaged during the 2-day period. A negative change from Baseline indicates improvement. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into the extension study who received at least 1 BOTOX treatment over the course of the total evaluation period, starting from their first treatment in Study 120. 'n' is the number of participants with evaluable data at the given time point.

| | |
|---|---------|
| End point type | Primary |
| End point timeframe: | |
| Study Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 2 | |
| 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: Statistical analyses were not available | |

| End point values | Onabotulinumt oxinA 50 U (Treatment Cycle 2) | Onabotulinumt oxinA 100 U (Treatment Cycle 2) | Onabotulinumt oxinA 200 U (Treatment Cycle 2) | |
|--|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 9 | 45 | 36 | |
| Units: urinary incontinence episodes per day | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=9, 45, 36) | 2.57 (± 0.937) | 2.80 (± 0.915) | 3.83 (± 4.623) | |
| Change from Baseline to Week 6 (n=6, 44, 34) | -1.07 (± 2.092) | -1.70 (± 1.331) | -1.64 (± 1.906) | |

Statistical analyses

No statistical analyses for this end point

Primary: Change From Study Baseline in the Daily Normalized Daytime Average Number of Urinary Incontinence Episodes in Treatment Cycle 3

| | |
|-----------------|--|
| End point title | Change From Study Baseline in the Daily Normalized Daytime Average Number of Urinary Incontinence Episodes in Treatment Cycle 3 ^[3] |
|-----------------|--|

End point description:

Urinary incontinence was defined as involuntary loss of urine as recorded by the participant in a bladder diary during 2 consecutive days in the week prior to the study visit (normalized to a 12 hour daytime period). Daytime is defined as the time between waking up to start the day and going to bed to sleep for the night. The number of daily daytime incontinence episodes were averaged during the 2-day period. A negative change from Baseline indicates improvement. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into the extension study who received at least 1 BOTOX treatment over the course of the total evaluation period, starting from their first treatment in Study 120. 'n' is the number of participants with evaluable data at the given time point.

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

End point timeframe:

Study Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 3

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: Statistical analyses were not available

| End point values | Onabotulinumt oxinA 50 U (Treatment Cycle 3) | Onabotulinumt oxinA 100 U (Treatment Cycle 3) | Onabotulinumt oxinA 200 U (Treatment Cycle 3) | |
|--|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 5 | 16 | 34 | |
| Units: urinary incontinence episodes per day | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=5, 16, 34) | 2.48 (± 0.228) | 2.94 (± 0.923) | 3.80 (± 4.678) | |
| Change from Baseline to Week 6 (n=5, 16, 33) | -1.92 (± 0.858) | -1.73 (± 1.057) | -2.74 (± 4.833) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment Emergent Adverse Events (TEAEs) and Serious Treatment Emergent Adverse Events (STEAEs)

| | |
|-----------------|--|
| End point title | Number of Participants with Treatment Emergent Adverse Events (TEAEs) and Serious Treatment Emergent Adverse Events (STEAEs) |
|-----------------|--|

End point description:

Adverse event: any untoward medical occurrence in patient or clinical investigation participant administered pharmaceutical product, which does not necessarily have causal relationship with treatment. It can therefore be any unfavorable and unintended sign (including abnormal laboratory finding), symptom, or disease temporally associated with use of medicinal (investigational) product, whether or not related to medicinal product. Serious AE (SAE): any AE resulted in death, inpatient hospitalization/prolongation of existing hospitalization, persistent or significant disability/incapacity, life threatening, congenital anomaly/birth defect or important medical event. TEAE/STEAE: any new AE/worsening of existing condition after initiation of treatment. Data summarized under respective treatments participants received in corresponding treatment cycles. BOTOX-treated Population: all participants enrolled into Study 121, received ≥ 1 BOTOX treatment during total evaluation period, from first treatment in Study 120.

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

End point timeframe:

First injection on Day 1 in Study 120 through completion of Study 121 (Up to 108 weeks)

| End point values | OnabotulinumtoxinA 50 U (Treatment Cycle 1) | OnabotulinumtoxinA 100 U (Treatment Cycle 1) | OnabotulinumtoxinA 200 U (Treatment Cycle 1) | OnabotulinumtoxinA 50 U (Treatment Cycle 2) |
|-----------------------------|---|--|--|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 31 | 39 | 25 | 9 |
| Units: participants | | | | |
| TEAEs | 23 | 31 | 19 | 7 |
| STEAEs | 2 | 3 | 1 | 0 |

| End point values | OnabotulinumtoxinA 100 U (Treatment Cycle 2) | OnabotulinumtoxinA 200 U (Treatment Cycle 2) | OnabotulinumtoxinA 50 U (Treatment Cycle 3) | OnabotulinumtoxinA 100 U (Treatment Cycle 3) |
|-----------------------------|--|--|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 45 | 36 | 5 | 16 |
| Units: participants | | | | |
| TEAEs | 34 | 31 | 4 | 10 |
| STEAEs | 5 | 6 | 0 | 1 |

| End point values | Onabotulinumt oxinA 200 U (Treatment Cycle 3) | Onabotulinumt oxinA 50 U (Treatment Cycle 4) | Onabotulinumt oxinA 100 U (Treatment Cycle 4) | Onabotulinumt oxinA 200 U (Treatment Cycle 4) |
|-----------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 34 | 3 | 4 | 4 |
| Units: participants | | | | |
| TEAEs | 21 | 3 | 2 | 4 |
| STAEs | 2 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with $\geq 50\%$, $\geq 75\%$, $\geq 90\%$, and $\geq 100\%$ Reduction from Baseline in the Number of Normalized Daytime Urinary Incontinence Episodes in Treatment Cycle 1

| | |
|-----------------|---|
| End point title | Percentage of Participants with $\geq 50\%$, $\geq 75\%$, $\geq 90\%$, and $\geq 100\%$ Reduction from Baseline in the Number of Normalized Daytime Urinary Incontinence Episodes in Treatment Cycle 1 |
|-----------------|---|

End point description:

Urinary incontinence was defined as involuntary loss of urine as recorded by the participant in a bladder diary during 2 consecutive days in the week prior to the study visit (normalized to a 12 hour daytime period). Daytime is defined as the time between waking up to start the day and going to bed to sleep for the night. The number of daily incontinence episodes were averaged during the 2-day period. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received at least 1 BOTOX treatment over the course of total evaluation period, starting from their first treatment in Study 120. Number analysed is the number of participants with evaluable data for the specific category.

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

End point timeframe:

Study Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 1

| End point values | Onabotulinumt oxinA 50 U (Treatment Cycle 1) | Onabotulinumt oxinA 100 U (Treatment Cycle 1) | Onabotulinumt oxinA 200 U (Treatment Cycle 1) | |
|---|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 30 | 36 | 23 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| $\geq 50\%$ Reduction from Baseline to Week 6 | 53.3 (34.33 to 71.66) | 55.6 (38.10 to 72.06) | 52.2 (30.59 to 73.18) | |
| $\geq 75\%$ Reduction from Baseline to Week 6 | 30.0 (14.73 to 49.40) | 41.7 (25.51 to 59.24) | 39.1 (19.71 to 61.46) | |
| $\geq 90\%$ Reduction from Baseline to Week 6 | 26.7 (12.28 to 45.89) | 30.6 (16.35 to 48.11) | 30.4 (13.21 to 52.92) | |

| | | | | |
|---|-----------------------|-----------------------|-----------------------|--|
| ≥100% Reduction from Baseline to Week 6 | 26.7 (12.28 to 45.89) | 27.8 (14.20 to 45.19) | 26.1 (10.23 to 48.41) | |
|---|-----------------------|-----------------------|-----------------------|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with ≥ 50%, ≥ 75%, ≥ 90%, and ≥ 100% Reduction from Baseline in the Number of Normalized Daytime Urinary Incontinence Episodes in Treatment Cycle 2

| | |
|-----------------|--|
| End point title | Percentage of Participants with ≥ 50%, ≥ 75%, ≥ 90%, and ≥ 100% Reduction from Baseline in the Number of Normalized Daytime Urinary Incontinence Episodes in Treatment Cycle 2 |
|-----------------|--|

End point description:

Urinary incontinence was defined as involuntary loss of urine as recorded by the participant in a bladder diary during 2 consecutive days in the week prior to the study visit (normalized to a 12 hour daytime period). Daytime is defined as the time between waking up to start the day and going to bed to sleep for the night. The number of daily incontinence episodes were averaged during the 2-day period. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received at least 1 BOTOX treatment over the course of total evaluation period, starting from their first treatment in Study 120. Number analysed is the number of participants with evaluable data for the specific category.

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

End point timeframe:

Study Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 2

| End point values | Onabotulinumt oxinA 50 U (Treatment Cycle 2) | Onabotulinumt oxinA 100 U (Treatment Cycle 2) | Onabotulinumt oxinA 200 U (Treatment Cycle 2) | |
|---|--|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 6 | 44 | 34 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| ≥50% Reduction from Baseline to Week 6 | 66.7 (22.28 to 95.67) | 65.9 (50.08 to 79.51) | 58.8 (40.70 to 75.35) | |
| ≥75% Reduction from Baseline to Week 6 | 50.0 (11.81 to 88.19) | 43.2 (28.35 to 58.97) | 47.1 (29.78 to 64.87) | |
| ≥90% Reduction from Baseline to Week 6 | 50.0 (11.81 to 88.19) | 27.3 (14.96 to 42.79) | 41.2 (24.65 to 59.30) | |
| ≥100% Reduction from Baseline to Week 6 | 50.0 (11.81 to 88.19) | 25.0 (13.19 to 40.34) | 38.2 (22.17 to 56.44) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with $\geq 50\%$, $\geq 75\%$, $\geq 90\%$, and $\geq 100\%$ Reduction from Baseline in the Number of Normalized Daytime Urinary Incontinence Episodes in Treatment Cycle 3

| | |
|-----------------|---|
| End point title | Percentage of Participants with $\geq 50\%$, $\geq 75\%$, $\geq 90\%$, and $\geq 100\%$ Reduction from Baseline in the Number of Normalized Daytime Urinary Incontinence Episodes in Treatment Cycle 3 |
|-----------------|---|

End point description:

Urinary incontinence was defined as involuntary loss of urine as recorded by the participant in a bladder diary during 2 consecutive days in the week prior to the study visit (normalized to a 12 hour daytime period). Daytime is defined as the time between waking up to start the day and going to bed to sleep for the night. The number of daily incontinence episodes were averaged during the 2-day period. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received at least 1 BOTOX treatment over the course of total evaluation period, starting from their first treatment in Study 120. Number analysed is the number of participants with evaluable data for the specific category.

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

End point timeframe:

Study Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 3

| End point values | Onabotulinumt oxinA 50 U (Treatment Cycle 3) | Onabotulinumt oxinA 100 U (Treatment Cycle 3) | Onabotulinumt oxinA 200 U (Treatment Cycle 3) | |
|--|--|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 5 | 16 | 33 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| $\geq 50\%$ Reduction from Baseline at Week 6 | 60.0 (14.66 to 94.73) | 75.0 (47.62 to 92.73) | 69.7 (51.29 to 84.41) | |
| $\geq 75\%$ Reduction from Baseline at Week 6 | 60.0 (14.66 to 94.73) | 37.5 (15.20 to 64.57) | 39.4 (22.91 to 57.86) | |
| $\geq 90\%$ Reduction from Baseline at Week 6 | 60.0 (14.66 to 94.73) | 18.8 (4.05 to 45.65) | 33.3 (17.96 to 51.83) | |
| $\geq 100\%$ Reduction from Baseline at Week 6 | 60.0 (14.66 to 94.73) | 18.8 (4.05 to 45.65) | 30.3 (15.59 to 48.71) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Average Urine Volume at First Morning Catheterization in Treatment Cycle 1

| | |
|-----------------|--|
| End point title | Change from Baseline in Average Urine Volume at First Morning Catheterization in Treatment Cycle 1 |
|-----------------|--|

End point description:

The change in urine volume at first morning catheterization was recorded by the participant in a bladder diary in the 2 consecutive days during the week prior to the study visit. The daily values were averaged during the 2-day period. A positive change from Baseline indicates improvement. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received ≥ 1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. Overall number of participants analysed is the number of participants with data available for analyses.

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

End point timeframe:

Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 1

| End point values | Onabotulinumt oxinA 50 U (Treatment Cycle 1) | Onabotulinumt oxinA 100 U (Treatment Cycle 1) | Onabotulinumt oxinA 200 U (Treatment Cycle 1) | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 30 | 36 | 21 | |
| Units: mL | | | | |
| arithmetic mean (standard deviation) | 14.68 (± 88.146) | 39.88 (± 72.787) | 96.90 (± 120.429) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Average Urine Volume at First Morning Catheterization in Treatment Cycle 2

| | |
|-----------------|--|
| End point title | Change from Baseline in Average Urine Volume at First Morning Catheterization in Treatment Cycle 2 |
|-----------------|--|

End point description:

The change in urine volume at first morning catheterization was recorded by the participant in a bladder diary in the 2 consecutive days during the week prior to the study visit. The daily values were averaged during the 2-day period. A positive change from Baseline indicates improvement. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received ≥ 1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. Overall number of participants analysed is the number of participants with data available for analyses.

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

End point timeframe:

Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 2

| End point values | Onabotulinumt oxinA 50 U (Treatment Cycle 2) | Onabotulinumt oxinA 100 U (Treatment Cycle 2) | Onabotulinumt oxinA 200 U (Treatment Cycle 2) | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 6 | 43 | 31 | |
| Units: mL | | | | |
| arithmetic mean (standard deviation) | 7.92 (± 148.597) | 79.53 (± 106.794) | 35.34 (± 98.209) | |

Statistical analyses

Secondary: Change from Baseline in Average Urine Volume at First Morning Catheterization in Treatment Cycle 3

| | |
|-----------------|--|
| End point title | Change from Baseline in Average Urine Volume at First Morning Catheterization in Treatment Cycle 3 |
|-----------------|--|

End point description:

The change in urine volume at first morning catheterization was recorded by the participant in a bladder diary in the 2 consecutive days during the week prior to the study visit. The daily values were averaged during the 2-day period. A positive change from Baseline indicates improvement. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received ≥ 1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. Overall number of participants analysed is the number of participants with data available for analyses.

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

End point timeframe:

Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 3

| End point values | Onabotulinumt oxinA 50 U (Treatment Cycle 3) | Onabotulinumt oxinA 100 U (Treatment Cycle 3) | Onabotulinumt oxinA 200 U (Treatment Cycle 3) | |
|--------------------------------------|--|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 5 | 10 | 31 | |
| Units: mL | | | | |
| arithmetic mean (standard deviation) | 58.50 (\pm 22.749) | 57.86 (\pm 74.762) | 92.39 (\pm 147.322) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Night Time Urinary Incontinence in Treatment Cycle 1

| | |
|-----------------|--|
| End point title | Percentage of Participants with Night Time Urinary Incontinence in Treatment Cycle 1 |
|-----------------|--|

End point description:

Urinary incontinence was defined as involuntary loss of urine. Night time urinary incontinence was recorded by the participant on the bladder diary as a presence or absence of urinary leakage upon waking, for 2 consecutive days in the week prior to the week 6 visit. Night time was defined as the time between going to bed to sleep for the night and waking up to start the day. The percentage of participants with night time urinary incontinence is presented in categories 0, 1, and 2 nights. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received ≥ 1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. 'n' is the number of participants with data available for analyses at the given time point.

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

End point timeframe:

Baseline (Prior to Day 1 in Study 120) and 2 consecutive days in the week prior to Week 6 in Treatment Cycle 1

| End point values | Onabotulinumt oxinA 50 U (Treatment Cycle 1) | Onabotulinumt oxinA 100 U (Treatment Cycle 1) | Onabotulinumt oxinA 200 U (Treatment Cycle 1) | |
|--|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 31 | 39 | 25 | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| 0 Nights of Incontinence at Baseline (n=31,39,23) | 0.0 | 15.4 | 4.3 | |
| 0 Nights of Incontinence at Week 6 (n=30,37,24) | 30.0 | 37.8 | 25.0 | |
| 1 Night of Incontinence at Baseline (n=31,39,23) | 12.9 | 2.6 | 17.4 | |
| 1 Night of Incontinence at Week 6 (n=30,37,24) | 20.0 | 16.2 | 29.2 | |
| 2 Nights of Incontinence at Baseline (n=31,39,23) | 87.1 | 82.1 | 78.3 | |
| 2 Nights of Incontinence at Week 6 (n=30,37,24) | 50.0 | 45.9 | 45.8 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Night Time Urinary Incontinence in Treatment Cycle 2

| | |
|-----------------|--|
| End point title | Percentage of Participants with Night Time Urinary Incontinence in Treatment Cycle 2 |
|-----------------|--|

End point description:

Urinary incontinence was defined as involuntary loss of urine. Night time urinary incontinence was recorded by the participant on the bladder diary as a presence or absence of urinary leakage upon waking, for 2 consecutive days in the week prior to the week 6 visit. Night time was defined as the time between going to bed to sleep for the night and waking up to start the day. The percentage of participants with night time urinary incontinence is presented in categories 0, 1, and 2 nights. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received ≥ 1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. 'n' is the number of participants with data available for analyses at the given time point.

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

End point timeframe:

Baseline (Prior to Day 1 in Study 120) and 2 consecutive days in the week prior to Week 6 in Treatment Cycle 2

| End point values | Onabotulinumt oxinA 50 U (Treatment Cycle 2) | Onabotulinumt oxinA 100 U (Treatment Cycle 2) | Onabotulinumt oxinA 200 U (Treatment Cycle 2) | |
|---|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 9 | 45 | 36 | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| 0 Nights of Incontinence at Baseline (n=9, 45, 34) | 0.0 | 8.9 | 5.9 | |
| 0 Nights of Incontinence at Week 6 (n=6, 44, 34) | 66.7 | 34.1 | 23.5 | |
| 1 Night of Incontinence at Baseline (n=9, 45, 34) | 22.2 | 6.7 | 8.8 | |
| 1 Night of Incontinence at Week 6 (n=6, 44, 34) | 16.7 | 22.7 | 8.8 | |
| 2 Nights of Incontinence at Baseline (n=9, 45, 34) | 77.8 | 84.4 | 85.3 | |
| 2 Nights of Incontinence at Week 6 (n=6, 44, 34) | 16.7 | 43.2 | 67.6 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Night Time Urinary Incontinence in Treatment Cycle 3

| | |
|-----------------|--|
| End point title | Percentage of Participants with Night Time Urinary Incontinence in Treatment Cycle 3 |
|-----------------|--|

End point description:

Urinary incontinence was defined as involuntary loss of urine. Night time urinary incontinence was recorded by the participant on the bladder diary as a presence or absence of urinary leakage upon waking, for 2 consecutive days in the week prior to the week 6 visit. Night time was defined as the time between going to bed to sleep for the night and waking up to start the day. The percentage of participants with night time urinary incontinence is presented in categories 0, 1, and 2 nights. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received ≥ 1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. 'n' is the number of participants with data available for analyses at the given time point.

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

End point timeframe:

Baseline (Prior to Day 1 in Study 120) and 2 consecutive days in the week prior to Week 6 in Treatment Cycle 3

| End point values | Onabotulinumt oxinA 50 U (Treatment Cycle 3) | Onabotulinumt oxinA 100 U (Treatment Cycle 3) | Onabotulinumt oxinA 200 U (Treatment Cycle 3) | |
|-----------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 5 | 16 | 34 | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |

| | | | | |
|--|-------|------|------|--|
| 0 Nights of Incontinence at Baseline (n=5, 16, 34) | 0.0 | 12.5 | 5.9 | |
| 0 Nights of Incontinence at Week 6 (n=5, 16, 33) | 20.0 | 31.3 | 21.2 | |
| 1 Night of Incontinence at Baseline (n=5, 16, 34) | 0.0 | 0.0 | 5.9 | |
| 1 Night of Incontinence at Week 6 (n=5, 16, 33) | 40.0 | 12.5 | 27.3 | |
| 2 Nights of Incontinence at Baseline (n=5, 16, 34) | 100.0 | 87.5 | 88.2 | |
| 2 Nights of Incontinence at Week 6 (n=5, 16, 33) | 40.0 | 56.3 | 51.5 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Average Time to Participant's Request for Retreatment

| | |
|-----------------|---|
| End point title | Average Time to Participant's Request for Retreatment |
|-----------------|---|

End point description:

Time to request for re-treatment is the time in weeks between last injection and request for next injection, regardless of fulfillment of the re-treatment criteria. Data are summarized under the respective treatments that participants received across entire study. Data is reported for only participants that had at least one request for retreatment while on a specified BOTOX dose. BOTOX-treated Population included all participants enrolled into extension study who received ≥ 1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. Overall number of participants analysed is the number of participants with data available for analyses.

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

End point timeframe:

First injection on Day 1 in Study 120 through to the date of completion of Study 121 (Up to 108 weeks)

| End point values | Onabotulinumt oxinA 50 U | Onabotulinumt oxinA 100 U | Onabotulinumt oxinA 200 U | |
|-------------------------------|--------------------------|---------------------------|---------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 30 | 53 | 35 | |
| Units: weeks | | | | |
| median (full range (min-max)) | 24.55 (11.9 to 89.7) | 24.64 (11.7 to 73.3) | 25.43 (11.1 to 78.9) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Average Time to Participant's Qualification for Retreatment

| | |
|-----------------|---|
| End point title | Average Time to Participant's Qualification for Retreatment |
|-----------------|---|

End point description:

The criteria for qualification of retreatment included 1) Participant/parent/caregiver requests retreatment; 2) Participant has a total of at least 2 daytime urinary incontinence episodes over the 2-day bladder diary collection period; 3) At least 12 weeks has elapsed since treatment 1 and 4)

Participant has not experienced a serious treatment-related adverse event at any time. Data are summarized under the respective treatments that participants received across entire study. Data is reported for only participants that had at least one request for retreatment while on a specified BOTOX dose. BOTOX-treated Population included all participants enrolled into extension study who received ≥ 1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. Overall number of participants analysed is the number of participants with data available for analyses.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| First injection on Day 1 in Study 120 through to the date of completion of Study 121 (Up to 108 weeks) | |

| End point values | Onabotulinumt oxinA 200 U | Onabotulinumt oxinA 100 U | Onabotulinumt oxinA 50 U | |
|----------------------------------|---------------------------|---------------------------|--------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 25 | 53 | 29 | |
| Units: weeks | | | | |
| median (confidence interval 95%) | 26.29 (11.1 to 78.9) | 25.43 (11.7 to 76.1) | 25.38 (11.9 to 84.4) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Positive Response on Modified Treatment Benefit Scale (TBS) in Treatment Cycle 1

| | |
|-----------------|--|
| End point title | Percentage of Participants with Positive Response on Modified Treatment Benefit Scale (TBS) in Treatment Cycle 1 |
|-----------------|--|

End point description:

The Modified TBS is a single-item scale which assesses the participant's condition (urinary problems, urinary incontinence) on a 4-point scale where 1 = greatly improved; 2 = improved; 3 = not changed; and 4 = worsened. A participant was considered to have a positive treatment response if they responded to the TBS question as either "greatly improved" or "improved". Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received ≥ 1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. Overall number of participants analysed is number of participants with data available for analyses.

| | |
|-----------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 6 in Treatment Cycle 1 | |

| End point values | Onabotulinumt oxinA 50 U (Treatment Cycle 1) | Onabotulinumt oxinA 100 U (Treatment Cycle 1) | Onabotulinumt oxinA 200 U (Treatment Cycle 1) | |
|-----------------------------------|--|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 30 | 35 | 24 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 80.0 (61.43 to 92.29) | 80.0 (63.06 to 91.56) | 75.0 (53.29 to 90.23) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Positive Response on Modified Treatment Benefit Scale (TBS) in Treatment Cycle 2

| | |
|-----------------|--|
| End point title | Percentage of Participants with Positive Response on Modified Treatment Benefit Scale (TBS) in Treatment Cycle 2 |
|-----------------|--|

End point description:

The Modified TBS is a single-item scale which assesses the participant's condition (urinary problems, urinary incontinence) on a 4-point scale where 1 = greatly improved; 2 = improved; 3 = not changed; and 4 = worsened. A participant was considered to have a positive treatment response if they responded to the TBS question as either "greatly improved" or "improved". Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received ≥ 1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. Overall number of participants analysed is the number of participants with data available for analyses.

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

End point timeframe:

Week 6 in Treatment Cycle 2

| End point values | Onabotulinumt oxinA 50 U (Treatment Cycle 2) | Onabotulinumt oxinA 100 U (Treatment Cycle 2) | Onabotulinumt oxinA 200 U (Treatment Cycle 2) | |
|-----------------------------------|--|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 8 | 42 | 30 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 75.0 (34.91 to 96.81) | 97.6 (87.43 to 99.94) | 83.3 (65.28 to 94.36) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Positive Response on Modified Treatment Benefit Scale (TBS) in Treatment Cycle 3

| | |
|-----------------|--|
| End point title | Percentage of Participants with Positive Response on Modified Treatment Benefit Scale (TBS) in Treatment Cycle 3 |
|-----------------|--|

End point description:

The Modified TBS is a single-item scale which assesses the participant's condition (urinary problems, urinary incontinence) on a 4-point scale where 1 = greatly improved; 2 = improved; 3 = not changed; and 4 = worsened. A participant was considered to have a positive treatment response if they responded to the TBS question as either "greatly improved" or "improved". Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-

treated Population included all participants enrolled into extension study who received ≥ 1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. Overall number of participants analysed is the number of participants with data available for analyses.

| | |
|-----------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 6 in Treatment Cycle 3 | |

| End point values | Onabotulinumt oxinA 50 U (Treatment Cycle 3) | Onabotulinumt oxinA 100 U (Treatment Cycle 3) | Onabotulinumt oxinA 200 U (Treatment Cycle 3) | |
|-----------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 5 | 15 | 33 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 100 (47.82 to 100.00) | 80.0 (51.91 to 95.67) | 84.8 (68.10 to 94.89) | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First injection on Day 1 in Study 120 through the completion of Study 121 (Up to 108 Weeks)

Adverse event reporting additional description:

BOTOX-treated Population included all participants enrolled into the extension study who received at least 1 BOTOX treatment over the course of the total evaluation period, starting from their first treatment in Study 191622-120. Data are summarized under the respective treatments that participants received in the corresponding treatment cycles.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | OnabotulinumtoxinA 100 U (Treatment Cycle 1) |
|-----------------------|--|

Reporting group description:

OnabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 1. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|-----------------------|---|
| Reporting group title | OnabotulinumtoxinA 50 U (Treatment Cycle 1) |
|-----------------------|---|

Reporting group description:

OnabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 1. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|-----------------------|--|
| Reporting group title | OnabotulinumtoxinA 200 U (Treatment Cycle 1) |
|-----------------------|--|

Reporting group description:

OnabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 1. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|-----------------------|---|
| Reporting group title | OnabotulinumtoxinA 50 U (Treatment Cycle 2) |
|-----------------------|---|

Reporting group description:

OnabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 2. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|-----------------------|--|
| Reporting group title | OnabotulinumtoxinA 100 U (Treatment Cycle 2) |
|-----------------------|--|

Reporting group description:

OnabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 2. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|-----------------------|--|
| Reporting group title | OnabotulinumtoxinA 200 U (Treatment Cycle 2) |
|-----------------------|--|

Reporting group description:

OnabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 2. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|-----------------------|---|
| Reporting group title | OnabotulinumtoxinA 50 U (Treatment Cycle 3) |
|-----------------------|---|

Reporting group description:

OnabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 3. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

| | |
|---|--|
| Reporting group title | OnabotulinumtoxinA 100 U (Treatment Cycle 3) |
| Reporting group description: OnabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 3. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg). | |
| Reporting group title | OnabotulinumtoxinA 200 U (Treatment Cycle 3) |
| Reporting group description: OnabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 3. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg). | |
| Reporting group title | OnabotulinumtoxinA 50 U (Treatment Cycle 4) |
| Reporting group description: OnabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 4. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg). | |
| Reporting group title | OnabotulinumtoxinA 100 U (Treatment Cycle 4) |
| Reporting group description: OnabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 4. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg). | |
| Reporting group title | OnabotulinumtoxinA 200 U (Treatment Cycle 4) |
| Reporting group description: OnabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 4. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg). | |

| Serious adverse events | OnabotulinumtoxinA 100 U (Treatment Cycle 1) | OnabotulinumtoxinA 50 U (Treatment Cycle 1) | OnabotulinumtoxinA 200 U (Treatment Cycle 1) |
|---|--|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 2 / 31 (6.45%) | 1 / 25 (4.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Arteriovenous fistula thrombosis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 31 (3.23%) | 0 / 25 (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 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (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 / 39 (0.00%) | 0 / 31 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Hydrocephalus | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 31 (0.00%) | 0 / 25 (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 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (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 |
| Renal and urinary disorders | | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (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 | | | |
| Fistula | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (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 |
| Hip deformity | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (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 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (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 | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 1 / 31 (3.23%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalitis viral | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 31 (0.00%) | 0 / 25 (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 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (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 |
| Bacterial diarrhoea | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (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 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (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 |
| Febrile infection | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (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 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (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 |
| Wound infection | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (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 |
| Product issues | | | |
| Device malfunction | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (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 | OnabotulinumtoxinA 50 U (Treatment Cycle 2) | OnabotulinumtoxinA 100 U (Treatment Cycle 2) | OnabotulinumtoxinA 200 U (Treatment Cycle 2) |
|---|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 5 / 45 (11.11%) | 6 / 36 (16.67%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Arteriovenous fistula thrombosis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 45 (0.00%) | 0 / 36 (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 / 9 (0.00%) | 1 / 45 (2.22%) | 0 / 36 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 45 (0.00%) | 0 / 36 (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 | | | |
| Hydrocephalus | | | |

| | | | |
|---|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 45 (0.00%) | 0 / 36 (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 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 45 (0.00%) | 0 / 36 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 45 (0.00%) | 1 / 36 (2.78%) |
| 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 | | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 45 (2.22%) | 0 / 36 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Fistula | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 45 (2.22%) | 0 / 36 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip deformity | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 45 (2.22%) | 0 / 36 (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 / 9 (0.00%) | 0 / 45 (0.00%) | 1 / 36 (2.78%) |
| 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 | | | |
| Urinary tract infection | | | |

| | | | |
|---|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 45 (2.22%) | 2 / 36 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalitis viral | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 45 (0.00%) | 0 / 36 (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 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 45 (4.44%) | 0 / 36 (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 |
| Bacterial diarrhoea | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 45 (2.22%) | 0 / 36 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 45 (2.22%) | 0 / 36 (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 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 45 (0.00%) | 1 / 36 (2.78%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 45 (0.00%) | 1 / 36 (2.78%) |
| 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 / 9 (0.00%) | 0 / 45 (0.00%) | 1 / 36 (2.78%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection | | | |

| | | | |
|---|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 45 (0.00%) | 1 / 36 (2.78%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Product issues | | | |
| Device malfunction | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 45 (0.00%) | 1 / 36 (2.78%) |
| 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 | OnabotulinumtoxinA 50 U (Treatment Cycle 3) | OnabotulinumtoxinA 100 U (Treatment Cycle 3) | OnabotulinumtoxinA 200 U (Treatment Cycle 3) |
|---|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 16 (6.25%) | 2 / 34 (5.88%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Arteriovenous fistula thrombosis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 | | | |
| Hydrocephalus | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 |
| Epilepsy | | | |

| | | | |
|---|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 16 (6.25%) | 0 / 34 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 |
| Renal and urinary disorders | | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 | | | |
| Fistula | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 |
| Hip deformity | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 2 / 34 (5.88%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalitis viral | | | |

| | | | |
|---|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 |
| Bacterial diarrhoea | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 |
| Febrile infection | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 |
| Wound infection | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 |
| Product issues | | | |
| Device malfunction | | | |

| | | | |
|---|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (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 | OnabotulinumtoxinA 50 U (Treatment Cycle 4) | OnabotulinumtoxinA 100 U (Treatment Cycle 4) | OnabotulinumtoxinA 200 U (Treatment Cycle 4) |
|---|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Arteriovenous fistula thrombosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 | | | |
| Hydrocephalus | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Psoriasis | | | |

| | | | |
|---|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 |
| Renal and urinary disorders | | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 | | | |
| Fistula | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 |
| Hip deformity | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 |
| Encephalitis viral | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 |

| | | | |
|---|---------------|---------------|---------------|
| Bacterial diarrhoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 |
| Febrile infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 |
| Wound infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 |
| Product issues | | | |
| Device malfunction | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (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 | OnabotulinumtoxinA 100 U (Treatment Cycle 1) | OnabotulinumtoxinA 50 U (Treatment Cycle 1) | OnabotulinumtoxinA 200 U (Treatment Cycle 1) |
|---|--|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 31 / 39 (79.49%) | 21 / 31 (67.74%) | 16 / 25 (64.00%) |
| Investigations Blood urine present subjects affected / exposed occurrences (all) Protein urine present subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 0 / 39 (0.00%) 0 | 0 / 31 (0.00%) 0 0 / 31 (0.00%) 0 | 0 / 25 (0.00%) 0 0 / 25 (0.00%) 0 |
| Injury, poisoning and procedural complications Procedural pain subjects affected / exposed occurrences (all) Eschar subjects affected / exposed occurrences (all) Foot fracture subjects affected / exposed occurrences (all) Skin laceration subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 0 / 39 (0.00%) 0 0 / 39 (0.00%) 0 0 / 39 (0.00%) 0 | 0 / 31 (0.00%) 0 0 / 31 (0.00%) 0 1 / 31 (3.23%) 2 0 / 31 (0.00%) 0 | 0 / 25 (0.00%) 0 0 / 25 (0.00%) 0 0 / 25 (0.00%) 0 0 / 25 (0.00%) 0 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 7 / 39 (17.95%) 15 | 2 / 31 (6.45%) 2 | 2 / 25 (8.00%) 4 |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) Suprapubic pain subjects affected / exposed occurrences (all) | 5 / 39 (12.82%) 7 0 / 39 (0.00%) 0 | 1 / 31 (3.23%) 1 2 / 31 (6.45%) 2 | 0 / 25 (0.00%) 0 1 / 25 (4.00%) 1 |
| Gastrointestinal disorders | | | |

| | | | |
|---|---|----------------|----------------|
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 2 / 31 (6.45%) | 2 / 25 (8.00%) |
| occurrences (all) | 8 | 3 | 2 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 2 / 31 (6.45%) | 1 / 25 (4.00%) |
| occurrences (all) | 1 | 2 | 2 |
| Nausea | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 31 (6.45%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 31 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Testicular retraction | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysmenorrhoea | Additional description: Number of participants at risk in the OnabotulinumtoxinA 200 U (Treatment Cycle 2) arm group is based on the female population. | | |
| subjects affected / exposed ^[1] | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 2 / 31 (6.45%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 31 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 2 | 0 | 1 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 31 (3.23%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | | |
|---|-----------------------------|------------------|-----------------|-----------------|
| Skin and subcutaneous tissue disorders | Acne | | | |
| | subjects affected / exposed | 1 / 39 (2.56%) | 2 / 31 (6.45%) | 1 / 25 (4.00%) |
| | occurrences (all) | 1 | 3 | 1 |
| | Rash | | | |
| Renal and urinary disorders | subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (0.00%) |
| | occurrences (all) | 0 | 0 | 0 |
| | Leukocyturia | | | |
| | subjects affected / exposed | 3 / 39 (7.69%) | 1 / 31 (3.23%) | 3 / 25 (12.00%) |
| Musculoskeletal and connective tissue disorders | occurrences (all) | 3 | 2 | 4 |
| | Haematuria | | | |
| | subjects affected / exposed | 1 / 39 (2.56%) | 1 / 31 (3.23%) | 1 / 25 (4.00%) |
| | occurrences (all) | 1 | 1 | 1 |
| Infections and infestations | Hydronephrosis | | | |
| | subjects affected / exposed | 0 / 39 (0.00%) | 2 / 31 (6.45%) | 0 / 25 (0.00%) |
| | occurrences (all) | 0 | 2 | 0 |
| | Back pain | | | |
| Infections and infestations | subjects affected / exposed | 2 / 39 (5.13%) | 1 / 31 (3.23%) | 0 / 25 (0.00%) |
| | occurrences (all) | 2 | 1 | 0 |
| | Neck pain | | | |
| | subjects affected / exposed | 1 / 39 (2.56%) | 0 / 31 (0.00%) | 0 / 25 (0.00%) |
| Infections and infestations | occurrences (all) | 1 | 0 | 0 |
| | Urinary tract infection | | | |
| | subjects affected / exposed | 13 / 39 (33.33%) | 9 / 31 (29.03%) | 5 / 25 (20.00%) |
| | occurrences (all) | 22 | 12 | 7 |
| Infections and infestations | Bacteriuria | | | |
| | subjects affected / exposed | 7 / 39 (17.95%) | 5 / 31 (16.13%) | 5 / 25 (20.00%) |
| | occurrences (all) | 12 | 10 | 10 |
| | Pharyngitis | | | |
| Infections and infestations | subjects affected / exposed | 4 / 39 (10.26%) | 3 / 31 (9.68%) | 0 / 25 (0.00%) |
| | occurrences (all) | 4 | 3 | 0 |
| | Nasopharyngitis | | | |
| | | | | |

| | | | |
|-----------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 31 (0.00%) | 4 / 25 (16.00%) |
| occurrences (all) | 1 | 0 | 4 |
| Gastroenteritis | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 1 / 31 (3.23%) | 0 / 25 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 0 / 31 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 3 | 0 | 1 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 31 (3.23%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Tinea capitis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 31 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 31 (6.45%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 2 | 1 |
| Asymptomatic bacteriuria | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 1 / 31 (3.23%) | 0 / 25 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Influenza | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 31 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 2 | 0 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 31 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 3 | 0 | 1 |

| Non-serious adverse events | OnabotulinumtoxinA 50 U (Treatment Cycle 2) | OnabotulinumtoxinA 100 U (Treatment Cycle 2) | OnabotulinumtoxinA 200 U (Treatment Cycle 2) |
|--|---|--|--|
| Total subjects affected by non-serious adverse events | | | |

| subjects affected / exposed | 7 / 9 (77.78%) | 32 / 45 (71.11%) | 27 / 36 (75.00%) |
|--|----------------|------------------|------------------|
| Investigations | | | |
| Blood urine present | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 4 / 45 (8.89%) | 2 / 36 (5.56%) |
| occurrences (all) | 2 | 4 | 2 |
| Protein urine present | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 45 (0.00%) | 2 / 36 (5.56%) |
| occurrences (all) | 0 | 0 | 2 |
| Injury, poisoning and procedural complications | | | |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 45 (0.00%) | 2 / 36 (5.56%) |
| occurrences (all) | 0 | 0 | 2 |
| Eschar | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 45 (0.00%) | 0 / 36 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 45 (0.00%) | 0 / 36 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 45 (2.22%) | 0 / 36 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 45 (6.67%) | 2 / 36 (5.56%) |
| occurrences (all) | 1 | 3 | 2 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 6 / 45 (13.33%) | 3 / 36 (8.33%) |
| occurrences (all) | 0 | 9 | 3 |
| Suprapubic pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 45 (0.00%) | 0 / 36 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 45 (4.44%) | 3 / 36 (8.33%) |
| occurrences (all) | 1 | 2 | 3 |
| Abdominal pain | | | |

| | | | |
|---|---|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 3 / 45 (6.67%) 3 | 1 / 36 (2.78%) 1 |
| Nausea subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 45 (2.22%) 1 | 0 / 36 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 2 | 2 / 45 (4.44%) 4 | 0 / 36 (0.00%) 0 |
| Constipation subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 3 / 45 (6.67%) 3 | 0 / 36 (0.00%) 0 |
| Reproductive system and breast disorders | | | |
| Testicular retraction subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 45 (0.00%) 0 | 0 / 36 (0.00%) 0 |
| Dysmenorrhoea | Additional description: Number of participants at risk in the OnabotulinumtoxinA 200 U (Treatment Cycle 2) arm group is based on the female population. | | |
| subjects affected / exposed ^[1] occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 45 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 45 (2.22%) 1 | 1 / 36 (2.78%) 1 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 5 / 45 (11.11%) 5 | 0 / 36 (0.00%) 0 |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 45 (0.00%) 0 | 2 / 36 (5.56%) 2 |
| Nasal congestion subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 45 (0.00%) 0 | 1 / 36 (2.78%) 1 |
| Skin and subcutaneous tissue disorders | | | |
| Acne subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 45 (0.00%) 0 | 0 / 36 (0.00%) 0 |

| | | | |
|--|---------------------|------------------------|----------------------|
| Rash subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 45 (2.22%) 1 | 0 / 36 (0.00%) 0 |
| Renal and urinary disorders Leukocyturia subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 2 | 1 / 45 (2.22%) 1 | 3 / 36 (8.33%) 4 |
| Haematuria subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 1 / 45 (2.22%) 1 | 0 / 36 (0.00%) 0 |
| Hydronephrosis subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 45 (2.22%) 1 | 0 / 36 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 45 (0.00%) 0 | 0 / 36 (0.00%) 0 |
| Neck pain subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 45 (0.00%) 0 | 0 / 36 (0.00%) 0 |
| Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 22 / 45 (48.89%) 33 | 6 / 36 (16.67%) 8 |
| Bacteriuria subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 9 / 45 (20.00%) 15 | 2 / 36 (5.56%) 3 |
| Pharyngitis subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 3 / 45 (6.67%) 3 | 2 / 36 (5.56%) 2 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 2 / 45 (4.44%) 2 | 3 / 36 (8.33%) 3 |
| Gastroenteritis subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 3 | 2 / 45 (4.44%) 2 | 0 / 36 (0.00%) 0 |

| | | | |
|-----------------------------------|----------------|----------------|----------------|
| Bronchitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 45 (2.22%) | 0 / 36 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 45 (2.22%) | 0 / 36 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 45 (2.22%) | 0 / 36 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 45 (0.00%) | 2 / 36 (5.56%) |
| occurrences (all) | 0 | 0 | 2 |
| Tinea capitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 45 (0.00%) | 0 / 36 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 45 (4.44%) | 0 / 36 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Asymptomatic bacteriuria | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 45 (2.22%) | 0 / 36 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 4 / 45 (8.89%) | 1 / 36 (2.78%) |
| occurrences (all) | 0 | 4 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 45 (4.44%) | 2 / 36 (5.56%) |
| occurrences (all) | 0 | 4 | 3 |

| Non-serious adverse events | OnabotulinumtoxinA 50 U (Treatment Cycle 3) | OnabotulinumtoxinA 100 U (Treatment Cycle 3) | OnabotulinumtoxinA 200 U (Treatment Cycle 3) |
|--|---|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 5 (80.00%) | 10 / 16 (62.50%) | 19 / 34 (55.88%) |
| Investigations | | | |
| Blood urine present | | | |
| subjects affected / exposed | 2 / 5 (40.00%) | 1 / 16 (6.25%) | 5 / 34 (14.71%) |
| occurrences (all) | 2 | 1 | 5 |
| Protein urine present | | | |

| | | | |
|--|--------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 16 (0.00%) 0 | 0 / 34 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eschar | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 16 (6.25%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 16 (6.25%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 2 / 5 (40.00%) | 0 / 16 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 2 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 3 / 34 (8.82%) |
| occurrences (all) | 0 | 0 | 3 |
| Suprapubic pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 16 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Nausea | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---------------------|---------------------|
| Vomiting subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 16 (0.00%) 0 | 1 / 34 (2.94%) 1 |
| Constipation subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 1 / 16 (6.25%) 1 | 0 / 34 (0.00%) 0 |
| Reproductive system and breast disorders | | | |
| Testicular retraction subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 16 (0.00%) 0 | 0 / 34 (0.00%) 0 |
| Dysmenorrhoea | Additional description: Number of participants at risk in the OnabotulinumtoxinA 200 U (Treatment Cycle 2) arm group is based on the female population. | | |
| subjects affected / exposed ^[1] occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 16 (0.00%) 0 | 0 / 34 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 16 (0.00%) 0 | 2 / 34 (5.88%) 2 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 16 (0.00%) 0 | 1 / 34 (2.94%) 1 |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 16 (0.00%) 0 | 0 / 34 (0.00%) 0 |
| Nasal congestion subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 1 / 16 (6.25%) 1 | 0 / 34 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Acne subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 16 (0.00%) 0 | 0 / 34 (0.00%) 0 |
| Rash subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 1 / 16 (6.25%) 1 | 0 / 34 (0.00%) 0 |
| Renal and urinary disorders | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| Leukocyturia | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 16 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 2 / 34 (5.88%) |
| occurrences (all) | 0 | 0 | 2 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 4 / 16 (25.00%) | 6 / 34 (17.65%) |
| occurrences (all) | 0 | 6 | 7 |
| Bacteriuria | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 3 / 16 (18.75%) | 4 / 34 (11.76%) |
| occurrences (all) | 0 | 3 | 8 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 16 (6.25%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 16 (6.25%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 1 | 1 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cystitis | | | |

| | | | |
|-----------------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 16 (6.25%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinea capitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Asymptomatic bacteriuria | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 16 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | OnabotulinumtoxinA 50 U (Treatment Cycle 4) | OnabotulinumtoxinA 100 U (Treatment Cycle 4) | OnabotulinumtoxinA 200 U (Treatment Cycle 4) |
|--|---|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 3 (100.00%) | 2 / 4 (50.00%) | 4 / 4 (100.00%) |
| Investigations | | | |
| Blood urine present | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 2 / 4 (50.00%) | 2 / 4 (50.00%) |
| occurrences (all) | 2 | 2 | 2 |
| Protein urine present | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |

| | | | |
|--|--------------------|---------------------|---------------------|
| Procedural pain subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Eschar subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Foot fracture subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Skin laceration subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 4 (25.00%) 1 | 1 / 4 (25.00%) 1 |
| Suprapubic pain subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Abdominal pain subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Nausea subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |

| | | | |
|---|---|--------------------|---------------------|
| Constipation subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Reproductive system and breast disorders | | | |
| Testicular retraction subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| Dysmenorrhoea | Additional description: Number of participants at risk in the OnabotulinumtoxinA 200 U (Treatment Cycle 2) arm group is based on the female population. | | |
| subjects affected / exposed ^[1] occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Nasal congestion subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Acne subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Rash subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Renal and urinary disorders | | | |
| Leukocyturia subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Haematuria | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Hydronephrosis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Neck pain subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Infections and infestations | | | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 1 / 4 (25.00%) 1 | 0 / 4 (0.00%) 0 |
| Bacteriuria subjects affected / exposed occurrences (all) | 2 / 3 (66.67%) 2 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Pharyngitis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| Gastroenteritis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Bronchitis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Cystitis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Gastroenteritis viral | | | |

| | | | |
|-----------------------------------|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinea capitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Asymptomatic bacteriuria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed in the OnabotulinumtoxinA 200 U (Treatment Cycle 2) arm group is based on the female population.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 04 October 2013 | Amendment 1 - The following changes were implemented with Amendment 1: Provided clarifications and guidance to investigators regarding entry criteria, study procedures, and prohibited medications/treatments. In addition, the following procedures were added to the protocol: <ul style="list-style-type: none">• Addition of renal function assessment [estimated glomerular filtration rate (eGFR)]• Added form for collecting 'Reason for Requesting Retreatment' at week 12 and later. |
| 05 May 2016 | Amendment 2 - The following changes were implemented with Amendment 1: Modified the inclusion criteria to change the minimum age to 5 years old from 8 years old and to include dosing information for a younger patient population. In addition, an update was made to the criteria which the investigator should consider when determining if a patient had a urinary track infection (UTI). According to the protocol, an adverse event of UTI was defined as 'a symptomatic UTI that required treatment in the opinion of the investigator'. The protocol also indicated that if urinalysis/culture results were reported which, in the opinion of the investigator, were considered clinically significant but did not fulfill the definition of UTI, the findings were to be recorded as adverse events (e.g., bacteriuria, leukocyturia). In addition, the investigator was required to describe the criteria used for qualifying 'leukocyturia' as an adverse event. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported