# Clinical trial results:
# BOTOX® in the Treatment of Urinary Incontinence Due to Overactive Bladder in Patients 12 to 17 Years of Age

## Summary

| | |
|---|---|
| EudraCT number | 2014-000464-17 |
| Trial protocol | GB CZ BE IT NL NO PL FR |
| Global end of trial date | 10 February 2022 |

**Results information**

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 08 February 2023 |
| First version publication date | 20 August 2022 |
| Version creation reason | • Correction of full data set<br>Edit to data table and arm descriptions. |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 191622-137 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02097121 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Allergan |
| Sponsor organisation address | 2525 Dupont Drive, Irvine, CA, United States, 92612 |
| Public contact | Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com |
| Scientific contact | Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.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 | 10 February 2022 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 10 February 2022 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

This was a multicenter, randomized, double-blind, parallel-group, multiple-dose study to evaluate the efficacy and safety of BOTOX in adolescents with urinary incontinence due to overactive bladder (OAB) with inadequate management with anticholinergic therapy. Subjects were randomized in a 1:1:1 ratio to receive a single Tx of 25 U, 50 U, or 100 U BOTOX (not to exceed 6 U/kg) on Day 1, were seen after each treatment at Wks 2, 6, and 12 post-treatment, and thereafter at alternating telephone and clinic visits every 6 weeks until they qualified for further retreatment/exited the study. Subjects could receive multiple treatments dependent upon the number and timing of patient requests/qualification for retreatment. At each retreatment the investigator could keep the dose the same or increase it one dose level in a blinded fashion. Subjects exited the study once 96 weeks have elapsed since entry on Day 1 and at least 12 weeks follow-up since their last study treatment had occurred.

Protection of trial subjects:

Written informed consent was to be obtained from each patient and/or from the patient’s legally authorized representative prior to initiating any study-related activities or procedures. If the patient was under the legal age of consent, the consent form must have been signed by the legally authorized representative in accordance with the relevant country and local regulatory requirements.

Written parental/legally authorized representative informed consent in addition to a separate written minor consent and/or assent (in accordance with any applicable state and local laws/regulations) was required for each minor study patient prior to study enrollment or any study-related procedures in the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 23 May 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Poland: 4 |
| Country: Number of subjects enrolled | Australia: 3 |
| Country: Number of subjects enrolled | Canada: 11 |
| Country: Number of subjects enrolled | United States: 4 |
| Country: Number of subjects enrolled | Czechia: 2 |
| Country: Number of subjects enrolled | Italy: 1 |
| Country: Number of subjects enrolled | Belgium: 10 |
| Country: Number of subjects enrolled | United Kingdom: 21 |

| | |
|---|---|
| Worldwide total number of subjects | 56 |
| EEA total number of subjects | 17 |

Notes:

| **Subjects enrolled per age group** | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 56 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The study included a 28-day screening period.

### Period 1

| | |
|---|---|
| Period 1 title | Overall Study |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Assessor |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Botox 25 U |

Arm description:

Participants randomized to receive 25 Units (U) BOTOX (not to exceed 6 U/kg), administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone. Posttreatment follow-up clinic visits occurred at Weeks 2, 6, and 12. Participants could request retreatment from Week 12 and 12 weeks after each subsequent treatment for up to 4 cycles. The retreatment dose was determined by the Investigator and could be at the same dose or at the next higher dose compared with the preceding treatment.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | BOTOX® |
| Investigational medicinal product code | 9060X |
| Other name | Botulinum Toxin Type A |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Each vial of BOTOX (Botulinum Toxin Type A) purified neurotoxin complex, formulation No. 9060X contains 100 U of Clostridium botulinum toxin Type A, 0.5 mg albumin (human), and 0.9 mg sodium chloride in a sterile, vacuum-dried form without a preservative. The study medication was to be reconstituted with 0.9% sodium chloride (preservative-free). The 10 mL of study drug was to be administered as 20 injections each of 0.5 mL. Under direct cystoscopic visualization, injections were to be distributed evenly across the detrusor wall and spaced approximately 1 cm apart. To avoid injecting the trigone, the injections were to be at least 1 cm above the trigone. The injection needle was to be inserted approximately 2 mm into the detrusor for each injection.

| | |
|---|---|
| **Arm title** | Botox 50 U |

Arm description:

Participants randomized to receive 50 Units (U) BOTOX (not to exceed 6 U/kg), administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone. Posttreatment follow-up clinic visits occurred at Weeks 2, 6, and 12. Participants could request retreatment from Week 12 and 12 weeks after each subsequent treatment for up to 4 cycles. The retreatment dose was determined by the Investigator and could be at the same dose or at the next higher dose compared with the preceding treatment.

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | BOTOX® |
| Investigational medicinal product code | 9060X |
| Other name | Botulinum Toxin Type A |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Each vial of BOTOX (Botulinum Toxin Type A) purified neurotoxin complex, formulation No. 9060X contains 100 U of Clostridium botulinum toxin Type A, 0.5 mg albumin (human), and 0.9 mg sodium chloride in a sterile, vacuum-dried form without a preservative. The study medication was to be reconstituted with 0.9% sodium chloride (preservative-free). The 10 mL of study drug was to be administered as 20 injections each of 0.5 mL. Under direct cystoscopic visualization, injections were to be distributed evenly across the detrusor wall and spaced approximately 1 cm apart. To avoid injecting the trigone, the injections were to be at least 1 cm above the trigone. The injection needle was to be inserted approximately 2 mm into the detrusor for each injection.

| | |
|---|---|
| **Arm title** | Botox 100 U |

Arm description:

Participants randomized to receive 100 Units (U) BOTOX (not to exceed 6 U/kg), administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone. Posttreatment follow-up clinic visits occurred at Weeks 2, 6, and 12. Participants could request retreatment from Week 12 and 12 weeks after each subsequent treatment for up to 4 cycles. The retreatment dose was determined by the Investigator and could be at the same dose or at the next higher dose compared with the preceding treatment.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | BOTOX® |
| Investigational medicinal product code | 9060X |
| Other name | Botulinum Toxin Type A |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Each vial of BOTOX (Botulinum Toxin Type A) purified neurotoxin complex, formulation No. 9060X contains 100 U of Clostridium botulinum toxin Type A, 0.5 mg albumin (human), and 0.9 mg sodium chloride in a sterile, vacuum-dried form without a preservative. The study medication was to be reconstituted with 0.9% sodium chloride (preservative-free). The 10 mL of study drug was to be administered as 20 injections each of 0.5 mL. Under direct cystoscopic visualization, injections were to be distributed evenly across the detrusor wall and spaced approximately 1 cm apart. To avoid injecting the trigone, the injections were to be at least 1 cm above the trigone. The injection needle was to be inserted approximately 2 mm into the detrusor for each injection.

| **Number of subjects in period 1[1]** | Botox 25 U | Botox 50 U | Botox 100 U |
|---|---|---|---|
| Started | 19 | 18 | 19 |
| Received any treatment | 19 | 17 | 19 |
| Actual Treatment Received in Cycle 1 | 18 | 17 | 20 |
| Actual Treatment Received in Cycle 2 | 1 [2] | 17 | 28 |
| Actual Treatment Received in Cycle 3 | 2 [3] | 7 [4] | 13 |
| Actual Treatment Received in Cycle 4 | 0 [5] | 1 [6] | 3 |
| Completed | 12 | 12 | 9 |
| Not completed | 7 | 6 | 19 |

| | | | |
|---|---|---|---|
| Adverse event, non-fatal | - | 1 | - |
| Other, not specified | 4 | 2 | 3 |
| Not specified | - | - | 9 |
| Lost to follow-up | 1 | 1 | 2 |
| Lack of efficacy | 2 | 1 | 3 |
| Withdrawal by subject | - | 1 | 2 |
| Joined | 0 | 0 | 9 |
| Subject assigned to 25 U rcvd 100 U in Cycle 2 | - | - | 1 |
| Transferred in from other group/arm | - | - | 7 |
| Subject assigned to 25 U rcvd 100 U in Cycle 1 | - | - | 1 |

Notes:

[1] - The number of subjects transferring in and out of the arms in the period are not the same. It is expected the net number of transfers in and out of the arms in a period, will be zero.
Justification: Subjects were randomized in a 1:1:1 ratio to 1 of 3 treatment arms. Randomization was stratified by baseline daytime urinary urgency incontinence episodes (a total of ≤6 episodes or > 6 episodes over the 2-day bladder diary collection period).

Subjects could request retreatment from Week 12 and 12 weeks after each subsequent treatment for up to 4 cycles. Retreatment dose was determined by the Investigator and could be at same dose or at the next higher dose compared with the preceding dose.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: One participant assigned to 25 U BOTOX received 100 U BOTOX in Cycle 1 in error.
One participant assigned to 25 U BOTOX received 100 U BOTOX in Cycle 2 in error.

Participants could request retreatment from Week 12 and 12 weeks after each subsequent treatment for up to 4 cycles. The retreatment dose was determined by the Investigator and could be at the same dose or at the next higher dose compared with the preceding treatment.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: One participant assigned to 25 U BOTOX received 100 U BOTOX in Cycle 1 in error.
One participant assigned to 25 U BOTOX received 100 U BOTOX in Cycle 2 in error.

Participants could request retreatment from Week 12 and 12 weeks after each subsequent treatment for up to 4 cycles. The retreatment dose was determined by the Investigator and could be at the same dose or at the next higher dose compared with the preceding treatment.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: One participant assigned to 100 U BOTOX received 50 U BOTOX in Cycle 2 in error.

Participants could request retreatment from Week 12 and 12 weeks after each subsequent treatment for up to 4 cycles. The retreatment dose was determined by the Investigator and could be at the same dose or at the next higher dose compared with the preceding treatment.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: One participant assigned to 25 U BOTOX received 100 U BOTOX in Cycle 1 in error. One participant assigned to 25 U BOTOX received 100 U BOTOX in Cycle 2 in error.

Participants could request retreatment from Week 12 and 12 weeks after each subsequent treatment for up to 4 cycles. The retreatment dose was determined by the Investigator and could be at the same dose or at the next higher dose compared with the preceding treatment.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: One participant assigned to 100 U BOTOX received 50 U BOTOX in Cycle 2 in error.

Participants could request retreatment from Week 12 and 12 weeks after each subsequent treatment for up to 4 cycles. The retreatment dose was determined by the Investigator and could be at the same dose or at the next higher dose compared with the preceding treatment.

## Period 2

| | |
|---|---|
| Period 2 title | BOTOX-treated population |
| Is this the baseline period? | Yes[7] |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Assessor |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | BOTOX 25 U (BOTOX-Treated Population) |

Arm description:

Participants received 25 U BOTOX in Treatment Cycle 1

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | BOTOX® |
| Investigational medicinal product code | 9060X |
| Other name | Botulinum Toxin Type A |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Each vial of BOTOX (Botulinum Toxin Type A) purified neurotoxin complex, formulation No. 9060X contains 100 U of Clostridium botulinum toxin Type A, 0.5 mg albumin (human), and 0.9 mg sodium chloride in a sterile, vacuum-dried form without a preservative. The study medication was to be reconstituted with 0.9% sodium chloride (preservative-free). The 10 mL of study drug was to be administered as 20 injections each of 0.5 mL. Under direct cystoscopic visualization, injections were to be distributed evenly across the detrusor wall and spaced approximately 1 cm apart. To avoid injecting the trigone, the injections were to be at least 1 cm above the trigone. The injection needle was to be inserted approximately 2 mm into the detrusor for each injection.

| | |
|---|---|
| **Arm title** | BOTOX 50 U (BOTOX-Treated Population) |

Arm description:

Participants received 50 U BOTOX in Treatment Cycle 1

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | BOTOX® |
| Investigational medicinal product code | 9060X |
| Other name | Botulinum Toxin Type A |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Each vial of BOTOX (Botulinum Toxin Type A) purified neurotoxin complex, formulation No. 9060X

contains 100 U of Clostridium botulinum toxin Type A, 0.5 mg albumin (human), and 0.9 mg sodium chloride in a sterile, vacuum-dried form without a preservative. The study medication was to be reconstituted with 0.9% sodium chloride (preservative-free). The 10 mL of study drug was to be administered as 20 injections each of 0.5 mL. Under direct cystoscopic visualization, injections were to be distributed evenly across the detrusor wall and spaced approximately 1 cm apart. To avoid injecting the trigone, the injections were to be at least 1 cm above the trigone. The injection needle was to be inserted approximately 2 mm into the detrusor for each injection.

| **Arm title** | BOTOX 100 U (BOTOX-Treated Population) |
|---|---|

Arm description:

Participants received 100 U BOTOX in Treatment Cycle 1

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | BOTOX® |
| Investigational medicinal product code | 9060X |
| Other name | Botulinum Toxin Type A |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Each vial of BOTOX (Botulinum Toxin Type A) purified neurotoxin complex, formulation No. 9060X contains 100 U of Clostridium botulinum toxin Type A, 0.5 mg albumin (human), and 0.9 mg sodium chloride in a sterile, vacuum-dried form without a preservative. The study medication was to be reconstituted with 0.9% sodium chloride (preservative-free). The 10 mL of study drug was to be administered as 20 injections each of 0.5 mL. Under direct cystoscopic visualization, injections were to be distributed evenly across the detrusor wall and spaced approximately 1 cm apart. To avoid injecting the trigone, the injections were to be at least 1 cm above the trigone. The injection needle was to be inserted approximately 2 mm into the detrusor for each injection.

Notes:

[7] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The BOTOX-treated population (all participants enrolled into the study who received at least 1 BOTOX treatment) is presented according to the dose received in the first treatment cycle

| **Number of subjects in period 2[8][9]** | BOTOX 25 U (BOTOX-Treated Population) | BOTOX 50 U (BOTOX-Treated Population) | BOTOX 100 U (BOTOX-Treated Population) |
|---|---|---|---|
| Started | 12 | 12 | 9 |
| Completed | 18 | 17 | 20 |
| Joined | 6 | 5 | 11 |
| BOTOX-treated subjects | 6 | 5 | 10 |
| Transferred in from other group/arm | - | - | 1 |

Notes:

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

Justification: The BOTOX-treated population (all participants enrolled into the study who received at least 1 BOTOX treatment) is presented according to the dose received in the first treatment cycle

[9] - The number of subjects transferring in and out of the arms in the period are not the same. It is expected the net number of transfers in and out of the arms in a period, will be zero.

Justification: The BOTOX-treated population (all participants enrolled into the study who received at least 1 BOTOX treatment) is presented according to the dose received in the first treatment cycle.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | BOTOX 25 U (BOTOX-Treated Population) |
| Reporting group description: | |
| Participants received 25 U BOTOX in Treatment Cycle 1 | |

| | |
|---|---|
| Reporting group title | BOTOX 50 U (BOTOX-Treated Population) |
| Reporting group description: | |
| Participants received 50 U BOTOX in Treatment Cycle 1 | |

| | |
|---|---|
| Reporting group title | BOTOX 100 U (BOTOX-Treated Population) |
| Reporting group description: | |
| Participants received 100 U BOTOX in Treatment Cycle 1 | |

| Reporting group values | BOTOX 25 U (BOTOX-Treated Population) | BOTOX 50 U (BOTOX-Treated Population) | BOTOX 100 U (BOTOX-Treated Population) |
|---|---|---|---|
| Number of subjects | 18 | 17 | 20 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 18 | 17 | 20 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 13.7 | 14.3 | 14.0 |
| standard deviation | ± 1.49 | ± 1.86 | ± 1.75 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 16 | 17 | 14 |
| Male | 2 | 0 | 6 |
| Race<br>Units: Subjects | | | |
| White | 12 | 12 | 17 |
| Black or African American | 0 | 0 | 0 |
| Asian | 0 | 1 | 0 |
| Hispanic | 0 | 0 | 0 |
| Other | 1 | 1 | 1 |
| Not Reported | 2 | 1 | 1 |
| Unknown | 3 | 2 | 1 |

| Daily Frequency of Daytime Urinary Incontinence Episodes | | | |
|---|---|---|---|
| A bladder diary was used to log each daytime urgency episode over 2 consecutive days during screening. | | | |
| Units: number of episodes | | | |
| arithmetic mean | 5.29 | 3.54 | 3.64 |
| standard deviation | ± 3.447 | ± 2.696 | ± 2.951 |

| **Reporting group values** | Total | | |
|---|---|---|---|
| Number of subjects | 55 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 55 | | |
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 47 | | |
| Male | 8 | | |
| Race | | | |
| Units: Subjects | | | |
| White | 41 | | |
| Black or African American | 0 | | |
| Asian | 1 | | |
| Hispanic | 0 | | |
| Other | 3 | | |
| Not Reported | 4 | | |
| Unknown | 6 | | |
| Daily Frequency of Daytime Urinary Incontinence Episodes | | | |
| A bladder diary was used to log each daytime urgency episode over 2 consecutive days during screening. | | | |
| Units: number of episodes | | | |
| arithmetic mean | | | |
| standard deviation | - | | |

## End points

### End points reporting groups

| Reporting group title | Botox 25 U |
|---|---|

Reporting group description:

Participants randomized to receive 25 Units (U) BOTOX (not to exceed 6 U/kg), administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone. Posttreatment follow-up clinic visits occurred at Weeks 2, 6, and 12. Participants could request retreatment from Week 12 and 12 weeks after each subsequent treatment for up to 4 cycles. The retreatment dose was determined by the Investigator and could be at the same dose or at the next higher dose compared with the preceding treatment.

| Reporting group title | Botox 50 U |
|---|---|

Reporting group description:

Participants randomized to receive 50 Units (U) BOTOX (not to exceed 6 U/kg), administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone. Posttreatment follow-up clinic visits occurred at Weeks 2, 6, and 12. Participants could request retreatment from Week 12 and 12 weeks after each subsequent treatment for up to 4 cycles. The retreatment dose was determined by the Investigator and could be at the same dose or at the next higher dose compared with the preceding treatment.

| Reporting group title | Botox 100 U |
|---|---|

Reporting group description:

Participants randomized to receive 100 Units (U) BOTOX (not to exceed 6 U/kg), administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone. Posttreatment follow-up clinic visits occurred at Weeks 2, 6, and 12. Participants could request retreatment from Week 12 and 12 weeks after each subsequent treatment for up to 4 cycles. The retreatment dose was determined by the Investigator and could be at the same dose or at the next higher dose compared with the preceding treatment.

| Reporting group title | BOTOX 25 U (BOTOX-Treated Population) |
|---|---|

Reporting group description:

Participants received 25 U BOTOX in Treatment Cycle 1

| Reporting group title | BOTOX 50 U (BOTOX-Treated Population) |
|---|---|

Reporting group description:

Participants received 50 U BOTOX in Treatment Cycle 1

| Reporting group title | BOTOX 100 U (BOTOX-Treated Population) |
|---|---|

Reporting group description:

Participants received 100 U BOTOX in Treatment Cycle 1

| Subject analysis set title | BOTOX 25 U (BOTOX-Treated Population) |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants received 25 U BOTOX in a given Treatment Cycle

| Subject analysis set title | BOTOX 50 U (BOTOX-Treated Population) |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants received 50 U BOTOX in a given Treatment Cycle

| Subject analysis set title | BOTOX 100 U (BOTOX-Treated Population) |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants received 100 U BOTOX in a given Treatment Cycle

## 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 |
|---|---|

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 per the respective treatments that participants received in the corresponding treatment cycle.

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

End point timeframe:

From Baseline to 2 consecutive days in the week prior to Week 12 in Treatment Cycle 1

| **End point values** | BOTOX 25 U (BOTOX-Treated Population) | BOTOX 50 U (BOTOX-Treated Population) | BOTOX 100 U (BOTOX-Treated Population) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 18[1] | 17[2] | 20[3] | |
| Units: urinary incontinence episodes per day | | | | |
| least squares mean (standard error) | -1.37 (± 0.801) | -0.97 (± 0.811) | -2.35 (± 0.746) | |

Notes:

[1] - Subjects with analysis values at both baseline and Week 12

[2] - Subjects with analysis values at both baseline and Week 12

[3] - Subjects with analysis values at both baseline and Week 12

### Statistical analyses

| **Statistical analysis title** | Treatment Difference of 100 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 100 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using an ANCOVA model with study baseline value as covariate, and treatment group as factor. A hierarchical analysis strategy to adjust for multiplicity was used.

| Comparison groups | BOTOX 25 U (BOTOX-Treated Population) v BOTOX 100 U (BOTOX-Treated Population) |
|---|---|
| Number of subjects included in analysis | 38 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3802 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.98 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.203 |
| upper limit | 1.243 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.107 |

| **Statistical analysis title** | Treatment Difference of 50 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 50 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using an ANCOVA model with study baseline value as covariate, and treatment group as factor. A hierarchical analysis strategy to adjust for multiplicity was used.

| | |
|---|---|
| Comparison groups | BOTOX 25 U (BOTOX-Treated Population) v BOTOX 50 U (BOTOX-Treated Population) |
| Number of subjects included in analysis | 35 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.733 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.921 |
| upper limit | 2.712 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.154 |

## Secondary: Change From Study Baseline in the Daily Average Frequency of Normalized Daytime Micturition Episodes

| End point title | Change From Study Baseline in the Daily Average Frequency of Normalized Daytime Micturition Episodes |
|---|---|

End point description:

Micturition was defined as toilet voids 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 micturition episodes were averaged during the 2-day period. A negative change from Baseline indicates improvement. Data are summarized per the respective treatments that participants received in the corresponding treatment cycle.

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

End point timeframe:

From Baseline to 2 consecutive days in the week prior to Week 12 in Treatment Cycle 1

| End point values | BOTOX 25 U (BOTOX-Treated Population) | BOTOX 50 U (BOTOX-Treated Population) | BOTOX 100 U (BOTOX-Treated Population) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 18[4] | 17[5] | 20[6] | |
| Units: micturition episodes per day | | | | |
| least squares mean (standard error) | -1.84 (± 1.027) | 0.31 (± 1.014) | -1.02 (± 0.983) | |

Notes:

[4] - Subjects with analysis values at both baseline and Week 12

[5] - Subjects with analysis values at both baseline and Week 12

[6] - Subjects with analysis values at both baseline and Week 12

## Statistical analyses

| Statistical analysis title | Treatment Difference of 100 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 100 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using an ANCOVA model with study baseline value as covariate, and treatment group and stratification (baseline daytime urinary urgency incontinence episodes [a total of ≤ 6 episodes or > 6 episodes over the 2-day diary collection period]) as factors. A hierarchical analysis strategy to adjust for multiplicity was not implemented.

| Comparison groups | BOTOX 100 U (BOTOX-Treated Population) v BOTOX 25 U (BOTOX-Treated Population) |
|---|---|
| Number of subjects included in analysis | 38 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5743 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.082 |
| upper limit | 3.713 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.442 |

| Statistical analysis title | Treatment Difference of 50 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 50 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using an ANCOVA model with study baseline value as covariate, and treatment group and stratification (baseline daytime urinary urgency incontinence episodes [a total of ≤ 6 episodes or > 6 episodes over the 2-day diary collection period]) as factors. A hierarchical analysis strategy to adjust for multiplicity was not implemented.

| Comparison groups | BOTOX 50 U (BOTOX-Treated Population) v BOTOX 25 U (BOTOX-Treated Population) |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 35 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1451 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | 2.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.769 |
| upper limit | 5.078 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.455 |

## Secondary: Change From Study Baseline in the Daily Average Frequency of Normalized Daytime Urgency Episodes

| | |
|---|---|
| End point title | Change From Study Baseline in the Daily Average Frequency of Normalized Daytime Urgency Episodes |

End point description:

Participants recorded daytime urgency episodes 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 urgency episodes were averaged during the 2-day period. A negative change from Baseline indicates improvement. Data are summarized per the respective treatments that participants received in the corresponding treatment cycle.

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

End point timeframe:

From Baseline to 2 consecutive days in the week prior to Week 12 in Treatment Cycle 1

| End point values | BOTOX 25 U (BOTOX-Treated Population) | BOTOX 50 U (BOTOX-Treated Population) | BOTOX 100 U (BOTOX-Treated Population) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 18[7] | 17[8] | 20[9] | |
| Units: urgency episodes per day | | | | |
| least squares mean (standard error) | -1.85 (± 1.014) | -1.78 (± 0.998) | -2.18 (± 0.945) | |

Notes:

[7] - Subjects with analysis values at both baseline and Week 12

[8] - Subjects with analysis values at both baseline and Week 12

[9] - Subjects with analysis values at both baseline and Week 12

### Statistical analyses

| Statistical analysis title | Treatment Difference of 100 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 100 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using an ANCOVA model with study baseline value as covariate, and treatment group and

stratification (baseline daytime urinary urgency incontinence episodes [a total of ≤ 6 episodes or > 6 episodes over the 2-day diary collection period]) as factors. A hierarchical analysis strategy to adjust for multiplicity was not implemented.

| | |
|---|---|
| Comparison groups | BOTOX 100 U (BOTOX-Treated Population) v BOTOX 25 U (BOTOX-Treated Population) |
| Number of subjects included in analysis | 38 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8206 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.33 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.205 |
| upper limit | 2.551 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.434 |

| **Statistical analysis title** | Treatment Difference of 50 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 50 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using an ANCOVA model with study baseline value as covariate, and treatment group and stratification (baseline daytime urinary urgency incontinence episodes [a total of ≤ 6 episodes or > 6 episodes over the 2-day diary collection period]) as factors. A hierarchical analysis strategy to adjust for multiplicity was not implemented.

| | |
|---|---|
| Comparison groups | BOTOX 25 U (BOTOX-Treated Population) v BOTOX 50 U (BOTOX-Treated Population) |
| Number of subjects included in analysis | 35 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9604 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.07 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.807 |
| upper limit | 2.95 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.434 |

## Secondary: Percentage of Participants With Night Time Urinary Incontinence

| | |
|---|---|
| End point title | Percentage of Participants With Night Time Urinary Incontinence |

End point description:

Urinary incontinence was defined as involuntary loss of urine. Participants recorded night time urinary incontinence episodes in a bladder diary during 2 consecutive days in the week prior to the study visit. Night time is defined as the time between going to bed to sleep for the night and waking up to start the next day. The number of daily night time urinary incontinence episodes were averaged during the 2-day period. Data are summarized per the respective treatments that participants received in the corresponding treatment cycle.

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

End point timeframe:

From Baseline to 2 consecutive days in the week prior to Week 12 in Treatment Cycle 1

| **End point values** | BOTOX 25 U (BOTOX-Treated Population) | BOTOX 50 U (BOTOX-Treated Population) | BOTOX 100 U (BOTOX-Treated Population) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 18[10] | 17[11] | 20[12] | |
| Units: percentage of partipants | | | | |
| number (not applicable) | | | | |
| Baseline—0 nights | 22.2 | 52.9 | 35.0 | |
| Baseline—1 night | 27.8 | 11.8 | 15.0 | |
| Baseline—2 nights | 50.0 | 35.3 | 50.0 | |
| Week 12—0 nights | 50.0 | 76.5 | 50.0 | |
| Week 12—1 night | 22.2 | 5.9 | 15.0 | |
| Week 12—2 nights | 27.8 | 17.6 | 35.0 | |

Notes:

[10] - Subjects with analysis values at both baseline and Week 12

[11] - Subjects with analysis values at both baseline and Week 12

[12] - Subjects with analysis values at both baseline and Week 12

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Study Baseline in the Daily Average Volume Voided Per Micturition (mL)

| End point title | Change From Study Baseline in the Daily Average Volume Voided Per Micturition (mL) |
|---|---|

End point description:

The volume per micturition was derived from the total urine volume voided over 1 daytime period during the 2-day bladder diary collection period divided by the number of voids in the same daytime period. Daytime is defined as the time between waking up to start the day and going to bed to sleep for the night. A negative change from Baseline indicates improvement. Data are summarized per the respective treatments that participants received in the corresponding treatment cycle.

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

End point timeframe:

From Baseline to 2 consecutive days in the week prior to Week 12 in Treatment Cycle 1

| End point values | BOTOX 25 U (BOTOX-Treated Population) | BOTOX 50 U (BOTOX-Treated Population) | BOTOX 100 U (BOTOX-Treated Population) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 18[13] | 17[14] | 20[15] | |
| Units: mL | | | | |
| least squares mean (standard error) | -9.17 (± 15.924) | 24.94 (± 17.047) | 26.16 (± 15.900) | |

Notes:

[13] - Subjects with analysis values at both baseline and Week 12

[14] - Subjects with analysis values at both baseline and Week 12

[15] - Subjects with analysis values at both baseline and Week 12

## Statistical analyses

| Statistical analysis title | Treatment Difference of 100 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 100 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using an ANCOVA model with study baseline value as covariate, and treatment group and stratification (baseline daytime urinary urgency incontinence episodes [a total of ≤ 6 episodes or > 6 episodes over the 2-day diary collection period]) as factors. A hierarchical analysis strategy to adjust for multiplicity was not implemented.

| | |
|---|---|
| Comparison groups | BOTOX 100 U (BOTOX-Treated Population) v BOTOX 25 U (BOTOX-Treated Population) |
| Number of subjects included in analysis | 38 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1174 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | 35.33 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.207 |
| upper limit | 79.873 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 22.175 |

| Statistical analysis title | Treatment Difference of 50 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 50 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using an ANCOVA model with study baseline value as covariate, and treatment group and stratification (baseline daytime urinary urgency incontinence episodes [a total of ≤ 6 episodes or > 6 episodes over the 2-day diary collection period]) as factors. A hierarchical analysis strategy to adjust for multiplicity was not implemented.

| | |
|---|---|
| Comparison groups | BOTOX 50 U (BOTOX-Treated Population) v BOTOX 25 U (BOTOX-Treated Population) |

| | |
|---|---|
| Number of subjects included in analysis | 35 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1567 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | 34.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.536 |
| upper limit | 81.76 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 23.722 |

## Secondary: Change From Study Baseline in Pediatric Urinary Incontinence Quality of Life Total Score (PinQ)

| | |
|---|---|
| End point title | Change From Study Baseline in Pediatric Urinary Incontinence Quality of Life Total Score (PinQ) |

End point description:

The PinQ is a 20-item questionnaire that asks about the subject's incontinence and its consequences in daily life and relationships. Items are answered on a Likert-type scale of 0 (no) to 4 (all of the time) and a total sum score is calculated (from 0 to 80), with higher scores indicating lower health-related quality of life. A negative change from Baseline indicates improvement.

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

End point timeframe:

From Day 1 Prior to Treatment to Week 12 in Treatment Cycle 1

| End point values | BOTOX 25 U (BOTOX-Treated Population) | BOTOX 50 U (BOTOX-Treated Population) | BOTOX 100 U (BOTOX-Treated Population) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 18[16] | 17[17] | 20[18] | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | -6.96 (± 2.841) | -5.11 (± 3.243) | -8.28 (± 2.979) | |

Notes:

[16] - Subjects with analysis values at both baseline and Week 12

[17] - Subjects with analysis values at both baseline and Week 12

[18] - Subjects with analysis values at both baseline and Week 12

### Statistical analyses

| Statistical analysis title | Treatment Difference of 100 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 100 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using an ANCOVA model with study baseline value as covariate, and treatment group and stratification (baseline daytime urinary urgency incontinence episodes [a total of ≤ 6 episodes or > 6 episodes over the 2-day diary collection period]) as factors. A hierarchical analysis strategy to adjust for

multiplicity was not implemented.

| | |
|---|---|
| Comparison groups | BOTOX 100 U (BOTOX-Treated Population) v BOTOX 25 U (BOTOX-Treated Population) |
| Number of subjects included in analysis | 38 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7481 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -1.32 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.553 |
| upper limit | 6.909 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.091 |

| **Statistical analysis title** | Treatment Difference of 50 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 50 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using an ANCOVA model with study baseline value as covariate, and treatment group and stratification (baseline daytime urinary urgency incontinence episodes [a total of ≤ 6 episodes or > 6 episodes over the 2-day diary collection period]) as factors. A hierarchical analysis strategy to adjust for multiplicity was not implemented.

| | |
|---|---|
| Comparison groups | BOTOX 25 U (BOTOX-Treated Population) v BOTOX 50 U (BOTOX-Treated Population) |
| Number of subjects included in analysis | 35 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6691 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | 1.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.799 |
| upper limit | 10.498 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.299 |

## Secondary: Change From Study Baseline in PinQ item 'I am worried that people might think my clothes smell like pee"

| | |
|---|---|
| End point title | Change From Study Baseline in PinQ item 'I am worried that people might think my clothes smell like pee" |

End point description:

The Pediatric Urinary Incontinence Quality of (PinQ) is a 20-item questionnaire that asks about the subject's incontinence and its consequences in daily life and relationships. Items are answered on a Likert-type scale of 0 (no) to 4 (all of the time), with higher scores indicating lower health-related quality of life. A negative change from Baseline indicates improvement.

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

End point timeframe:

From Day 1 Prior to Treatment to Week 12 in Treatment Cycle 1

| **End point values** | BOTOX 25 U (BOTOX-Treated Population) | BOTOX 50 U (BOTOX-Treated Population) | BOTOX 100 U (BOTOX-Treated Population) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 18[19] | 17[20] | 20[21] | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | -0.06 (± 0.238) | -0.37 (± 0.273) | -0.09 (± 0.251) | |

Notes:

[19] - Subjects with analysis values at both baseline and Week 12

[20] - Subjects with analysis values at both baseline and Week 12

[21] - Subjects with analysis values at both baseline and Week 12

## Statistical analyses

| **Statistical analysis title** | Treatment Difference of 100 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 100 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using an ANCOVA model with study baseline value as covariate, and treatment group and stratification (baseline daytime urinary urgency incontinence episodes [a total of ≤ 6 episodes or > 6 episodes over the 2-day diary collection period]) as factors. A hierarchical analysis strategy to adjust for multiplicity was not implemented.

| Comparison groups | BOTOX 100 U (BOTOX-Treated Population) v BOTOX 25 U (BOTOX-Treated Population) |
|---|---|
| Number of subjects included in analysis | 38 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9297 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.721 |
| upper limit | 0.661 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.343 |

| Statistical analysis title | Treatment Difference of 50 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 50 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using an ANCOVA model with study baseline value as covariate, and treatment group and stratification (baseline daytime urinary urgency incontinence episodes [a total of ≤ 6 episodes or > 6 episodes over the 2-day diary collection period]) as factors. A hierarchical analysis strategy to adjust for multiplicity was not implemented.

| | |
|---|---|
| Comparison groups | BOTOX 25 U (BOTOX-Treated Population) v BOTOX 50 U (BOTOX-Treated Population) |
| Number of subjects included in analysis | 35 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3976 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.022 |
| upper limit | 0.413 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.357 |

## Secondary: Change From Study Baseline in PinQ item 'My bladder problem makes me feel bad about myself"

| End point title | Change From Study Baseline in PinQ item 'My bladder problem makes me feel bad about myself" |
|---|---|

End point description:

The Pediatric Urinary Incontinence Quality of (PinQ) is a 20-item questionnaire that asks about the subject's incontinence and its consequences in daily life and relationships. Items are answered on a Likert-type scale of 0 (no) to 4 (all of the time), with higher scores indicating lower health-related quality of life. A negative change from Baseline indicates improvement.

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

End point timeframe:

From Day 1 Prior to Treatment to Week 12 in Treatment Cycle 1

| End point values | BOTOX 25 U (BOTOX-Treated Population) | BOTOX 50 U (BOTOX-Treated Population) | BOTOX 100 U (BOTOX-Treated Population) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 18[22] | 17[23] | 20[24] | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | -0.54 (± 0.209) | -0.15 (± 0.238) | -0.24 (± 0.220) | |

Notes:

[22] - Subjects with analysis values at both baseline and Week 12

[23] - Subjects with analysis values at both baseline and Week 12

[24] - Subjects with analysis values at both baseline and Week 12

## Statistical analyses

| **Statistical analysis title** | Treatment Difference of 100 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 100 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using an ANCOVA model with study baseline value as covariate, and treatment group and stratification (baseline daytime urinary urgency incontinence episodes [a total of ≤ 6 episodes or > 6 episodes over the 2-day diary collection period]) as factors. A hierarchical analysis strategy to adjust for multiplicity was not implemented.

| | |
|---|---|
| Comparison groups | BOTOX 100 U (BOTOX-Treated Population) v BOTOX 25 U (BOTOX-Treated Population) |
| Number of subjects included in analysis | 38 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3309 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.311 |
| upper limit | 0.904 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.302 |

| **Statistical analysis title** | Treatment Difference of 50 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 50 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using an ANCOVA model with study baseline value as covariate, and treatment group and stratification (baseline daytime urinary urgency incontinence episodes [a total of ≤ 6 episodes or > 6 episodes over the 2-day diary collection period]) as factors. A hierarchical analysis strategy to adjust for multiplicity was not implemented.

| | |
|---|---|
| Comparison groups | BOTOX 25 U (BOTOX-Treated Population) v BOTOX 50 U (BOTOX-Treated Population) |
| Number of subjects included in analysis | 35 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2235 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.39 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.245 |
| upper limit | 1.024 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.315 |

## Secondary: Change From Study Baseline in PinQ item 'I miss out on being with friends because of my bladder problems"

| | |
|---|---|
| End point title | Change From Study Baseline in PinQ item 'I miss out on being with friends because of my bladder problems" |

End point description:

The Pediatric Urinary Incontinence Quality of (PinQ) is a 20-item questionnaire that asks about the subject's incontinence and its consequences in daily life and relationships. Items are answered on a Likert-type scale of 0 (no) to 4 (all of the time), with higher scores indicating lower health-related quality of life. A negative change from Baseline indicates improvement.

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

End point timeframe:

From Day 1 Prior to Treatment to Week 12 in Treatment Cycle 1

| End point values | BOTOX 25 U (BOTOX-Treated Population) | BOTOX 50 U (BOTOX-Treated Population) | BOTOX 100 U (BOTOX-Treated Population) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 18[25] | 17[26] | 20[27] | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | -0.39 (± 0.193) | -0.24 (± 0.218) | -0.27 (± 0.201) | |

Notes:

[25] - Subjects with analysis values at both baseline and Week 12

[26] - Subjects with analysis values at both baseline and Week 12

[27] - Subjects with analysis values at both baseline and Week 12

### Statistical analyses

| Statistical analysis title | Treatment Difference of 100 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 100 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using an ANCOVA model with study baseline value as covariate, and treatment group and stratification (baseline daytime urinary urgency incontinence episodes [a total of ≤ 6 episodes or > 6 episodes over the 2-day diary collection period]) as factors. A hierarchical analysis strategy to adjust for multiplicity was not implemented.

| | |
|---|---|
| Comparison groups | BOTOX 100 U (BOTOX-Treated Population) v BOTOX 25 U (BOTOX-Treated Population) |

| | |
|---|---|
| Number of subjects included in analysis | 38 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6689 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.434 |
| upper limit | 0.67 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.274 |

| **Statistical analysis title** | Treatment Difference of 50 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 50 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using an ANCOVA model with study baseline value as covariate, and treatment group and stratification (baseline daytime urinary urgency incontinence episodes [a total of ≤ 6 episodes or > 6 episodes over the 2-day diary collection period]) as factors. A hierarchical analysis strategy to adjust for multiplicity was not implemented.

| | |
|---|---|
| Comparison groups | BOTOX 25 U (BOTOX-Treated Population) v BOTOX 50 U (BOTOX-Treated Population) |
| Number of subjects included in analysis | 35 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6076 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.431 |
| upper limit | 0.729 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.288 |

## Secondary: Percentage of Participants with a Positive Treatment Response in the Modified Treatment Benefit Scale

| End point title | Percentage of Participants with a Positive Treatment Response in the Modified Treatment Benefit Scale |
|---|---|

End point description:

The Modified Treatment Benefit Scale (Modified TBS) is a single-item scale designed to assess the change in the subject's overactive bladder (OAB) condition following treatment. The subject's current condition (urinary problems, urinary incontinence) is compared to their condition prior to receipt of any study treatment by selection of "greatly improved", "improved", "not changed" or "worsened". Subjects who selected "greatly improved" or "improved" were considered to have a positive treatment response.

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

End point timeframe:

At Week 12 in Treatment Cycle 1

| **End point values** | BOTOX 25 U (BOTOX-Treated Population) | BOTOX 50 U (BOTOX-Treated Population) | BOTOX 100 U (BOTOX-Treated Population) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 17[28] | 17[29] | 19[30] | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 52.9 (27.81 to 77.02) | 70.6 (44.04 to 89.69) | 68.4 (43.45 to 87.42) | |

Notes:

[28] - Subjects with non-missing values at Week 12.

[29] - Subjects with non-missing values at Week 12.

[30] - Subjects with non-missing values at Week 12.

### Statistical analyses

| **Statistical analysis title** | Treatment Difference of 100 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 100 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using the Cochran-Mantel-Haenszel (CMH) method stratified by baseline daytime urinary urgency incontinence episodes (a total of ≤ 6 episodes or > 6 episodes over the 2-day diary collection period).

| | |
|---|---|
| Comparison groups | BOTOX 100 U (BOTOX-Treated Population) v BOTOX 25 U (BOTOX-Treated Population) |
| Number of subjects included in analysis | 36 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6092 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference % |
| Point estimate | 15.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -18.94 |
| upper limit | 46.19 |

| **Statistical analysis title** | Treatment Difference of 50 U versus 25 U |
|---|---|

Statistical analysis description:

Pairwise comparisons of 50 U versus 25 U of BOTOX up to Week 12 in Treatment Cycle 1 was evaluated using the Cochran-Mantel-Haenszel (CMH) method stratified by baseline daytime urinary urgency incontinence episodes (a total of ≤ 6 episodes or > 6 episodes over the 2-day diary collection period).

| | |
|---|---|
| Comparison groups | BOTOX 50 U (BOTOX-Treated Population) v BOTOX 25 U (BOTOX-Treated Population) |

| | |
|---|---|
| Number of subjects included in analysis | 34 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4824 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference % |
| Point estimate | 17.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16.2 |
| upper limit | 48.9 |

## Secondary: Time to Subject's First Request for Retreatment

| | |
|---|---|
| End point title | Time to Subject's First Request for Retreatment |

End point description:

The time from the day of BOTOX treatment to the request for the subsequent treatment was estimated using a Kaplan-Meier survival method for each treatment group. Subjects who did not request retreatment were treated as censored at the time of their last study visit or study exit.

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

End point timeframe:

From the day of BOTOX treatment in Treatment Cycle 1 to the request for subsequent treatment

| **End point values** | BOTOX 25 U (BOTOX-Treated Population) | BOTOX 50 U (BOTOX-Treated Population) | BOTOX 100 U (BOTOX-Treated Population) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 17[31] | 14[32] | 17[33] | |
| Units: weeks | | | | |
| median (confidence interval 95%) | 16.6 (12.71 to 25.29) | 17.6 (11.29 to 38.57) | 21.3 (12.86 to 30.14) | |

Notes:

[31] - BOTOX-treated subjects who requested retreatment

[32] - BOTOX-treated subjects who requested retreatment

[33] - BOTOX-treated subjects who requested retreatment

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Subject's Qualification for Retreatment

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

End point description:

The time from the day of BOTOX treatment to the qualification for retreatment was estimated using a Kaplan-Meier survival method for each treatment group. Subjects who did not qualify for retreatment were treated as censored at the time of their last study visit or study exit.

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

End point timeframe:

From the day of BOTOX treatment in Treatment Cycle 1 to the qualification for retreatment

| End point values | BOTOX 25 U (BOTOX-Treated Population) | BOTOX 50 U (BOTOX-Treated Population) | BOTOX 100 U (BOTOX-Treated Population) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 16[34] | 14[35] | 17[36] | |
| Units: weeks | | | | |
| median (confidence interval 95%) | 22.5 (13.57 to 36.29) | 18.1 (12.29 to 52.57) | 24.1 (12.86 to 41.57) | |

Notes:

[34] - BOTOX-treated subjects who qualified for retreatment

[35] - BOTOX-treated subjects who qualified for retreatment

[36] - BOTOX-treated subjects who qualified for retreatment

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Number of Participants With Treatment Emergent Adverse Events

| End point title | Number of Participants With Treatment Emergent Adverse Events |
|---|---|

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product which does not necessarily have a causal relationship with this treatment. The investigator assesses the relationship of each event to the use of study drug. A serious adverse event (SAE) is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the participant and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment-emergent adverse events/treatment-emergent serious adverse events (TEAEs/TESAEs) are defined as any event that began or worsened in severity on or after the first dose of study drug.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

From the first dose of study drug until the last dose, up to 147 weeks

| End point values | BOTOX 25 U (BOTOX-Treated Population) | BOTOX 50 U (BOTOX-Treated Population) | BOTOX 100 U (BOTOX-Treated Population) | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 18[37] | 17[38] | 28[39] | |
| Units: number of participants | | | | |
| Cycle 1 (n=18, 17, 20) | 13 | 12 | 14 | |
| Cycle 2 (n=1, 17, 28) | 1 | 13 | 18 | |
| Cycle 3 (n=2, 7, 13) | 1 | 3 | 8 | |
| Cycle 4 (n=0, 1, 3) | 0 | 1 | 1 | |

Notes:
[37] - All participants enrolled into the study who received at least 1 BOTOX treatment

[38] - All participants enrolled into the study who received at least 1 BOTOX treatment

[39] - All participants enrolled into the study who received at least 1 BOTOX treatment

## Statistical analyses

No statistical analyses for this end point

## Adverse events information

Timeframe for reporting adverse events:

All-cause mortality is reported from enrollment to the end of study; median time on follow-up was up to 724 days. TEAEs/SAEs were collected from the first dose of study drug until the last dose, up to 147 weeks.

Adverse event reporting additional description:

For safety analyses, participants were assigned to a treatment group based on the treatment actually received, regardless of the treatment randomized.

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

## Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 24.1 |

## Reporting groups

| | |
|---|---|
| Reporting group title | 25 U BOTOX All |

Reporting group description:

All participants who received 25 U BOTOX (not to exceed 6 U/kg), administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone.

| | |
|---|---|
| Reporting group title | 50 U BOTOX All |

Reporting group description:

All participants who received 50 U BOTOX (not to exceed 6 U/kg), administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone.

| | |
|---|---|
| Reporting group title | 50 U BOTOX Cycle 1 |

Reporting group description:

Participants who received 50 U BOTOX (not to exceed 6 U/kg) in Treatment Cycle 1, administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone.

| | |
|---|---|
| Reporting group title | 100 U BOTOX All |

Reporting group description:

All participants who received 100 U BOTOX (not to exceed 6 U/kg), administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone.

| | |
|---|---|
| Reporting group title | 25 U BOTOX Cycle 1 |

Reporting group description:

Participants who received 25 U BOTOX (not to exceed 6 U/kg) in Treatment Cycle 1, administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone.

| | |
|---|---|
| Reporting group title | 100 U BOTOX Cycle 1 |

Reporting group description:

Participants who received 100 U BOTOX (not to exceed 6 U/kg) in Treatment Cycle 1, administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone.

| | |
|---|---|
| Reporting group title | All BOTOX Cycle 1 |

Reporting group description:

All BOTOX-treated participants in Treatment Cycle 1

| | |
|---|---|
| Reporting group title | 25 U BOTOX Cycle 2 |

Reporting group description:

Participants who received 25 U BOTOX (not to exceed 6 U/kg) in Treatment Cycle 2, administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone.

| | |
|---|---|
| Reporting group title | 50 U BOTOX Cycle 2 |

Reporting group description:

Participants who received 50 U BOTOX (not to exceed 6 U/kg) in Treatment Cycle 2, administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone.

| | |
|---|---|
| Reporting group title | All BOTOX Cycle 2 |

Reporting group description:

All BOTOX-treated participants in Treatment Cycle 2

| | |
|---|---|
| Reporting group title | 100 U BOTOX Cycle 2 |

Reporting group description:

Participants who received 100 U BOTOX (not to exceed 6 U/kg) in Treatment Cycle 2, administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone.

| Reporting group title | 25 U BOTOX Cycle 3 |
|---|---|

Reporting group description:

Participants who received 25 U BOTOX (not to exceed 6 U/kg) in Treatment Cycle 3, administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone.

| Reporting group title | 50 U BOTOX Cycle 3 |
|---|---|

Reporting group description:

Participants who received 50 U BOTOX (not to exceed 6 U/kg) in Treatment Cycle 3, administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone.

| Reporting group title | 100 U BOTOX Cycle 3 |
|---|---|

Reporting group description:

Participants who received 100 U BOTOX (not to exceed 6 U/kg) in Treatment Cycle 3, administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone.

| Reporting group title | All BOTOX Cycle 3 |
|---|---|

Reporting group description:

All BOTOX-treated participants in Treatment Cycle 3

| Reporting group title | 50 U BOTOX Cycle 4 |
|---|---|

Reporting group description:

Participants who received 50 U BOTOX (not to exceed 6 U/kg) in Treatment Cycle 4, administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone

| Reporting group title | 100 U BOTOX Cycle 4 |
|---|---|

Reporting group description:

Participants who received 100 U BOTOX (not to exceed 6 U/kg) in Treatment Cycle 4, administered via cystoscopy as 20 intradetrusor injections of 0.5 mL each, sparing the trigone.

| Reporting group title | All BOTOX Cycle 4 |
|---|---|

Reporting group description:

All BOTOX-treated participants in Treatment Cycle 4

| **Serious adverse events** | 25 U BOTOX All | 50 U BOTOX All | 50 U BOTOX Cycle 1 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Vascular disorders | | | |
| PALLOR | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| MALAISE | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (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 |

| | | | |
|---|---|---|---|
| Social circumstances | | | |
| SOCIAL PROBLEM | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (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 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (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 |
| Psychiatric disorders | | | |
| ANXIETY DISORDER | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (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 |

| **Serious adverse events** | 100 U BOTOX All | 25 U BOTOX Cycle 1 | 100 U BOTOX Cycle 1 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Vascular disorders | | | |
| PALLOR | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| MALAISE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (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 |
| Social circumstances | | | |
| SOCIAL PROBLEM | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| ANXIETY DISORDER | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 0 / 20 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (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 |

| **Serious adverse events** | All BOTOX Cycle 1 | 25 U BOTOX Cycle 2 | 50 U BOTOX Cycle 2 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Vascular disorders | | | |
| PALLOR | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| MALAISE | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (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 |
| Social circumstances | | | |
| SOCIAL PROBLEM | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (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 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (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 |
| Psychiatric disorders | | | |
| ANXIETY DISORDER | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (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 |

| **Serious adverse events** | All BOTOX Cycle 2 | 100 U BOTOX Cycle 2 | 25 U BOTOX Cycle 3 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 1 / 28 (3.57%) | 0 / 2 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Vascular disorders | | | |
| PALLOR | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration | | | |

| | | | |
|---|---|---|---|
| site conditions | | | |
| MALAISE | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (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 |
| Social circumstances | | | |
| SOCIAL PROBLEM | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| ANXIETY DISORDER | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 1 / 28 (3.57%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (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** | 50 U BOTOX Cycle 3 | 100 U BOTOX Cycle 3 | All BOTOX Cycle 3 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 13 (7.69%) | 1 / 22 (4.55%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Vascular disorders | | | |
| PALLOR | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 13 (7.69%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| General disorders and administration site conditions | | | |
| MALAISE | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 13 (7.69%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Social circumstances | | | |
| SOCIAL PROBLEM | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| ANXIETY DISORDER | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (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** | 50 U BOTOX Cycle 4 | 100 U BOTOX Cycle 4 | All BOTOX Cycle 4 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Vascular disorders | | | |
| PALLOR | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (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 |
| General disorders and administration site conditions | | | |
| MALAISE | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (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 |
| Social circumstances | | | |
| SOCIAL PROBLEM | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (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 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (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 |
| Psychiatric disorders | | | |
| ANXIETY DISORDER | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (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 | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (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** | 25 U BOTOX All | 50 U BOTOX All | 50 U BOTOX Cycle 1 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 18 (66.67%) | 23 / 29 (79.31%) | 12 / 17 (70.59%) |
| Vascular disorders | | | |
| FLUSHING | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 1 | 1 |
| HAEMATOMA | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| RAYNAUD'S PHENOMENON | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 1 | 1 |
| General disorders and administration site conditions | | | |
| CHRONIC FATIGUE SYNDROME | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FATIGUE | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ILLNESS | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| MALAISE | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PAIN | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 1 | 1 |
| PERIPHERAL SWELLING | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Reproductive system and breast disorders | | | |

| | | | |
|---|---|---|---|
| DYSMENORRHOEA | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GENITAL PAIN | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 1 | 1 |
| HAEMORRHAGIC OVARIAN CYST | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HEAVY MENSTRUAL BLEEDING | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OEDEMA GENITAL | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| VAGINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| VULVOVAGINAL DISCOMFORT | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NASAL CONGESTION | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 1 | 3 | 3 |
| Psychiatric disorders | | | |
| ANOREXIA NERVOSA | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 1 | 1 |
| ANXIETY | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Investigations | | | |
| BLOOD ALKALINE PHOSPHATASE INCREASED | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLOOD BILIRUBIN INCREASED | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLOOD URINE PRESENT | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| CRYSTAL URINE PRESENT | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CYTOMEGALOVIRUS TEST POSITIVE | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| EPSTEIN-BARR VIRUS TEST POSITIVE | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| RED BLOOD CELLS URINE POSITIVE | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RESIDUAL URINE VOLUME | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINE LEUKOCYTE ESTERASE POSITIVE | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| ANIMAL BITE | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| ANIMAL SCRATCH | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CLAVICLE FRACTURE | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| CONTUSION | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FALL | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| JOINT INJURY | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LIGAMENT SPRAIN | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 1 | 1 | 1 |
| POST PROCEDURAL DISCOMFORT | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| POST PROCEDURAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PROCEDURAL PAIN | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| TENDON INJURY | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| TACHYCARDIA | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 2 / 29 (6.90%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 2 | 1 |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 2 / 29 (6.90%) | 2 / 17 (11.76%) |
| occurrences (all) | 0 | 2 | 2 |
| MIGRAINE | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| HYPERACUSIS | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MISOPHONIA | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| EYE PAIN | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 1 | 1 |
| OCULAR HYPERAEMIA | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 1 | 1 |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISTENSION | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 2 / 29 (6.90%) | 1 / 17 (5.88%) |
| occurrences (all) | 2 | 2 | 1 |
| ABDOMINAL PAIN LOWER | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 1 | 1 |

| | | | |
|---|---|---|---|
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CONSTIPATION | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 1 | 1 |
| DIARRHOEA | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| DYSPEPSIA | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| IRRITABLE BOWEL SYNDROME | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAUSEA | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| TOOTHACHE | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| VOMITING | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 3 / 29 (10.34%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| ACNE | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| ALOPECIA | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DERMATITIS CONTACT | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ECZEMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 1 | 1 |
| NAIL BED INFLAMMATION | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| RASH | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| URTICARIA | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal and urinary disorders | | | |
| BLADDER DISCOMFORT | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLADDER SPASM | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DYSURIA | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 5 / 29 (17.24%) | 1 / 17 (5.88%) |
| occurrences (all) | 2 | 5 | 1 |
| HAEMATURIA | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| LEUKOCYTURIA | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 2 / 29 (6.90%) | 1 / 17 (5.88%) |
| occurrences (all) | 1 | 3 | 1 |
| POLLAKIURIA | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 1 | 1 | 1 |
| PROTEINURIA | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URETHRAL PAIN | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| URINARY INCONTINENCE | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BACK PAIN | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 2 | 1 | 1 |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| JOINT SWELLING | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 2 | 2 |
| MUSCULOSKELETAL CHEST PAIN | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MYALGIA | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 1 | 1 |
| SACRAL PAIN | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| SPONDYLOLISTHESIS | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| BACTERIURIA | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| EAR INFECTION | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 2 / 29 (6.90%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 2 | 1 |
| FUNGAL SKIN INFECTION | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 2 / 29 (6.90%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 2 | 1 |
| GASTROENTERITIS VIRAL | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| INFLUENZA | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 1 | 1 |
| LARYNGITIS | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 1 | 1 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 2 / 29 (6.90%) | 2 / 17 (11.76%) |
| occurrences (all) | 1 | 4 | 4 |
| PARONYCHIA | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PHARYNGITIS | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 1 | 3 | 3 |
| RESPIRATORY TRACT INFECTION VIRAL | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| RHINOVIRUS INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| SINUSITIS | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| TONSILLITIS | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 2 / 29 (6.90%) | 2 / 17 (11.76%) |
| occurrences (all) | 0 | 4 | 4 |
| TRACHEOBRONCHITIS | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 1 | 1 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 6 / 29 (20.69%) | 2 / 17 (11.76%) |
| occurrences (all) | 3 | 11 | 4 |
| VIRAL INFECTION | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VULVOVAGINAL CANDIDIASIS | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| ABNORMAL WEIGHT GAIN | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 29 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VITAMIN D DEFICIENCY | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 29 (3.45%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| **Non-serious adverse events** | 100 U BOTOX All | 25 U BOTOX Cycle 1 | 100 U BOTOX Cycle 1 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 24 / 33 (72.73%) | 12 / 18 (66.67%) | 14 / 20 (70.00%) |
| Vascular disorders | | | |

| | | | |
|---|---|---|---|
| FLUSHING | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HAEMATOMA | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| RAYNAUD'S PHENOMENON | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| CHRONIC FATIGUE SYNDROME | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FATIGUE | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| ILLNESS | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| MALAISE | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| PAIN | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PERIPHERAL SWELLING | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| PYREXIA | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Reproductive system and breast disorders | | | |
| DYSMENORRHOEA | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 2 | 0 | 1 |
| GENITAL PAIN | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HAEMORRHAGIC OVARIAN CYST | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HEAVY MENSTRUAL BLEEDING | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OEDEMA GENITAL | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| VAGINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| VULVOVAGINAL DISCOMFORT | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| NASAL CONGESTION | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 2 / 18 (11.11%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 1 / 18 (5.56%) | 2 / 20 (10.00%) |
| occurrences (all) | 2 | 1 | 2 |
| Psychiatric disorders | | | |
| ANOREXIA NERVOSA | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ANXIETY | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Investigations | | | |

| | | | |
|---|---|---|---|
| BLOOD ALKALINE PHOSPHATASE INCREASED | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| BLOOD BILIRUBIN INCREASED | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| BLOOD URINE PRESENT | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| CRYSTAL URINE PRESENT | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| CYTOMEGALOVIRUS TEST POSITIVE | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| EPSTEIN-BARR VIRUS TEST POSITIVE | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RED BLOOD CELLS URINE POSITIVE | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RESIDUAL URINE VOLUME | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINE LEUKOCYTE ESTERASE POSITIVE | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| ANIMAL BITE | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ANIMAL SCRATCH | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| CLAVICLE FRACTURE | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CONTUSION | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FALL | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| JOINT INJURY | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 18 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all) | 2 | 0 | 2 |
| LIGAMENT SPRAIN | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| POST PROCEDURAL DISCOMFORT | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| POST PROCEDURAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| PROCEDURAL PAIN | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| TENDON INJURY | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Cardiac disorders | | | |
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Nervous system disorders | | | |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HEADACHE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 33 (12.12%) | 0 / 18 (0.00%) | 3 / 20 (15.00%) |
| occurrences (all) | 4 | 0 | 3 |
| MIGRAINE | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| HYPERACUSIS | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MISOPHONIA | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| EYE PAIN | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OCULAR HYPERAEMIA | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISTENSION | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 2 / 18 (11.11%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| ABDOMINAL PAIN LOWER | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| CONSTIPATION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DIARRHOEA | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 1 / 18 (5.56%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 1 | 1 |
| DYSPEPSIA | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| IRRITABLE BOWEL SYNDROME | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| NAUSEA | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 1 / 18 (5.56%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 1 | 1 |
| TOOTHACHE | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VOMITING | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| ACNE | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| ALOPECIA | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| DERMATITIS CONTACT | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ECZEMA | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAIL BED INFLAMMATION | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| RASH | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URTICARIA | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 1 / 18 (5.56%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 1 | 1 |
| Renal and urinary disorders | | | |
| BLADDER DISCOMFORT | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| BLADDER SPASM | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| DYSURIA | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 2 / 18 (11.11%) | 2 / 20 (10.00%) |
| occurrences (all) | 3 | 2 | 2 |
| HAEMATURIA | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 2 / 18 (11.11%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| LEUKOCYTURIA | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| POLLAKIURIA | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| PROTEINURIA | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| URETHRAL PAIN | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 18 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all) | 2 | 0 | 2 |
| URINARY INCONTINENCE | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|---|---|---|
| ARTHRALGIA | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| JOINT SWELLING | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCULOSKELETAL CHEST PAIN | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MYALGIA | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| SACRAL PAIN | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SPONDYLOLISTHESIS | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infections and infestations | | | |
| BACTERIURIA | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 1 / 18 (5.56%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 1 | 1 |
| EAR INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FUNGAL SKIN INFECTION | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 2 | 0 | 1 |
| GASTROENTERITIS VIRAL | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| INFLUENZA | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| LARYNGITIS | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 6 / 33 (18.18%) | 1 / 18 (5.56%) | 3 / 20 (15.00%) |
| occurrences (all) | 8 | 1 | 4 |
| PARONYCHIA | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| PHARYNGITIS | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| RESPIRATORY TRACT INFECTION VIRAL | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RHINOVIRUS INFECTION | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| SINUSITIS | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| TONSILLITIS | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| TRACHEOBRONCHITIS | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 6 / 33 (18.18%) | 2 / 18 (11.11%) | 2 / 20 (10.00%) |
| occurrences (all) | 9 | 3 | 5 |
| VIRAL INFECTION | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VULVOVAGINAL CANDIDIASIS | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolism and nutrition disorders | | | |
| ABNORMAL WEIGHT GAIN | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| VITAMIN D DEFICIENCY | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | All BOTOX Cycle 1 | 25 U BOTOX Cycle 2 | 50 U BOTOX Cycle 2 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 38 / 55 (69.09%) | 1 / 1 (100.00%) | 13 / 17 (76.47%) |
| Vascular disorders | | | |
| FLUSHING | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| HAEMATOMA | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| RAYNAUD'S PHENOMENON | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| General disorders and administration site conditions | | | |
| CHRONIC FATIGUE SYNDROME | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 1 (100.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| FATIGUE | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| ILLNESS | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| MALAISE | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| PAIN | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| PERIPHERAL SWELLING | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| PYREXIA | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 1 | 0 | 1 |
| Reproductive system and breast disorders | | | |
| DYSMENORRHOEA | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| GENITAL PAIN | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| HAEMORRHAGIC OVARIAN CYST | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HEAVY MENSTRUAL BLEEDING | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OEDEMA GENITAL | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| VAGINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| VULVOVAGINAL DISCOMFORT | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NASAL CONGESTION | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 4 / 55 (7.27%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Psychiatric disorders | | | |
| ANOREXIA NERVOSA | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| ANXIETY | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 1 | 0 | 1 |
| Investigations | | | |
| BLOOD ALKALINE PHOSPHATASE INCREASED | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| BLOOD BILIRUBIN INCREASED | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| BLOOD URINE PRESENT | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| CRYSTAL URINE PRESENT | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| CYTOMEGALOVIRUS TEST POSITIVE | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| EPSTEIN-BARR VIRUS TEST POSITIVE | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| RED BLOOD CELLS URINE POSITIVE | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RESIDUAL URINE VOLUME | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINE LEUKOCYTE ESTERASE POSITIVE | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| ANIMAL BITE | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| ANIMAL SCRATCH | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CLAVICLE FRACTURE | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| CONTUSION | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FALL | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 2 | 0 | 1 |
| JOINT INJURY | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| LIGAMENT SPRAIN | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| POST PROCEDURAL DISCOMFORT | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| POST PROCEDURAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| PROCEDURAL PAIN | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| TENDON INJURY | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cardiac disorders | | | |
| TACHYCARDIA | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Nervous system disorders | | | |
| DIZZINESS | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 1 | 0 | 1 |
| HEADACHE | | | |
| subjects affected / exposed | 5 / 55 (9.09%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| MIGRAINE | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|---|---|---|
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| HYPERACUSIS | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| MISOPHONIA | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| Eye disorders | | | |
| EYE PAIN | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| OCULAR HYPERAEMIA | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISTENSION | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 3 | 0 | 1 |
| ABDOMINAL PAIN LOWER | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| CONSTIPATION | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| DIARRHOEA | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 2 | 0 | 1 |
| DYSPEPSIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| IRRITABLE BOWEL SYNDROME | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| NAUSEA | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 2 | 0 | 1 |
| TOOTHACHE | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| VOMITING | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 3 / 17 (17.65%) |
| occurrences (all) | 0 | 0 | 3 |
| Skin and subcutaneous tissue disorders | | | |
| ACNE | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 1 | 0 | 1 |
| ALOPECIA | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| DERMATITIS CONTACT | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ECZEMA | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| NAIL BED INFLAMMATION | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 2 |
| RASH | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| URTICARIA | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |

| | | | |
|---|---|---|---|
| Renal and urinary disorders | | | |
| BLADDER DISCOMFORT | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| BLADDER SPASM | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| DYSURIA | | | |
| subjects affected / exposed | 5 / 55 (9.09%) | 0 / 1 (0.00%) | 4 / 17 (23.53%) |
| occurrences (all) | 5 | 0 | 4 |
| HAEMATURIA | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| LEUKOCYTURIA | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 2 | 0 | 2 |
| POLLAKIURIA | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| PROTEINURIA | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| URETHRAL PAIN | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| URINARY INCONTINENCE | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 1 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BACK PAIN | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| FLANK PAIN | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| JOINT SWELLING | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| MUSCULOSKELETAL CHEST PAIN | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MYALGIA | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| SACRAL PAIN | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| SPONDYLOLISTHESIS | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infections and infestations | | | |
| BACTERIURIA | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| EAR INFECTION | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 2 / 17 (11.76%) |
| occurrences (all) | 1 | 0 | 2 |
| FUNGAL SKIN INFECTION | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 2 | 0 | 1 |

| | | | |
|---|---|---|---|
| GASTROENTERITIS VIRAL | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| INFLUENZA | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| LARYNGITIS | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 6 / 55 (10.91%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 9 | 0 | 0 |
| PARONYCHIA | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| PHARYNGITIS | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| RESPIRATORY TRACT INFECTION VIRAL | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| RHINOVIRUS INFECTION | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| SINUSITIS | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| TONSILLITIS | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| TRACHEOBRONCHITIS | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| UPPER RESPIRATORY TRACT INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 6 / 55 (10.91%) | 0 / 1 (0.00%) | 4 / 17 (23.53%) |
| occurrences (all) | 12 | 0 | 7 |
| VIRAL INFECTION | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VULVOVAGINAL CANDIDIASIS | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| ABNORMAL WEIGHT GAIN | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 1 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| VITAMIN D DEFICIENCY | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 1 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |

| **Non-serious adverse events** | All BOTOX Cycle 2 | 100 U BOTOX Cycle 2 | 25 U BOTOX Cycle 3 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 32 / 46 (69.57%) | 18 / 28 (64.29%) | 1 / 2 (50.00%) |
| Vascular disorders | | | |
| FLUSHING | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HAEMATOMA | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RAYNAUD'S PHENOMENON | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| CHRONIC FATIGUE SYNDROME | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| FATIGUE | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ILLNESS | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MALAISE | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PAIN | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PERIPHERAL SWELLING | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PYREXIA | | | |
| subjects affected / exposed | 2 / 46 (4.35%) | 1 / 28 (3.57%) | 0 / 2 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Reproductive system and breast disorders | | | |
| DYSMENORRHOEA | | | |
| subjects affected / exposed | 2 / 46 (4.35%) | 2 / 28 (7.14%) | 0 / 2 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| GENITAL PAIN | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HAEMORRHAGIC OVARIAN CYST | | | |
| subjects affected / exposed | 2 / 46 (4.35%) | 2 / 28 (7.14%) | 0 / 2 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| HEAVY MENSTRUAL BLEEDING | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OEDEMA GENITAL | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VAGINAL HAEMORRHAGE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VULVOVAGINAL DISCOMFORT | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 1 / 28 (3.57%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| NASAL CONGESTION | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| ANOREXIA NERVOSA | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ANXIETY | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Investigations | | | |
| BLOOD ALKALINE PHOSPHATASE INCREASED | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLOOD BILIRUBIN INCREASED | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLOOD URINE PRESENT | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CRYSTAL URINE PRESENT | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CYTOMEGALOVIRUS TEST POSITIVE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| EPSTEIN-BARR VIRUS TEST POSITIVE | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| RED BLOOD CELLS URINE POSITIVE | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RESIDUAL URINE VOLUME | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINE LEUKOCYTE ESTERASE POSITIVE | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| ANIMAL BITE | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| ANIMAL SCRATCH | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CLAVICLE FRACTURE | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| CONTUSION | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FALL | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| JOINT INJURY | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LIGAMENT SPRAIN | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| POST PROCEDURAL DISCOMFORT | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| POST PROCEDURAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PROCEDURAL PAIN | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 1 / 28 (3.57%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| TENDON INJURY | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| DIZZINESS | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all) | 1 | 0 | 2 |
| HEADACHE | | | |
| subjects affected / exposed | 3 / 46 (6.52%) | 3 / 28 (10.71%) | 0 / 2 (0.00%) |
| occurrences (all) | 4 | 4 | 0 |
| MIGRAINE | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Ear and labyrinth disorders | | | |
| HYPERACUSIS | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| MISOPHONIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye disorders | | | |
| EYE PAIN | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OCULAR HYPERAEMIA | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISTENSION | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 3 / 46 (6.52%) | 2 / 28 (7.14%) | 0 / 2 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| ABDOMINAL PAIN LOWER | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CONSTIPATION | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all) | 0 | 0 | 1 |
| DIARRHOEA | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| DYSPEPSIA | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| IRRITABLE BOWEL SYNDROME | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAUSEA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 46 (4.35%) | 1 / 28 (3.57%) | 0 / 2 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| TOOTHACHE | | | |
| subjects affected / exposed | 2 / 46 (4.35%) | 1 / 28 (3.57%) | 0 / 2 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| VOMITING | | | |
| subjects affected / exposed | 3 / 46 (6.52%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| ACNE | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| ALOPECIA | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DERMATITIS CONTACT | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ECZEMA | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAIL BED INFLAMMATION | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| RASH | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| URTICARIA | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| BLADDER DISCOMFORT | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLADDER SPASM | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DYSURIA | | | |
| subjects affected / exposed | 6 / 46 (13.04%) | 2 / 28 (7.14%) | 1 / 2 (50.00%) |
| occurrences (all) | 6 | 2 | 1 |
| HAEMATURIA | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LEUKOCYTURIA | | | |
| subjects affected / exposed | 2 / 46 (4.35%) | 1 / 28 (3.57%) | 0 / 2 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| POLLAKIURIA | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PROTEINURIA | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URETHRAL PAIN | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINARY INCONTINENCE | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 2 / 46 (4.35%) | 2 / 28 (7.14%) | 0 / 2 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| JOINT SWELLING | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCULOSKELETAL CHEST PAIN | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MYALGIA | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 1 / 28 (3.57%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| SACRAL PAIN | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| SPONDYLOLISTHESIS | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| BACTERIURIA | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| EAR INFECTION | | | |
| subjects affected / exposed | 2 / 46 (4.35%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| FUNGAL SKIN INFECTION | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all) | 0 | 0 | 1 |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 2 / 46 (4.35%) | 1 / 28 (3.57%) | 0 / 2 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| GASTROENTERITIS VIRAL | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| INFLUENZA | | | |
| subjects affected / exposed | 3 / 46 (6.52%) | 3 / 28 (10.71%) | 0 / 2 (0.00%) |
| occurrences (all) | 3 | 3 | 0 |
| LARYNGITIS | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 4 / 46 (8.70%) | 4 / 28 (14.29%) | 0 / 2 (0.00%) |
| occurrences (all) | 6 | 6 | 0 |
| PARONYCHIA | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PHARYNGITIS | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 1 / 28 (3.57%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| RESPIRATORY TRACT INFECTION VIRAL | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| RHINOVIRUS INFECTION | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SINUSITIS | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TONSILLITIS | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TRACHEOBRONCHITIS | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 2 / 46 (4.35%) | 2 / 28 (7.14%) | 0 / 2 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| URINARY TRACT INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 13 / 46 (28.26%) | 9 / 28 (32.14%) | 0 / 2 (0.00%) |
| occurrences (all) | 19 | 12 | 0 |
| VIRAL INFECTION | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VULVOVAGINAL CANDIDIASIS | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| ABNORMAL WEIGHT GAIN | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VITAMIN D DEFICIENCY | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 28 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| **Non-serious adverse events** | 50 U BOTOX Cycle 3 | 100 U BOTOX Cycle 3 | All BOTOX Cycle 3 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 8 / 13 (61.54%) | 12 / 22 (54.55%) |
| Vascular disorders | | | |
| FLUSHING | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HAEMATOMA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RAYNAUD'S PHENOMENON | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| CHRONIC FATIGUE SYNDROME | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FATIGUE | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| ILLNESS | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MALAISE | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PAIN | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PERIPHERAL SWELLING | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| DYSMENORRHOEA | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 13 (7.69%) | 2 / 22 (9.09%) |
| occurrences (all) | 2 | 1 | 3 |
| GENITAL PAIN | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HAEMORRHAGIC OVARIAN CYST | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HEAVY MENSTRUAL BLEEDING | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 13 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 1 | 0 | 1 |
| OEDEMA GENITAL | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VAGINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VULVOVAGINAL DISCOMFORT | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 13 (7.69%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 1 | 1 |
| NASAL CONGESTION | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 13 (7.69%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 1 | 1 |
| Psychiatric disorders | | | |
| ANOREXIA NERVOSA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ANXIETY | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| BLOOD ALKALINE PHOSPHATASE INCREASED | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLOOD BILIRUBIN INCREASED | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLOOD URINE PRESENT | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CRYSTAL URINE PRESENT | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CYTOMEGALOVIRUS TEST POSITIVE | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| EPSTEIN-BARR VIRUS TEST | | | |

| | | | |
|---|---|---|---|
| POSITIVE | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RED BLOOD CELLS URINE POSITIVE | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 13 (7.69%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 1 | 1 |
| RESIDUAL URINE VOLUME | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINE LEUKOCYTE ESTERASE POSITIVE | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| ANIMAL BITE | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ANIMAL SCRATCH | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 13 (7.69%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 1 | 1 |
| CLAVICLE FRACTURE | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CONTUSION | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 13 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 1 | 0 | 1 |
| FALL | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 13 (7.69%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 1 | 1 |
| JOINT INJURY | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LIGAMENT SPRAIN | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 13 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 1 | 0 | 1 |
| POST PROCEDURAL DISCOMFORT | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| POST PROCEDURAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PROCEDURAL PAIN | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TENDON INJURY | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 2 |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 3 / 13 (23.08%) | 3 / 22 (13.64%) |
| occurrences (all) | 0 | 4 | 4 |
| MIGRAINE | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| Ear and labyrinth disorders | | | |
| HYPERACUSIS | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MISOPHONIA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |

| | | | |
|---|---|---|---|
| EYE PAIN | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OCULAR HYPERAEMIA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISTENSION | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ABDOMINAL PAIN LOWER | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CONSTIPATION | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| DIARRHOEA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DYSPEPSIA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| IRRITABLE BOWEL SYNDROME | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAUSEA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TOOTHACHE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VOMITING | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| ACNE | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ALOPECIA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DERMATITIS CONTACT | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 13 (7.69%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 1 | 1 |
| ECZEMA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAIL BED INFLAMMATION | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RASH | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URTICARIA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| BLADDER DISCOMFORT | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLADDER SPASM | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DYSURIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| HAEMATURIA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LEUKOCYTURIA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| POLLAKIURIA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PROTEINURIA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URETHRAL PAIN | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINARY INCONTINENCE | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 13 (7.69%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 1 | 1 |
| JOINT SWELLING | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCLE SPASMS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCULOSKELETAL CHEST PAIN | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MYALGIA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SACRAL PAIN | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SPONDYLOLISTHESIS | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| BACTERIURIA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| EAR INFECTION | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FUNGAL SKIN INFECTION | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTROENTERITIS VIRAL | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INFLUENZA | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 13 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 1 | 0 | 1 |

| | | | |
|---|---|---|---|
| LARYNGITIS | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 13 (7.69%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 1 | 1 |
| PARONYCHIA | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PHARYNGITIS | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 13 (7.69%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 1 | 1 |
| RESPIRATORY TRACT INFECTION VIRAL | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RHINOVIRUS INFECTION | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SINUSITIS | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TONSILLITIS | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 13 (7.69%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 1 | 1 |
| TRACHEOBRONCHITIS | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 13 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 1 | 0 | 1 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 4 / 13 (30.77%) | 6 / 22 (27.27%) |
| occurrences (all) | 3 | 5 | 8 |
| VIRAL INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 13 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 1 | 0 | 1 |
| VULVOVAGINAL CANDIDIASIS | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| ABNORMAL WEIGHT GAIN | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VITAMIN D DEFICIENCY | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 13 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | 50 U BOTOX Cycle 4 | 100 U BOTOX Cycle 4 | All BOTOX Cycle 4 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1 / 1 (100.00%) | 1 / 3 (33.33%) | 2 / 4 (50.00%) |
| Vascular disorders | | | |
| FLUSHING | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HAEMATOMA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RAYNAUD'S PHENOMENON | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| CHRONIC FATIGUE SYNDROME | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FATIGUE | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ILLNESS | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| MALAISE | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PAIN | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PERIPHERAL SWELLING | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 3 (33.33%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 1 |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| DYSMENORRHOEA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GENITAL PAIN | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HAEMORRHAGIC OVARIAN CYST | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HEAVY MENSTRUAL BLEEDING | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OEDEMA GENITAL | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VAGINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VULVOVAGINAL DISCOMFORT | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|---|---|---|
| COUGH | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NASAL CONGESTION | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| ANOREXIA NERVOSA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ANXIETY | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| BLOOD ALKALINE PHOSPHATASE INCREASED | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLOOD BILIRUBIN INCREASED | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLOOD URINE PRESENT | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CRYSTAL URINE PRESENT | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CYTOMEGALOVIRUS TEST POSITIVE | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| EPSTEIN-BARR VIRUS TEST POSITIVE | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RED BLOOD CELLS URINE POSITIVE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RESIDUAL URINE VOLUME | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 3 (33.33%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 1 |
| URINE LEUKOCYTE ESTERASE POSITIVE | | | |
| subjects affected / exposed | 1 / 1 (100.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Injury, poisoning and procedural complications | | | |
| ANIMAL BITE | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ANIMAL SCRATCH | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CLAVICLE FRACTURE | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CONTUSION | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FALL | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| JOINT INJURY | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LIGAMENT SPRAIN | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| POST PROCEDURAL DISCOMFORT | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| POST PROCEDURAL HAEMORRHAGE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PROCEDURAL PAIN | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TENDON INJURY | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MIGRAINE | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| HYPERACUSIS | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MISOPHONIA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| EYE PAIN | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| OCULAR HYPERAEMIA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISTENSION | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ABDOMINAL PAIN LOWER | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CONSTIPATION | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DIARRHOEA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DYSPEPSIA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| IRRITABLE BOWEL SYNDROME | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAUSEA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TOOTHACHE | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VOMITING | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| ACNE | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ALOPECIA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DERMATITIS CONTACT | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ECZEMA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAIL BED INFLAMMATION | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RASH | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URTICARIA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| BLADDER DISCOMFORT | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLADDER SPASM | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DYSURIA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HAEMATURIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LEUKOCYTURIA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| POLLAKIURIA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PROTEINURIA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URETHRAL PAIN | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINARY INCONTINENCE | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| JOINT SWELLING | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCULOSKELETAL CHEST PAIN | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 3 (33.33%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 1 |
| MYALGIA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SACRAL PAIN | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SPONDYLOLISTHESIS | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| BACTERIURIA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| EAR INFECTION | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FUNGAL SKIN INFECTION | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTROENTERITIS VIRAL | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INFLUENZA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LARYNGITIS | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PARONYCHIA | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PHARYNGITIS | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RESPIRATORY TRACT INFECTION VIRAL | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RHINOVIRUS INFECTION | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SINUSITIS | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TONSILLITIS | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TRACHEOBRONCHITIS | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VIRAL INFECTION | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VULVOVAGINAL CANDIDIASIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| ABNORMAL WEIGHT GAIN | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VITAMIN D DEFICIENCY | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 06 February 2014 | Amendment 1<br><br>Details were added to clarify primary analysis and final analysis details including unblinding after primary analysis. |
| 05 September 2014 | Amendment 2/Version 3<br><br>Exclusion criteria regarding medical conditions that may put patients at increased risk with exposure to BOTOX were inadvertently omitted in the original protocol and Amendment 1, these were added. Details from investigator's meeting were also added. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported