ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 12/09/2013

ClinicalTrials.gov ID: NCT00439140

Study Identification

Unique Protocol ID:	191622-082
Brief Title:	Safety and Efficacy Study of Botulinum Toxin Type A for the Treatment of Neurogenic Overactive Bladder
Official Title:	
Secondary IDs:	

Study Status

Record Verification:	December 2013
Overall Status:	Terminated [In agreement with FDA the study was terminated based on data available.]
Study Start:	June 2007
Primary Completion:	December 2012 [Actual]
Study Completion:	December 2012 [Actual]

Sponsor/Collaborators

Sponsor:	Allergan
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? No Delayed Posting? No

IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 12430 Serial Number: Has Expanded Access? No
Review Board:	Approval Status: Board Name: Board Affiliation: Phone: Email:
Data Monitoring?:	Yes
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	This study will assess the safety and efficacy of botulinum toxin Type A for the treatment of urinary incontinence overactive bladder in patients with a spinal cord injury or multiple sclerosis.
Detailed Description:	Botulinum toxin Type A 300U has been discontinued from the study after regulatory approval of botulinum toxin Type A 200U. Patients remaining in the study who were allocated to receive botulinum toxin Type A 300U at treatment 2 (and had not yet received it) will receive botulinum toxin Type A 200U instead.

Conditions

Conditions:	Overactive Bladder
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Parallel Assignment
Number of Arms:	4
Masking:	Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)

Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	41 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: botulinum toxin Type A 200U Botulinum toxin Type A 200U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 200U injection after a minimum of 12 weeks (if applicable).	Biological/Vaccine: botulinum toxin Type A Botulinum toxin Type A injection into the detrusor. Other Names: • BOTOX® • onabotulinumtoxinA
Experimental: botulinum toxin Type A 300U Botulinum toxin Type A 300U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 300U injection after a minimum of 12 weeks (if applicable).	Biological/Vaccine: botulinum toxin Type A Botulinum toxin Type A injection into the detrusor. Other Names: • BOTOX® • onabotulinumtoxinA
Placebo/botulinum toxin Type A 200U Placebo (Normal Saline) injection into the detrusor on Day 1 followed by a botulinum toxin Type A 200U injection after a minimum of 12 weeks (if applicable).	Biological/Vaccine: botulinum toxin Type A Botulinum toxin Type A injection into the detrusor. Other Names: • BOTOX® • onabotulinumtoxinA Drug: Normal Saline (Placebo) Placebo (Normal Saline) injection into the detrusor.
Placebo/botulinum toxin Type A 300U Placebo (Normal Saline) injection into the detrusor on Day 1 followed by a botulinum toxin Type A 300U injection (200U after discontinuation of 300U) after a minimum of 12 weeks (if applicable).	Biological/Vaccine: botulinum toxin Type A Botulinum toxin Type A injection into the detrusor. Other Names: • BOTOX® • onabotulinumtoxinA Drug: Normal Saline (Placebo) Placebo (Normal Saline) injection into the detrusor.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 80 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Urinary incontinence as a result of neurogenic overactive bladder due to spinal cord injury or multiple sclerosis
- Inadequate response to anticholinergic medication used to treat overactive bladder.
- Neurological respiratory impairment and abnormal pulmonary function test results

Exclusion Criteria:

- History or evidence of pelvic or urologic abnormality
- Previous or current diagnosis of bladder or prostate cancer
- Symptomatic or untreated urinary tract infection at time of enrollment

Contacts/Locations

Study Officials: Medical Director
Study Director
Allergan, Inc

Locations: United States, Illinois
Hines, Illinois, United States

Canada, Alberta
Edmonton, Alberta, Canada

Australia, Queensland
Herston, Queensland, Australia

France
Nimes Cedex, France

Netherlands
Amsterdam, Netherlands

India
Bangalore, India

Canada, British Columbia

Victoria, British Columbia, Canada

United States, Pennsylvania
Philadelphia, Pennsylvania, United States

India
Chennai, India

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Pre-Assignment Details	Botulinum toxin Type A 300U was discontinued from the study after regulatory approval of botulinum toxin Type A 200U. Patients remaining in the study who were allocated to receive botulinum toxin Type A 300U at treatment 2 (and had not yet received it) received botulinum toxin Type A 200U instead.

Reporting Groups

	Description
Botulinum Toxin Type A 200U	Botulinum toxin Type A 200U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 200U injection after a minimum of 12 weeks (if applicable).
Botulinum Toxin Type A 300U	Botulinum toxin Type A 300U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 300U injection after a minimum of 12 weeks (if applicable).
Placebo	Placebo (Normal Saline) injection into the detrusor on Day 1. (If applicable after 12 weeks, participants received either botulinum toxin Type A 200U or 300U in Treatment Cycle 2.)

Treatment Cycle 1

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo
Started	15	14	12
Completed	14	10	11 [1]

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo
Not Completed	1	4	1
Lost to Follow-up	1	1	1
Personal reasons	0	2	0
Withdrawal by Subject	0	1	0

[1] 5 patients did not enter Cycle 2. 6 patients received botulinum toxin Type A in Cycle 2.

Treatment Cycle 2

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo
Started	13 [1]	7 [2]	0 [3]
Completed	11	6	0
Not Completed	2	1	0
Withdrawal by Subject	1	0	0
Lost to Follow-up	1	1	0

[1] 8 patients from the 200U arm plus 5 patients from the placebo arm in Cycle 1 entered Cycle 2.
[2] 6 patients from the 300U arm plus 1 patient from the placebo arm in Cycle 1 entered Cycle 2.
[3] No patients received placebo in Cycle 2.

Baseline Characteristics

Reporting Groups

	Description
Botulinum Toxin Type A 200U	Botulinum toxin Type A 200U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 200U injection after a minimum of 12 weeks (if applicable).
Botulinum Toxin Type A 300U	Botulinum toxin Type A 300U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 300U injection after a minimum of 12 weeks (if applicable).
Placebo/Botulinum Toxin Type A	Placebo (Normal Saline) injection into the detrusor on Day 1 followed by a botulinum toxin Type A 200U or 300U injection after a minimum of 12 weeks (if applicable).

Baseline Measures

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo/Botulinum Toxin Type A	Total
Number of Participants	15	14	12	41
Age, Customized [units: participants]				
< 40 Years	9	8	6	23
40-64 Years	4	6	6	16
≥ 65 Years	2	0	0	2
Gender, Male/Female [units: participants]				
Female	7	6	3	16
Male	8	8	9	25

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change From Baseline in Forced Vital Capacity (FVC)
Measure Description	Spirometry was conducted according to American Thoracic Society standards. A spirometer was used to measure FVC, the maximum amount of air exhaled from the lungs after taking the deepest breath possible, at Baseline and Week 6. A positive change from Baseline indicated improvement.
Time Frame	Baseline, Week 6
Safety Issue?	Yes

Analysis Population Description

Safety Population included all randomized participants who received treatment.

Reporting Groups

	Description
Botulinum Toxin Type A 200U	Botulinum toxin Type A 200U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 200U injection after a minimum of 12 weeks (if applicable).
Botulinum Toxin Type A 300U	Botulinum toxin Type A 300U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 300U injection after a minimum of 12 weeks (if applicable).
Placebo	Placebo (Normal Saline) injection into the detrusor on Day 1.

Measured Values

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo
Number of Participants Analyzed	15	14	12
Change From Baseline in Forced Vital Capacity (FVC) [units: Liters] Mean (Standard Deviation)			
Baseline	2.659 (0.5308)	2.955 (0.7733)	3.095 (0.6868)
Change from Baseline at Week 6	-0.124 (0.2758)	-0.096 (0.2248)	-0.025 (0.2391)

2. Primary Outcome Measure:

Measure Title	Change From Baseline in Forced Expiratory Volume in One Second (FEV1)
Measure Description	Spirometry was conducted according to American Thoracic Society standards. A spirometer was used to measure FEV1, the maximum amount of air exhaled in one second, at Baseline and Week 6. The highest value at each time-point was recorded. A positive change from Baseline indicated improvement.
Time Frame	Baseline, Week 6
Safety Issue?	Yes

Analysis Population Description

Safety population included all randomized participants who received treatment.

Reporting Groups

	Description
Botulinum Toxin Type A 200U	Botulinum toxin Type A 200U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 200U injection after a minimum of 12 weeks (if applicable).
Botulinum Toxin Type A 300U	Botulinum toxin Type A 300U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 300U injection after a minimum of 12 weeks (if applicable).
Placebo	Placebo (Normal Saline) injection into the detrusor on Day 1.

Measured Values

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo
Number of Participants Analyzed	15	14	12
Change From Baseline in Forced Expiratory Volume in One Second (FEV1) [units: Liters]			

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo
Mean (Standard Deviation)			
Baseline	2.290 (0.5815)	2.534 (0.7227)	2.535 (0.7626)
Change from Baseline at Week 6	-0.067 (0.2525)	-0.094 (0.2196)	-0.052 (0.1926)

3. Primary Outcome Measure:

Measure Title	Change From Baseline in FEV1/FVC Ratio
Measure Description	The FEV1/FVC ratio was calculated by dividing the FEV1 value by the FVC value representing the portion (or ratio) of FVC exhaled in one second. A positive change from Baseline indicated improvement.
Time Frame	Baseline, Week 6
Safety Issue?	Yes

Analysis Population Description

Safety population included all randomized participants who received treatment.

Reporting Groups

	Description
Botulinum Toxin Type A 200U	Botulinum toxin Type A 200U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 200U injection after a minimum of 12 weeks (if applicable).
Botulinum Toxin Type A 300U	Botulinum toxin Type A 300U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 300U injection after a minimum of 12 weeks (if applicable).
Placebo	Placebo (Normal Saline) injection into the detrusor on Day 1.

Measured Values

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo
Number of Participants Analyzed	15	14	12
Change From Baseline in FEV1/FVC Ratio [units: Ratio] Mean (Standard Deviation)			
Baseline	0.857 (0.1093)	0.857 (0.1214)	0.818 (0.1574)
Change from Baseline at Week 6	0.017 (0.0668)	-0.007 (0.0578)	-0.018 (0.0676)

4. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Number of Urinary Incontinence Episodes
Measure Description	The number of urinary incontinence episodes or leakage occurring over the previous 3 days was recorded in the patient bladder diary at Baseline and prior to Week 6. A negative change from Baseline indicated improvement (less incontinence/leakage).
Time Frame	Baseline, Week 6
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat population (all randomized participants) using observed data for analysis.

Reporting Groups

	Description
Botulinum Toxin Type A 200U	Botulinum toxin Type A 200U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 200U injection after a minimum of 12 weeks (if applicable).
Botulinum Toxin Type A 300U	Botulinum toxin Type A 300U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 300U injection after a minimum of 12 weeks (if applicable).
Placebo	Placebo (Normal Saline) injection into the detrusor on Day 1.

Measured Values

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo
Number of Participants Analyzed	15	13	11
Change From Baseline in the Number of Urinary Incontinence Episodes [units: Episodes] Mean (Standard Deviation)			
Baseline	12.5 (9.78)	13.5 (6.48)	9.3 (6.59)
Change from Baseline at Week 6 (n=13,11,11)	-10.2 (7.70)	-9.5 (6.96)	-3.4 (4.57)

5. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Maximum (Amplitude) Detrusor Pressure (MDP)

Measure Description	MDP was measured at the first involuntary detrusor contraction using urodynamic testing. A catheter was inserted into the bladder at Baseline and Week 6 and the pressure [measured in centimeters water (cm H20)] was determined as the bladder filled. A negative change from Baseline indicated improvement (less Detrusor pressure).
Time Frame	Baseline, Week 6
Safety Issue?	No

Analysis Population Description

Intent-to-treat population included all randomized participants.

Reporting Groups

	Description
Botulinum Toxin Type A 200U	Botulinum toxin Type A 200U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 200U injection after a minimum of 12 weeks (if applicable).
Botulinum Toxin Type A 300U	Botulinum toxin Type A 300U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 300U injection after a minimum of 12 weeks (if applicable).
Placebo	Placebo (Normal Saline) injection into the detrusor on Day 1.

Measured Values

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo
Number of Participants Analyzed	15	14	12
Change From Baseline in the Maximum (Amplitude) Detrusor Pressure (MDP) [units: cm H2O] Mean (Standard Deviation)			
Baseline	39.1 (30.45)	42.6 (22.65)	41.9 (18.91)
Change from Baseline at Week 6 (n=4,9,9)	-23.3 (28.96)	0.3 (32.67)	8.7 (23.91)

6. Secondary Outcome Measure:

Measure Title	Change From Baseline in Maximum Cystometric Capacity (MCC)
Measure Description	MCC (the maximum amount of urine the bladder could hold) was measured using urodynamic testing. The amount of urine collected was subtracted from the total volume infused measured as milliliters (mL) of urine. A positive change from Baseline indicated improvement (fuller bladder/ less incontinence).
Time Frame	Baseline, Week 6

Safety Issue?	No

Analysis Population Description

Intent-to-treat population included all randomized participants.

Reporting Groups

	Description
Botulinum Toxin Type A 200U	Botulinum toxin Type A 200U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 200U injection after a minimum of 12 weeks (if applicable).
Botulinum Toxin Type A 300U	Botulinum toxin Type A 300U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 300U injection after a minimum of 12 weeks (if applicable).
Placebo	Placebo (Normal Saline) injection into the detrusor on Day 1.

Measured Values

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo
Number of Participants Analyzed	15	14	12
Change From Baseline in Maximum Cystometric Capacity (MCC) [units: mL] Mean (Standard Deviation)			
Baseline	161.4 (80.29)	216.7 (168.41)	266.2 (191.41)
Change from Baseline at Week 6 (n=12,13,11)	213.2 (135.58)	60.2 (222.35)	-64.5 (136.98)

7. Other Pre-specified Outcome Measure:

Measure Title	Number of Participants With at Least a 15% Decrease From Baseline in FVC
Measure Description	Spirometry was conducted according to American Thoracic Society standards. A spirometer was used to measure FVC, the maximum amount of air exhaled from the lungs after taking the deepest breath possible at Baseline, Weeks 2, 6 and 12.
Time Frame	Baseline, Weeks 2, 6 and 12
Safety Issue?	Yes

Analysis Population Description

Safety population included all randomized participants who received treatment.

Reporting Groups

	Description
Botulinum Toxin Type A 200U	Botulinum toxin Type A 200U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 200U injection after a minimum of 12 weeks (if applicable).
Botulinum Toxin Type A 300U	Botulinum toxin Type A 300U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 300U injection after a minimum of 12 weeks (if applicable).
Placebo	Placebo (Normal Saline) injection into the detrusor on Day 1.

Measured Values

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo
Number of Participants Analyzed	15	14	12
Number of Participants With at Least a 15% Decrease From Baseline in FVC [units: Participants]			
Week 2 (n=15,14,12)	0	1	1
Week 6 (n=15,14,12)	2	1	0
Week 12 (n=14,12,9)	0	1	0

8. Other Pre-specified Outcome Measure:

Measure Title	Number of Participants With at Least a 20% Decrease From Baseline in FVC
Measure Description	Spirometry was conducted according to American Thoracic Society standards. A spirometer was used to measure FVC, the maximum amount of air exhaled from the lungs after taking the deepest breath possible at Baseline, Weeks 2, 6 and 12.
Time Frame	Baseline, Weeks 2, 6 and 12
Safety Issue?	Yes

Analysis Population Description

Safety population included all randomized participants who received treatment.

Reporting Groups

	Description
Botulinum Toxin Type A 200U	Botulinum toxin Type A 200U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 200U injection after a minimum of 12 weeks (if applicable).

	Description
Botulinum Toxin Type A 300U	Botulinum toxin Type A 300U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 300U injection after a minimum of 12 weeks (if applicable).
Placebo	Placebo (Normal Saline) injection into the detrusor on Day 1.

Measured Values

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo
Number of Participants Analyzed	15	14	12
Number of Participants With at Least a 20% Decrease From Baseline in FVC [units: Participants]			
Week 2 (n=15,14,12)	0	1	0
Week 6 (n=15,14,12)	1	0	0
Week 12 (n=14,12,9)	0	1	0

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	Serious Adverse Events (SAEs) and Adverse Events (AEs) were reported based on the treatment the participant received. SAEs and AEs reported for participants in the Placebo/Botulinum Toxin Type A arm may have occurred while the participant received placebo in Cycle 1 or botulinum toxin Type A in Cycle 2.

Reporting Groups

	Description
Botulinum Toxin Type A 200U	Botulinum toxin Type A 200U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 200U injection after a minimum of 12 weeks (if applicable).
Botulinum Toxin Type A 300U	Botulinum toxin Type A 300U injection into the detrusor on Day 1 followed by a repeat botulinum toxin Type A 300U injection after a minimum of 12 weeks (if applicable).
Placebo/Botulinum Toxin Type A	Placebo (Normal Saline) injection into the detrusor on Day 1 followed by a botulinum toxin Type A 200U or 300U injection after a minimum of 12 weeks (if applicable).

Serious Adverse Events

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo/Botulinum Toxin Type A
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	4/15 (26.67%)	6/14 (42.86%)	1/12 (8.33%)
Infections and infestations			
Cellulitis [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Leptospirosis [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Lower respiratory tract infection [A] [1] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Septic shock [A] [1] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Typhoid fever [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Upper respiratory tract infection [A] [1] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Urinary tract infection [A] †	2/15 (13.33%)	2/14 (14.29%)	0/12 (0%)
Urinary tract infection pseudomonal [A] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Urosepsis [A] [1] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Investigations			
Renal function test abnormal [A] [1] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Spinal cord neoplasm [A] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Renal and urinary disorders			
Calculus ureteric [A] [1] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Hydronephrosis [A] [1] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Urinary incontinence [A] *	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Urinary retention [A] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Skin and subcutaneous tissue disorders			
Decubitus ulcer [A] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)

† Indicates events were collected by systematic assessment.

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (15.1)

[1] Event not related to treatment.

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo/Botulinum Toxin Type A
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	12/15 (80%)	12/14 (85.71%)	10/12 (83.33%)
Blood and lymphatic system disorders			
Anaemia [A] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Congenital, familial and genetic disorders			
Syringomyelia [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Endocrine disorders			
Thyroid cyst [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Eye disorders			
Conjunctivitis [A] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Diplopia [A] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Vision blurred [A] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Visual acuity reduced [A] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Gastrointestinal disorders			
Abdominal discomfort [A] *	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Abdominal distension [A] †	0/15 (0%)	2/14 (14.29%)	0/12 (0%)
Abdominal pain [A] *	2/15 (13.33%)	1/14 (7.14%)	1/12 (8.33%)
Constipation [A] †	2/15 (13.33%)	1/14 (7.14%)	0/12 (0%)
Diarrhoea [A] *	2/15 (13.33%)	0/14 (0%)	2/12 (16.67%)
Dry mouth [A] *	0/15 (0%)	1/14 (7.14%)	0/12 (0%)

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo/Botulinum Toxin Type A
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Haemorrhoids [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Nausea [A] *	2/15 (13.33%)	0/14 (0%)	1/12 (8.33%)
Toothache [A] *	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Vomiting [A] *	1/15 (6.67%)	0/14 (0%)	1/12 (8.33%)
General disorders			
Asthenia [A] †	1/15 (6.67%)	0/14 (0%)	1/12 (8.33%)
Chills [A] *	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Fatigue [A] *	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Malaise [A] *	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Oedema [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Oedema peripheral [A] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Pyrexia [A] †	2/15 (13.33%)	5/14 (35.71%)	1/12 (8.33%)
Infections and infestations			
Bronchitis [A] [1] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Cellulitis [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Gastroenteritis viral [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Influenza [A] †	2/15 (13.33%)	1/14 (7.14%)	0/12 (0%)
Kidney infection [A] [1] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Leptospirosis [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Lower respiratory tract infection [A] [1] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Nasopharyngitis [A] †	1/15 (6.67%)	0/14 (0%)	1/12 (8.33%)
Paronychia [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo/Botulinum Toxin Type A
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Septic shock [A] [1] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Sinusitis [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Staphylococcal infection [A] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Typhoid fever [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Upper respiratory tract infection [A] [2] †	0/15 (0%)	2/14 (14.29%)	0/12 (0%)
Urinary tract infection [A] †	9/15 (60%)	8/14 (57.14%)	9/12 (75%)
Urinary tract infection pseudomonal [A] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Urosepsis [A] [1] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Vaginal infection [A] †	0/7 (0%)	0/6 (0%)	1/3 (33.33%)
Viral rhinitis [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Vulvovaginal mycotic infection [A] †	2/7 (28.57%)	0/6 (0%)	0/3 (0%)
Injury, poisoning and procedural complications			
Fall [A] *	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Ligament sprain [A] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Open wound [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Procedural pain [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Investigations			
Alanine aminotransferase increased [A] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Blood alkaline phosphatase increased [A] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Blood potassium decreased [A] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Blood urine present [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Cardiac murmur [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo/Botulinum Toxin Type A
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Gamma-glutamyltransferase increased [A] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Heart rate increased [A] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Neutrophil count decreased [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Pulmonary function test decreased [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Renal function test abnormal [A] [1] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Residual urine volume [A] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
White blood cells urine positive [A] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Metabolism and nutrition disorders			
Dehydration [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Musculoskeletal and connective tissue disorders			
Back pain [A] *	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Groin pain [A] *	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Intervertebral disc disorder [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Muscle spasms [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Muscular weakness [A] †	1/15 (6.67%)	1/14 (7.14%)	1/12 (8.33%)
Musculoskeletal pain [A] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Pain in extremity [A] *	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Dysplastic naevus [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Spinal cord neoplasm [A] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Nervous system disorders			
Burning sensation [A] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Carotid artery disease [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo/Botulinum Toxin Type A
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Dizziness [A] *	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Dysgeusia [A] *	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Headache [A] *	1/15 (6.67%)	0/14 (0%)	1/12 (8.33%)
Hemiplegia [A] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Multiple sclerosis [A] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Muscle spasticity [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Neuropathy peripheral [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Psychiatric disorders			
Insomnia [A] *	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Mood altered [A] *	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Renal and urinary disorders			
Bladder pain [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Calculus ureteric [A] [1] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Dysuria [A] *	2/15 (13.33%)	0/14 (0%)	0/12 (0%)
Haematuria [A] †	0/15 (0%)	1/14 (7.14%)	1/12 (8.33%)
Hydronephrosis [A] [2] †	1/15 (6.67%)	0/14 (0%)	1/12 (8.33%)
Micturition urgency [A] *	2/15 (13.33%)	0/14 (0%)	1/12 (8.33%)
Nephrolithiasis [A] [2] †	2/15 (13.33%)	0/14 (0%)	2/12 (16.67%)
Pollakiuria [A] *	2/15 (13.33%)	0/14 (0%)	2/12 (16.67%)
Renal failure [A] [1] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Urethral haemorrhage [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Urinary incontinence [A] *	1/15 (6.67%)	1/14 (7.14%)	0/12 (0%)

	Botulinum Toxin Type A 200U	Botulinum Toxin Type A 300U	Placebo/Botulinum Toxin Type A
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Urinary retention [A] †	1/15 (6.67%)	2/14 (14.29%)	0/12 (0%)
Vesicoureteric reflux [A] [1] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Reproductive system and breast disorders			
Atrophic vulvovaginitis [A] †	1/7 (14.29%)	0/6 (0%)	0/3 (0%)
Epididymitis [A] †	0/8 (0%)	1/8 (12.5%)	0/9 (0%)
Respiratory, thoracic and mediastinal disorders			
Cough [A] *	0/15 (0%)	2/14 (14.29%)	1/12 (8.33%)
Dysphonia [A] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)
Dyspnoea [A] *	1/15 (6.67%)	1/14 (7.14%)	2/12 (16.67%)
Nasal congestion [A] *	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Nasal obstruction [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Oropharyngeal pain [A] *	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Respiratory tract congestion [A] †	0/15 (0%)	0/14 (0%)	1/12 (8.33%)
Skin and subcutaneous tissue disorders			
Acne [A] †	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Decubitus ulcer [A] †	0/15 (0%)	2/14 (14.29%)	0/12 (0%)
Dry skin [A] *	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Night sweats [A] *	1/15 (6.67%)	0/14 (0%)	0/12 (0%)
Vascular disorders			
Hypotension [A] †	0/15 (0%)	1/14 (7.14%)	0/12 (0%)

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (15.1)

[1] Event not related to treatment.
[2] Events not related to treatment.

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

A disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 90 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

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