ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 09/17/2015

ClinicalTrials.gov ID: NCT00461292

Study Identification

Unique Protocol ID:	191622-516
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:	September 2015
Overall Status:	Completed
Study Start:	May 2007
Primary Completion:	March 2010 [Actual]
Study Completion:	April 2010 [Actual]

Sponsor/Collaborators

Sponsor:	Allergan
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes 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?:	
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	The purpose of this study is to assess the safety and effectiveness of botulinum toxin type A in treating overactive bladder in spinal cord injury or multiple sclerosis patients
Detailed Description:	

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: 275 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1 botulinum toxin Type A (200U)	Biological/Vaccine: botulinum toxin Type A (200U) botulinum toxin Type A 200 U injection at Day 1 followed by botulinum toxin Type A 200 U injection > Week 12; injections into detrusor Other Names: • BOTOX®
Experimental: 2 botulinum toxin Type A (300U)	Biological/Vaccine: botulinum toxin Type A (300U) botulinum toxin Type A 300 U injection on Day 1 followed by botulinum toxin Type A 300 U injection > Week 12; injections into detrusor Other Names: • BOTOX®
3 placebo; botulinum toxin Type A (200U)	Normal saline (Placebo); botulinum toxin Type A (200U) Placebo injection on Day 1 followed by botulinum toxin Type A 200 U injection > 12 weeks; injections into detrusor Other Names: • BOTOX®
4 placebo; botulinum toxin Type A (300U)	Normal saline (Placebo); botulinum toxin Type A (300U) Placebo injection on Day 1 followed by botulinum toxin Type A 300 U injection > Week 12; injections into detrusor Other Names: • BOTOX®

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

Exclusion Criteria:

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

Contacts/Locations

Study Officials: Medical Director
Study Director
Allergan, Inc.

Locations: United States, Connecticut
Middlebury, Connecticut, United States

Brazil
Rio de Janeiro, Brazil

Canada, British Columbia
Victoria, British Columbia, Canada

France
Salouel, France

Italy
Milan, Italy

Netherlands
Amsterdam, Netherlands

Portugal
Porto, Portugal

Singapore
Singapore, Singapore

South Africa
Pretoria, South Africa

Spain
Tenerife, Spain

Taiwan
Hualien, Taiwan

United Kingdom
Scunthorpe, United Kingdom

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Botulinum Toxin Type A (300U)	botulinum toxin Type A (300U)
Botulinum Toxin Type A (200U)	botulinum toxin Type A (200U)
Placebo	Normal saline (placebo)

Treatment Cycle 1

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo
Started	91	92	92
Completed	76	80	81
Not Completed	15	12	11

Treatment Cycle 2

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo
Started	63 [1]	74 [2]	0 [3]
Completed	58	72	0
Not Completed	5	2	0

[1] 32 from the 300U group + 31 from the Placebo group entered Cycle 2
[2] 42 from the 200U group + 32 from the Placebo group entered Cycle 2
[3] Cycle 1 Placebo pts were randomized to receive 300U or 200 U in Cycle 2

Baseline Characteristics

Reporting Groups

	Description
Botulinum Toxin Type A (300U)	botulinum toxin Type A (300U)
Botulinum Toxin Type A (200U)	botulinum toxin Type A (200U)
Placebo	Normal saline (placebo)

Baseline Measures

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo	Total
Number of Participants	91	92	92	275
Age, Customized [units: participants]				
< 40 years	30	31	25	86
Between 40 and 64 years	56	55	61	172
Between 65 and 74 years	4	5	5	14
>= 75 years	1	1	1	3
Gender, Male/Female [units: participants]				
Female	52	54	49	155
Male	39	38	43	120

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change From Baseline in Number of Weekly Episodes of Urinary Incontinence
Measure Description	Change from baseline in the weekly frequency of incontinence episodes at Week 6 after the first treatment. Incontinence is defined as involuntary loss of urine as recorded in a patient bladder diary. A negative number change from baseline indicates a reduction in incontinence episodes (improvement).
Time Frame	Baseline, Week 6
Safety Issue?	No

Analysis Population Description

Intent-To-Treat, defined as all patients who started the study (randomized)

Reporting Groups

	Description
Botulinum Toxin Type A (300U)	botulinum toxin Type A (300U)
Botulinum Toxin Type A (200U)	botulinum toxin Type A (200U)
Placebo	Normal saline (placebo)

Measured Values

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo
Number of Participants Analyzed	91	92	92
Change From Baseline in Number of Weekly Episodes of Urinary Incontinence [units: Number of Weekly Episodes] Mean (Standard Deviation)			
Baseline	31.2 (18.14)	32.5 (18.44)	36.7 (30.67)
Week 6	-19.4 (25.67)	-21.8 (18.06)	-13.2 (20.02)

2. Secondary Outcome Measure:

Measure Title	Change From Baseline in Maximum Cystometric Capacity (MCC)

Measure Description	Change from baseline in MCC at Week 6. MCC represents the maximum volume of urine the bladder holds. A positive number change from baseline represents an improvement (increase) in maximum volume of urine the bladder holds.
Time Frame	Baseline, Week 6
Safety Issue?	No

Analysis Population Description

Intent-To-Treat, defined as all patients who started the study (randomized)

Reporting Groups

	Description
Botulinum Toxin Type A (300U)	botulinum toxin Type A (300U)
Botulinum Toxin Type A (200U)	botulinum toxin Type A (200U)
Placebo	Normal saline (placebo)

Measured Values

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo
Number of Participants Analyzed	91	92	92
Change From Baseline in Maximum Cystometric Capacity (MCC) [units: Milliliters (mL) of urine] Mean (Standard Deviation)			
Baseline	246.8 (149.06)	247.3 (147.61)	249.4 (139.29)
Week 6	157.2 (185.18)	157.0 (164.75)	6.5 (144.77)

3. Secondary Outcome Measure:

Measure Title	Change From Baseline in Maximum Detrusor Pressure (MDP)
Measure Description	Change from baseline in MDP during the first involuntary detrusor contraction at week 6. MDP represents the maximum pressure (peak amplitude) in the bladder during the first involuntary contraction of the bladder muscle. The greater the negative number change from baseline, the better the improvement.
Time Frame	Baseline, Week 6
Safety Issue?	No

Analysis Population Description

Intent-To-Treat, defined as all patients who started the study (randomized)

Reporting Groups

	Description
Botulinum Toxin Type A (300U)	botulinum toxin Type A (300U)
Botulinum Toxin Type A (200U)	botulinum toxin Type A (200U)
Placebo	Normal saline (placebo)

Measured Values

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo
Number of Participants Analyzed	91	92	92
Change From Baseline in Maximum Detrusor Pressure (MDP) [units: Centimeters of water (cm H2O)] Mean (Standard Deviation)			
Baseline	42.1 (33.21)	51.7 (40.95)	41.5 (31.17)
Week 6	-26.9 (33.17)	-28.5 (47.82)	6.4 (41.10)

4. Secondary Outcome Measure:

Measure Title	Change From Baseline in Total Score on Incontinence Quality of Life (I-QOL) Questionnaire
Measure Description	Change from baseline in I-QOL questionnaire total score at Week 6, as completed by the patient. The I-QOL is a validated, disease-specific quality of life (QOL) questionnaire containing 22 questions designed to measure impact of urinary incontinence on patients' lives. Each question is answered on a 5-point scale (1 = worst QOL, and 5 = best QOL). The scores are totaled over the 22 questions and normalized to a score of 0-100 (0=worst QOL and 100=best QOL). A positive change from baseline represents an improvement.
Time Frame	Baseline, Week 6
Safety Issue?	No

Analysis Population Description

Intent-To-Treat, defined as all patients who started the study (randomized)

Reporting Groups

	Description
Botulinum Toxin Type A (300U)	botulinum toxin Type A (300U)
Botulinum Toxin Type A (200U)	botulinum toxin Type A (200U)
Placebo	Normal saline (placebo)

Measured Values

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo
Number of Participants Analyzed	91	92	92
Change From Baseline in Total Score on Incontinence Quality of Life (I-QOL) Questionnaire [units: Number on a Scale (Score)] Mean (Standard Deviation)			
Baseline	36.32 (18.685)	37.46 (20.109)	35.72 (18.656)
Week 6	24.26 (28.981)	24.43 (25.372)	11.71 (20.163)

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	The safety population was used to calculate the number of participants at risk for SAEs and AEs and is the total number of patients that were randomized AND treated. S(AE)s are displayed for the placebo-controlled treatment Cycle 1.

Reporting Groups

	Description
Botulinum Toxin Type A (300U)	botulinum toxin Type A (300U)
Botulinum Toxin Type A (200U)	botulinum toxin Type A (200U)
Placebo	Normal saline (placebo)

Serious Adverse Events

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	18/89 (20.22%)	17/91 (18.68%)	23/90 (25.56%)
Blood and lymphatic system disorders			
Anaemia [A] †	1/89 (1.12%)	0/91 (0%)	0/90 (0%)
Cardiac disorders			
Acute myocardial infarction [A] †	0/89 (0%)	1/91 (1.1%)	0/90 (0%)
Coronary artery disease [A] †	0/89 (0%)	1/91 (1.1%)	0/90 (0%)
Myocardial infarction [A] †	1/89 (1.12%)	0/91 (0%)	0/90 (0%)
Gastrointestinal disorders			
Abdominal Pain [A] *	1/89 (1.12%)	0/91 (0%)	0/90 (0%)
Diarrhoea [A] *	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Hepatobiliary disorders			
Cholecystitis acute [A] †	0/89 (0%)	1/91 (1.1%)	0/90 (0%)
Infections and infestations			
Bacteraemia [A] †	0/89 (0%)	1/91 (1.1%)	0/90 (0%)
Endocarditis enterococcal [A] †	0/89 (0%)	1/91 (1.1%)	0/90 (0%)
Extradural abscess [A] †	0/89 (0%)	1/91 (1.1%)	0/90 (0%)
Osteomyelitis [A] †	0/89 (0%)	1/91 (1.1%)	0/90 (0%)
Paronychia [A] *	0/89 (0%)	1/91 (1.1%)	0/90 (0%)
Pneumonia [A] †	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Pyelonephritis [A] †	0/89 (0%)	0/91 (0%)	2/90 (2.22%)
Sepsis [A] †	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Septic shock [A] [1] †	1/89 (1.12%)	0/91 (0%)	0/90 (0%)

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Upper respiratory tract infection [A] †	1/89 (1.12%)	0/91 (0%)	0/90 (0%)
Urinary tract infection [A] †	5/89 (5.62%)	1/91 (1.1%)	0/90 (0%)
Urosepsis [A] †	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Injury, poisoning and procedural complications			
Ankle fracture [A] †	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Bursa injury [A] †	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Fall [A] *	0/89 (0%)	1/91 (1.1%)	0/90 (0%)
Procedural pain [A] *	1/89 (1.12%)	0/91 (0%)	0/90 (0%)
Urethral injury [A] †	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Investigations			
International normalised ratio increased [A] †	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Urine cytology abnormal [A] †	0/89 (0%)	1/91 (1.1%)	0/90 (0%)
Metabolism and nutrition disorders			
Acidosis [A] †	0/89 (0%)	1/91 (1.1%)	0/90 (0%)
Failure to thrive [A] *	1/89 (1.12%)	0/91 (0%)	0/90 (0%)
Musculoskeletal and connective tissue disorders			
Foot deformity [A] †	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Intervertebral disc protrusion [A] †	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Joint contracture [A] *	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Muscular weakness [A] *	1/89 (1.12%)	0/91 (0%)	0/90 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm malignant [A] †	1/89 (1.12%)	0/91 (0%)	0/90 (0%)
Ovarian cancer [A] †	1/89 (1.12%)	0/91 (0%)	0/90 (0%)

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Nervous system disorders			
Multiple sclerosis relapse [A] †	0/89 (0%)	2/91 (2.2%)	3/90 (3.33%)
Psychiatric disorders			
Suicidal ideation [A] *	1/89 (1.12%)	0/91 (0%)	0/90 (0%)
Renal and urinary disorders			
Calculus bladder [A] †	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Calculus urinary [A] †	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Haematuria [A] †	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Renal failure acute [A] [1] †	0/89 (0%)	1/91 (1.1%)	0/90 (0%)
Renal impairment [A] [1] †	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease [A] †	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Respiratory failure [A] [1] †	0/89 (0%)	1/91 (1.1%)	0/90 (0%)
Skin and subcutaneous tissue disorders			
Decubitus ulcer [A] *	1/89 (1.12%)	1/91 (1.1%)	0/90 (0%)
Skin ulcer [A] *	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Surgical and medical procedures			
Abortion induced [A] †	0/89 (0%)	0/91 (0%)	1/90 (1.11%)
Vascular disorders			
Thrombosis [A] †	1/89 (1.12%)	0/91 (0%)	0/90 (0%)

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (13.0)

[1] Event not related to study drug

Other Adverse Events

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

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	70/89 (78.65%)	63/91 (69.23%)	52/90 (57.78%)
Gastrointestinal disorders			
Constipation [A] *	6/89 (6.74%)	5/91 (5.49%)	2/90 (2.22%)
Diarrhoea [A] *	6/89 (6.74%)	3/91 (3.3%)	6/90 (6.67%)
General disorders			
Fatigue [A] *	3/89 (3.37%)	8/91 (8.79%)	1/90 (1.11%)
Pyrexia [A] †	1/89 (1.12%)	6/91 (6.59%)	3/90 (3.33%)
Infections and infestations			
Influenza [A] †	1/89 (1.12%)	5/91 (5.49%)	0/90 (0%)
Nasopharyngitis [A] †	6/89 (6.74%)	6/91 (6.59%)	3/90 (3.33%)
Urinary tract infection [A] †	57/89 (64.04%)	51/91 (56.04%)	36/90 (40%)
Musculoskeletal and connective tissue disorders			
Arthralgia [A] *	1/89 (1.12%)	3/91 (3.3%)	5/90 (5.56%)
Muscle spasms [A] *	6/89 (6.74%)	4/91 (4.4%)	1/90 (1.11%)
Muscular weakness [A] *	4/89 (4.49%)	6/91 (6.59%)	1/90 (1.11%)
Pain in extremity [A] *	2/89 (2.25%)	5/91 (5.49%)	3/90 (3.33%)
Renal and urinary disorders			
Dysuria [A] *	7/89 (7.87%)	5/91 (5.49%)	2/90 (2.22%)
Haematuria [A] †	9/89 (10.11%)	5/91 (5.49%)	4/90 (4.44%)
Urinary incontinence [A] *	1/89 (1.12%)	5/91 (5.49%)	2/90 (2.22%)
Urinary retention [A] †	28/89 (31.46%)	18/91 (19.78%)	3/90 (3.33%)

† Indicates events were collected by systematic assessment.

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA (13.0)

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

Results Point of Contact:

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