ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 11/05/2015

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Study Identification

Unique Protocol ID:	191622-515
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:	November 2015
Overall Status:	Completed
Study Start:	August 2006
Primary Completion:	May 2010 [Actual]
Study Completion:	May 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: 416 [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 (tx 1) followed by botulinum toxin Type A 200 U (tx 2); injections into detrusor, at > 12 weeks interval Other Names: • BOTOX®
Experimental: 2 botulinum toxin Type A (300U)	Biological/Vaccine: botulinum toxin Type A (300U) botulinum toxin Type A 300 U (tx 1) followed by botulinum toxin Type A 300 U (tx 2); injections into detrusor, at > 12 weeks interval Other Names: • BOTOX®
3 placebo; botulinum toxin Type A (200U)	Normal Saline (Placebo); botulinum toxin Type A (200U) Placebo (tx 1) followed by botulinum toxin Type A 200 U (tx 2); injections into detrusor, at > 12 weeks interval Other Names: • BOTOX®
4 placebo; botulinum toxin Type A (300U)	Normal Saline (Placebo); botulinum toxin Type A (300U) Placebo (tx 1) followed by botulinum toxin Type A 300 U (tx 2), injections into detrusor, at > 12 weeks interval 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 of 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, Michigan
Royal Oak, Michigan, United States

Canada
Sherbrooke, Canada

Austria
Innsbruck, Austria

Belgium
Gent, Belgium

Czech Republic
Ostrava, Czech Republic

France
Garches, France

Germany
Halle (Saale), Germany

Poland
Wroclaw, Poland

Russian Federation
Moscow, Russian Federation

Slovakia
Martin, Slovakia

Ukraine
Lviv, Ukraine

United Kingdom
London, United Kingdom

Australia, New South Wales
Randwick, New South Wales, Australia

New Zealand
Christchurch, New Zealand

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	132	135	149
Completed	105	118	132

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo
Not Completed	27	17	17

Treatment Cycle 2

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo
Started	115 [1]	125 [2]	0 [3]
Completed	106	112	0
Not Completed	9	13	0

[1] 69 from the 300U group + 46 from the Placebo group entered Cycle 2
[2] 74 from the 200U group + 51 from the Placebo group entered Cycle 2
[3] Cycle 1 Placebo pts were randomized to receive 300U or 200U 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	132	135	149	416
Age, Customized [units: participants]				
<40 years	40	48	45	133
Between 40 and 64 years	83	73	95	251
Between 65 and 74 years	9	14	9	32
>=75 years	0	0	0	0

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo	Total
Gender, Male/Female [units: participants]				
Female	89	80	76	245
Male	43	55	73	171

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	132	135	149
Change From Baseline in Number of Weekly Episodes of Urinary Incontinence [units: Number of Weekly Episodes] Mean (Standard Deviation)			
Baseline	31.1 (17.02)	32.3 (22.76)	28.3 (15.82)
Week 6	-22.7 (17.10)	-21.0 (23.77)	-8.8 (16.18)

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	132	135	149
Change From Baseline in Maximum Cystometric Capacity (MCC) [units: Millimeters (mL) of urine] Mean (Standard Deviation)			
Baseline	255.8 (144.99)	252.3 (154.37)	256.0 (143.83)
Week 6	167.7 (169.56)	151.2 (170.59)	15.5 (127.31)

3. Secondary Outcome Measure:

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

Measure Description	Change from baseline in MDP during 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	132	135	149
Change From Baseline in Maximum Detrusor Pressure (MDP) [units: Centimeters of water (cm H20)] Mean (Standard Deviation)			
Baseline	47.1 (36.30)	51.3 (34.66)	50.9 (38.08)
Week 6	-33.3 (37.75)	-35.1 (35.67)	-2.4 (43.41)

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	132	135	149
Change From Baseline in Total Score on Incontinence Quality of Life (I-QOL) Questionnaire [units: Number on a Scale (Score)] Mean (Standard Deviation)			
Baseline	32.18 (18.609)	33.95 (18.021)	35.06 (18.066)
Week 6	32.92 (23.849)	26.90 (26.813)	10.81 (18.413)

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)

	Description
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	30/127 (23.62%)	24/135 (17.78%)	22/145 (15.17%)
Blood and lymphatic system disorders			
Neutropenia [A] †	1/127 (0.79%)	0/135 (0%)	0/145 (0%)
Gastrointestinal disorders			
Diarrhoea [A] *	1/127 (0.79%)	0/135 (0%)	0/145 (0%)
Faecaloma [A] †	0/127 (0%)	1/135 (0.74%)	0/145 (0%)
Gastritis [A] *	0/127 (0%)	0/135 (0%)	1/145 (0.69%)
Intestinal obstruction [A] †	1/127 (0.79%)	0/135 (0%)	0/145 (0%)
General disorders			
Adverse Drug Reaction [A] [1] †	1/127 (0.79%)	0/135 (0%)	0/145 (0%)
Death [A] †	1/127 (0.79%)	0/135 (0%)	0/145 (0%)
Non-cardiac chest pain [A] †	0/127 (0%)	1/135 (0.74%)	0/145 (0%)
Infections and infestations			
Appendicitis [A] †	0/127 (0%)	1/135 (0.74%)	0/145 (0%)
Bacteraemia [A] †	1/127 (0.79%)	0/135 (0%)	0/145 (0%)
Cellulitis [A] †	1/127 (0.79%)	0/135 (0%)	1/145 (0.69%)
Central nervous system abscess [A] †	0/127 (0%)	0/135 (0%)	1/145 (0.69%)
Clostridium difficile colitis [A] †	0/127 (0%)	0/135 (0%)	1/145 (0.69%)
Cystitis [A] †	0/127 (0%)	0/135 (0%)	1/145 (0.69%)

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Device related sepsis [A] [2] †	1/127 (0.79%)	0/135 (0%)	0/145 (0%)
Escherichia sepsis [A] †	0/127 (0%)	1/135 (0.74%)	0/145 (0%)
Extradural abscess [A] †	0/127 (0%)	0/135 (0%)	1/145 (0.69%)
Osteomyelitis [A] †	0/127 (0%)	0/135 (0%)	1/145 (0.69%)
Osteomyelitis chronic [A] †	0/127 (0%)	0/135 (0%)	1/145 (0.69%)
Pneumonia [A] †	0/127 (0%)	0/135 (0%)	1/145 (0.69%)
Pyelonephritis [A] †	1/127 (0.79%)	0/135 (0%)	0/145 (0%)
Staphylococcal bacteraemia [A] †	1/127 (0.79%)	0/135 (0%)	0/145 (0%)
Urinary tract infection [A] †	2/127 (1.57%)	3/135 (2.22%)	2/145 (1.38%)
Urinary tract infection bacterial [A] †	1/127 (0.79%)	0/135 (0%)	0/145 (0%)
Urosepsis [A] †	0/127 (0%)	0/135 (0%)	1/145 (0.69%)
Injury, poisoning and procedural complications			
Ankle fracture [A] †	0/127 (0%)	2/135 (1.48%)	0/145 (0%)
Concussion [A] †	0/127 (0%)	1/135 (0.74%)	0/145 (0%)
Eschar [A] *	0/127 (0%)	1/135 (0.74%)	0/145 (0%)
Forearm fracture [A] †	0/127 (0%)	1/135 (0.74%)	0/145 (0%)
Lower limb fracture [A] †	0/127 (0%)	1/135 (0.74%)	0/145 (0%)
Tendon rupture [A] †	0/127 (0%)	0/135 (0%)	1/145 (0.69%)
Thermal burn [A] *	0/127 (0%)	0/135 (0%)	1/145 (0.69%)
Investigations			
Oxygen saturation decreased [A] †	0/127 (0%)	0/135 (0%)	1/145 (0.69%)
Metabolism and nutrition disorders			

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Obesity [A] †	0/127 (0%)	1/135 (0.74%)	0/145 (0%)
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion [A] †	1/127 (0.79%)	1/135 (0.74%)	0/145 (0%)
Spondylolisthesis [A] †	0/127 (0%)	1/135 (0.74%)	0/145 (0%)
Vertebral foraminal stenosis [A] †	0/127 (0%)	1/135 (0.74%)	0/145 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma [A] †	1/127 (0.79%)	0/135 (0%)	0/145 (0%)
Breast cancer [A] †	1/127 (0.79%)	0/135 (0%)	0/145 (0%)
Nervous system disorders			
Epilepsy [A] †	0/127 (0%)	0/135 (0%)	1/145 (0.69%)
Metabolic encephalopathy [A] †	0/127 (0%)	0/135 (0%)	1/145 (0.69%)
Multiple sclerosis relapse [A] †	10/127 (7.87%)	0/135 (0%)	3/145 (2.07%)
Psychiatric disorders			
Mental status changes [A] [3] †	0/127 (0%)	1/135 (0.74%)	0/145 (0%)
Renal and urinary disorders			
Calculus ureteric [A] †	1/127 (0.79%)	0/135 (0%)	0/145 (0%)
Haematuria [A] †	1/127 (0.79%)	0/135 (0%)	0/145 (0%)
Hydronephrosis [A] †	0/127 (0%)	1/135 (0.74%)	0/145 (0%)
Renal failure chronic [A] †	0/127 (0%)	0/135 (0%)	1/145 (0.69%)
Stress urinary incontinence [A] †	0/127 (0%)	1/135 (0.74%)	0/145 (0%)
Urinary retention [A] †	1/127 (0.79%)	0/135 (0%)	0/145 (0%)
Reproductive system and breast disorders			
Epididymitis [A] †	0/127 (0%)	1/135 (0.74%)	0/145 (0%)

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease [A] †	0/127 (0%)	0/135 (0%)	1/145 (0.69%)
Pulmonary embolism [A] †	1/127 (0.79%)	0/135 (0%)	0/145 (0%)
Skin and subcutaneous tissue disorders			
Decubitus ulcer [A] *	0/127 (0%)	3/135 (2.22%)	0/145 (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, but to concomitant medication
[2] Event related to central intravenous catheter
[3] Event not related to study medication; related to underlying adverse event of urinary tract infection

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	82/127 (64.57%)	92/135 (68.15%)	70/145 (48.28%)
Gastrointestinal disorders			
Diarrhoea [A] *	7/127 (5.51%)	8/135 (5.93%)	4/145 (2.76%)
Nausea [A] *	8/127 (6.3%)	6/135 (4.44%)	3/145 (2.07%)
General disorders			
Fatigue [A] *	4/127 (3.15%)	8/135 (5.93%)	6/145 (4.14%)
Pyrexia [A] †	4/127 (3.15%)	10/135 (7.41%)	5/145 (3.45%)
Infections and infestations			
Urinary tract infection [A] †	64/127 (50.39%)	66/135 (48.89%)	49/145 (33.79%)
Vulvovaginal mycotic infection [A] [1] †	3/89 (3.37%)	6/80 (7.5%)	2/76 (2.63%)

	Botulinum Toxin Type A (300U)	Botulinum Toxin Type A (200U)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Musculoskeletal and connective tissue disorders			
Muscular weakness [A] *	9/127 (7.09%)	4/135 (2.96%)	4/145 (2.76%)
Nervous system disorders			
Headache [A] *	7/127 (5.51%)	4/135 (2.96%)	4/145 (2.76%)
Multiple sclerosis relapse [A] †	12/127 (9.45%)	1/135 (0.74%)	3/145 (2.07%)
Renal and urinary disorders			
Bladder pain [A] *	7/127 (5.51%)	2/135 (1.48%)	2/145 (1.38%)
Haematuria [A] †	6/127 (4.72%)	7/135 (5.19%)	4/145 (2.76%)
Urinary retention [A] †	22/127 (17.32%)	27/135 (20%)	5/145 (3.45%)
Vascular disorders			
Hypertension [A] †	7/127 (5.51%)	3/135 (2.22%)	0/145 (0%)

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

[1] Percentages for this adverse event were calculated based on the number of female patients in each group

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:

Name/Official Title: Therapeutic area Head

Organization: Allergan, Inc.

Phone: 714-246-4500

Email: clinicaltrials@allergan.com