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

ClinicalTrials.gov ID: NCT00575016

Study Identification

Unique Protocol ID:	191622-518
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:	Terminated [The study was terminated early due to enrollment challenges.]
Study Start:	December 2007
Primary Completion:	February 2010 [Actual]
Study Completion:	July 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?:	No
Review Board:	Approval Status: Approved Approval Number: 345/2007/4000 Board Name: Agency for Drugs and Medicinal Devices of Serbia Board Affiliation: Ministry of Health, Republic of Serbia Phone: +381 11 3114949 Email: hygia@alims.sr.gov.yu
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	India: Drugs Controller General, India, Directorate General of Health Services Greece: National Drug Organization Turkey: Turkish Republic Ministry of Health Egypt: Ministry of Health and Population

Study Description

Brief Summary:	The purpose of this study is to explore the effectiveness and safety of several doses of botulinum toxin type A in treating overactive bladder in patients with spinal cord injury.
Detailed Description:	

Conditions

Conditions:	Overactive Bladder
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Parallel Assignment
Number of Arms:	4
Masking:	Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Efficacy Study

Enrollment: 74 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1 botulinum toxin Type A (50U); botulinum toxin Type A (200U)	Biological/Vaccine: botulinum toxin Type A (50U); botulinum toxin Type A (200U) botulinum toxin Type A 50 U on Day 1 followed by botulinum toxin Type A 200 U > 12 weeks; injections into the detrusor Other Names: • BOTOX®
Experimental: 2 botulinum toxin Type A (100U); botulinum toxin Type A (200U)	Biological/Vaccine: botulinum toxin Type A (100U); botulinum toxin Type A (200U) botulinum toxin Type A 100 U on Day 1 followed by botulinum toxin Type A 200 U > 12 weeks; injections into the detrusor Other Names: • BOTOX®
Experimental: 3 botulinum toxin Type A (200U)	Biological/Vaccine: botulinum toxin Type A (200U) botulinum toxin Type A 200 U on Day 1 followed by botulinum toxin Type A 200 U > 12 weeks; injections into the detrusor Other Names: • BOTOX®
4 placebo; botulinum toxin Type A (200U)	Biological/Vaccine: Normal saline (Placebo); botulinum toxin Type A (200U) Placebo injection on Day 1 and botulinum toxin Type A injection 200 U > Week 12; injection into the 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
- 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

Locations: Serbia
Belgrade, Serbia

Greece
Thessaloniki, Greece

Turkey
Ankara, Turkey

Egypt
Cairo, Egypt

Lebanon
Beirut, Lebanon

India
Ahmadabad, India

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Pre-Assignment Details	Of the 74 patients enrolled into the study, 73 patients received study medication and are included in the analyses. One patient was enrolled but did not receive study medication.

Reporting Groups

	Description
Botulinum Toxin Type A (200U)	botulinum toxin Type A (200U)
Botulinum Toxin Type A (100U)	botulinum toxin Type A (100U)
Botulinum Toxin Type A (50U)	botulinum toxin Type A (50U)
Placebo	Normal saline (placebo)

Treatment Cycle 1

	Botulinum Toxin Type A (200U)	Botulinum Toxin Type A (100U)	Botulinum Toxin Type A (50U)	Placebo
Started	17	21	19	17 [1]
Completed	8 [2]	16 [3]	15 [4]	12 [5]
Not Completed	9	5	4	5

[1] 1 pt randomized to Placebo never received treatment
[2] 3 pts from 200U group entered Cycle 2
[3] 11 pts from 100U group entered Cycle 2
[4] 8 pts from 50U group entered Cycle 2
[5] 9 pts from Placebo group entered Cycle 2

Treatment Cycle 2

	Botulinum Toxin Type A (200U)	Botulinum Toxin Type A (100U)	Botulinum Toxin Type A (50U)	Placebo
Started	31 [1]	0 [1]	0 [1]	0 [1]
Completed	30	0	0	0

	Botulinum Toxin Type A (200U)	Botulinum Toxin Type A (100U)	Botulinum Toxin Type A (50U)	Placebo
Not Completed	1	0	0	0

[1] All patients received 200U in Treatment Cycle 2.

Baseline Characteristics

Reporting Groups

	Description
Botulinum Toxin Type A (200U)	botulinum toxin Type A (200U)
Botulinum Toxin Type A (100U)	botulinum toxin Type A (100U)
Botulinum Toxin Type A (50U)	botulinum toxin Type A (50U)
Placebo	Normal saline (placebo)

Baseline Measures

	Botulinum Toxin Type A (200U)	Botulinum Toxin Type A (100U)	Botulinum Toxin Type A (50U)	Placebo	Total
Number of Participants	17	21	19	17	74
Age, Customized [units: participants]					
< 40 years	13	13	16	11	53
Between 40 and 64 years	4	8	3	6	21
Between 65 and 74 years	0	0	0	0	0
>= 75 years	0	0	0	0	0
Gender, Male/Female [units: participants]					
Female	3	4	2	1	10
Male	14	17	17	16	64

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

Modified Intent-To-Treat: defined as all patients who were randomized (started study) and received treatment

Reporting Groups

	Description
Botulinum Toxin Type A (200U)	botulinum toxin Type A (200U)
Botulinum Toxin Type A (100U)	botulinum toxin Type A (100U)
Botulinum Toxin Type A (50U)	botulinum toxin Type A (50U)
Placebo	Normal saline (placebo)

Measured Values

	Botulinum Toxin Type A (200U)	Botulinum Toxin Type A (100U)	Botulinum Toxin Type A (50U)	Placebo
Number of Participants Analyzed	17	21	19	16
Change From Baseline in Number of Weekly Episodes of Urinary Incontinence [units: Number of Weekly Episodes] Mean (Standard Deviation)				
Baseline	28.8 (20.26)	37.8 (27.63)	26.3 (19.29)	24.6 (9.08)
Week 6	-15.8 (18.01)	-14.1 (23.90)	-7.7 (11.52)	-8.6 (8.12)

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

Modified Intent-To-Treat: defined as all patients who were randomized (started study) and received treatment

Reporting Groups

	Description
Botulinum Toxin Type A (200U)	botulinum toxin Type A (200U)
Botulinum Toxin Type A (100U)	botulinum toxin Type A (100U)
Botulinum Toxin Type A (50U)	botulinum toxin Type A (50U)
Placebo	Normal saline (placebo)

Measured Values

	Botulinum Toxin Type A (200U)	Botulinum Toxin Type A (100U)	Botulinum Toxin Type A (50U)	Placebo
Number of Participants Analyzed	17	21	19	16
Change From Baseline in Maximum Cystometric Capacity (MCC) [units: Milliliters (mL) of urine] Mean (Standard Deviation)				
Baseline	214.2 (96.56)	161.6 (66.13)	213.9 (135.41)	189.8 (103.56)
Week 6	183.7 (197.63)	220.1 (183.05)	136.8 (189.37)	117.4 (173.51)

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

Modified Intent-To-Treat: defined as all patients who were randomized (started study) and received treatment

Reporting Groups

	Description
Botulinum Toxin Type A (200U)	botulinum toxin Type A (200U)
Botulinum Toxin Type A (100U)	botulinum toxin Type A (100U)
Botulinum Toxin Type A (50U)	botulinum toxin Type A (50U)
Placebo	Normal saline (placebo)

Measured Values

	Botulinum Toxin Type A (200U)	Botulinum Toxin Type A (100U)	Botulinum Toxin Type A (50U)	Placebo
Number of Participants Analyzed	17	21	19	16
Change From Baseline in Maximum Detrusor Pressure (MDP) [units: Centimeters of water (cm H2O)] Mean (Standard Deviation)				
Baseline	62.9 (72.05)	54.2 (41.47)	52.7 (39.51)	45.9 (36.82)
Week 6	-33.0 (58.06)	-29.4 (39.67)	-20.1 (22.07)	-2.1 (27.65)

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 (200U)	botulinum toxin Type A (200U)

	Description
Botulinum Toxin Type A (100U)	botulinum toxin Type A (100U)
Botulinum Toxin Type A (50U)	botulinum toxin Type A (50U)
Placebo	Normal saline (placebo)

Serious Adverse Events

	Botulinum Toxin Type A (200U)	Botulinum Toxin Type A (100U)	Botulinum Toxin Type A (50U)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	2/17 (11.76%)	2/21 (9.52%)	2/19 (10.53%)	6/16 (37.5%)
Gastrointestinal disorders				
Intestinal obstruction [A] †	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
General disorders				
Sudden death [A] [1] *	1/17 (5.88%)	1/21 (4.76%)	0/19 (0%)	0/16 (0%)
Infections and infestations				
Lower respiratory tract infection [A] †	0/17 (0%)	1/21 (4.76%)	0/19 (0%)	0/16 (0%)
Malaria [A] †	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Urinary tract infection [A] †	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Testis cancer [A] †	0/17 (0%)	0/21 (0%)	1/19 (5.26%)	0/16 (0%)
Renal and urinary disorders				
Calculus ureteric [A] †	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Nephrolithiasis [A] †	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Respiratory, thoracic and mediastinal disorders				
Respiratory disorder [A] †	0/17 (0%)	0/21 (0%)	1/19 (5.26%)	0/16 (0%)
Skin and subcutaneous tissue disorders				
Skin ulcer [A] *	1/17 (5.88%)	0/21 (0%)	0/19 (0%)	0/16 (0%)

	Botulinum Toxin Type A (200U)	Botulinum Toxin Type A (100U)	Botulinum Toxin Type A (50U)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Surgical and medical procedures				
Intestinal stoma [A] †	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)

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

[1] Both events not related to study medication.

Other Adverse Events

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

	Botulinum Toxin Type A (200U)	Botulinum Toxin Type A (100U)	Botulinum Toxin Type A (50U)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	11/17 (64.71%)	17/21 (80.95%)	11/19 (57.89%)	13/16 (81.25%)
Blood and lymphatic system disorders				
Anaemia [A] †	1/17 (5.88%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Gastrointestinal disorders				
Anal inflammation [A] †	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Constipation [A] *	1/17 (5.88%)	0/21 (0%)	0/19 (0%)	0/16 (0%)
Dyspepsia [A] *	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Gastritis [A] *	1/17 (5.88%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Hyperchlorhydria [A] †	1/17 (5.88%)	2/21 (9.52%)	1/19 (5.26%)	2/16 (12.5%)
Intestinal obstruction [A] †	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Vomiting [A] *	0/17 (0%)	1/21 (4.76%)	0/19 (0%)	1/16 (6.25%)
General disorders				
Asthenia [A] *	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Pain [A] *	0/17 (0%)	0/21 (0%)	1/19 (5.26%)	0/16 (0%)

	Botulinum Toxin Type A (200U)	Botulinum Toxin Type A (100U)	Botulinum Toxin Type A (50U)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Pyrexia [A] †	1/17 (5.88%)	2/21 (9.52%)	0/19 (0%)	3/16 (18.75%)
Sudden death [A] [1] *	1/17 (5.88%)	1/21 (4.76%)	0/19 (0%)	0/16 (0%)
Infections and infestations				
Acute tonsillitis [A] †	0/17 (0%)	0/21 (0%)	1/19 (5.26%)	0/16 (0%)
Gastroenteritis [A] †	0/17 (0%)	0/21 (0%)	1/19 (5.26%)	0/16 (0%)
Infected skin ulcer [A] †	1/17 (5.88%)	0/21 (0%)	0/19 (0%)	0/16 (0%)
Malaria [A] †	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Nasopharyngitis [A] †	1/17 (5.88%)	0/21 (0%)	0/19 (0%)	0/16 (0%)
Orchitis [A] †	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Urinary tract infection [A] †	7/17 (41.18%)	11/21 (52.38%)	7/19 (36.84%)	10/16 (62.5%)
Injury, poisoning and procedural complications				
Muscle rupture [A] †	0/17 (0%)	0/21 (0%)	1/19 (5.26%)	0/16 (0%)
Post procedural haematuria [A] †	1/17 (5.88%)	1/21 (4.76%)	2/19 (10.53%)	2/16 (12.5%)
Procedural pain [A] *	1/17 (5.88%)	0/21 (0%)	0/19 (0%)	0/16 (0%)
Investigations				
Blood creatinine increased [A] †	1/17 (5.88%)	0/21 (0%)	0/19 (0%)	0/16 (0%)
Red blood cells urine positive [A] †	0/17 (0%)	0/21 (0%)	1/19 (5.26%)	0/16 (0%)
White blood cells urine positive [A] †	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Musculoskeletal and connective tissue disorders				
Arthralgia [A] *	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Tendonitis [A] †	0/17 (0%)	0/21 (0%)	1/19 (5.26%)	0/16 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				

	Botulinum Toxin Type A (200U)	Botulinum Toxin Type A (100U)	Botulinum Toxin Type A (50U)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Testis cancer [A] †	0/17 (0%)	0/21 (0%)	1/19 (5.26%)	0/16 (0%)
Nervous system disorders				
Headache [A] *	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Psychiatric disorders				
Panic disorder [A] †	0/17 (0%)	0/21 (0%)	1/19 (5.26%)	0/16 (0%)
Renal and urinary disorders				
Calculus ureteric [A] †	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Dysuria [A] *	0/17 (0%)	2/21 (9.52%)	1/19 (5.26%)	5/16 (31.25%)
Haematuria [A] †	1/17 (5.88%)	0/21 (0%)	2/19 (10.53%)	1/16 (6.25%)
Hydronephrosis [A] †	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Nephrolithiasis [A] †	0/17 (0%)	1/21 (4.76%)	0/19 (0%)	1/16 (6.25%)
Vesical fistula [A] †	1/17 (5.88%)	0/21 (0%)	0/19 (0%)	0/16 (0%)
Reproductive system and breast disorders				
Epididymitis [A] †	0/17 (0%)	1/21 (4.76%)	0/19 (0%)	0/16 (0%)
Respiratory, thoracic and mediastinal disorders				
Respiratory disorder [A] †	0/17 (0%)	0/21 (0%)	1/19 (5.26%)	0/16 (0%)
Skin and subcutaneous tissue disorders				
Decubitus ulcer [A] †	0/17 (0%)	0/21 (0%)	1/19 (5.26%)	0/16 (0%)
Dermatitis [A] *	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)
Petechiae [A] *	0/17 (0%)	0/21 (0%)	1/19 (5.26%)	0/16 (0%)
Skin ulcer [A] *	1/17 (5.88%)	0/21 (0%)	0/19 (0%)	0/16 (0%)
Surgical and medical procedures				

	Botulinum Toxin Type A (200U)	Botulinum Toxin Type A (100U)	Botulinum Toxin Type A (50U)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Intestinal stoma [A] †	0/17 (0%)	0/21 (0%)	0/19 (0%)	1/16 (6.25%)

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

[1] Both events not related to study drug

Limitations and Caveats

Due to recruitment difficulties, study enrollment was stopped early.

More Information

Certain Agreements:

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

The only 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 60 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