ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 10/24/2013

ClinicalTrials.gov ID: NCT00168428

Study Identification

Unique Protocol ID:	191622-080
Brief Title:	A Study Using Botulinum Toxin Type A as Headache Prophylaxis for Migraine Patients With Frequent Headaches
Official Title:	
Secondary IDs:	

Study Status

Record Verification:	October 2013
Overall Status:	Completed
Study Start:	March 2006
Primary Completion:	December 2007 [Actual]
Study Completion:	August 2008 [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: CBER IND/IDE Number: 7480 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:	This is a 60 week study including a double-blind phase followed by an open-label phase.
Detailed Description:	

Conditions

Conditions:	Migraine Disorders
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Double Blind (Subject, Investigator)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study

Enrollment: 705 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: botulinum toxin Type A Two treatment sessions in the double-blind phase and three treatment sessions in the open-label extension phase. Total minimum dose is 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas with the total maximum dose of 195 U with 39 head/neck injections.	Biological/Vaccine: Botulinum Toxin Type A Two treatment sessions in the double-blind phase and three treatment sessions in the open-label phase. Total minimum dose is 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas with the total maximum dose of 195 U with 39 head/neck injections. Other Names: • BOTOX®
Placebo Comparator: Placebo (saline) Two treatment sessions in the double-blind phase. Total minimum dose in 155 U with 31 fixed-site, fixed dose injections across seven specific head/ neck muscle areas and the total maximum dose is 195 U with 39 head/ neck injections.	placebo (saline) Two treatment sessions in the double-blind phase. Total minimum dose in 155 U with 31 fixed-site, fixed dose injections across seven specific head/ neck muscle areas and the total maximum dose is 195 U with 39 head/ neck injections.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 65 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Frequent migraine (>=15 headache days per month)
- >=4 distinct headache episodes lasting >=4 hours
- >=50% of baseline headache days migraine/probable migraine days

Exclusion Criteria:

- Previous use of botulinum toxin of any serotype or immunization to any botulinum toxin serotype
- Any medical condition that puts the patient at increased risk with exposure to BOTOX
- Diagnosis of complicated migraine, chronic tension-type headache, hypnic headache, hemicrania continua, new daily persistent headache
- Use of prophylactic headache medication within 28 days prior to week -4

- Unremitting headache lasting continuously throughout the 4-week baseline period
- Known or suspected TMD
- Diagnosis of fibromyalgia
- Beck depression inventory score >24 at week-4
- Psychiatric problems that may have interfered with study participation

Contacts/Locations

Study Officials: Medical Director
Study Director
Allergan, Inc.

Locations: United States, California
Walnut Creek, California, United States

Croatia
Zagreb, Croatia

Germany
Essen, Germany

Switzerland
Zurich, Switzerland

United Kingdom
London, United Kingdom

Canada, Alberta
Calgary, Alberta, Canada

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
Botulinum Toxin Type A	Two treatment sessions in the double-blind phase and three treatment sessions in the open-label extension phase. Total minimum dose is 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas with the total maximum dose of 195 U with 39 head/neck injections.
Placebo (Saline)	Two treatment sessions in the double-blind phase. Total minimum dose in 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas and the total maximum dose is 195 U with 39 head/neck injections.

Double-Blind Phase (DB)

	Botulinum Toxin Type A	Placebo (Saline)
Started	347	358
Completed	311 [1]	334 [1]
Not Completed	36	24

[1] Completed Week 24

Open-Label Phase (OL)

	Botulinum Toxin Type A	Placebo (Saline)
Started	305 [1]	329 [2]
Completed	261	261
Not Completed	44	68

[1] Number of DB Botulinum toxin type A patients who rolled into OL phase
[2] Number of DB Placebo patients who rolled into OL phase

Baseline Characteristics

Reporting Groups

	Description
Botulinum Toxin Type A	Two treatment sessions in the double-blind phase and three treatment sessions in the open-label extension phase. Total minimum dose is 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas with the total maximum dose of 195 U with 39 head/neck injections.
Placebo (Saline)	Two treatment sessions in the double-blind phase. Total minimum dose in 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas and the total maximum dose is 195 U with 39 head/neck injections.

Baseline Measures

	Botulinum Toxin Type A	Placebo (Saline)	Total
Number of Participants	347	358	705
Age, Customized [units: participants]			
< 40 years	149	160	309
>= 40 years	198	198	396
Gender, Male/Female [units: participants]			
Female	299	303	602
Male	48	55	103

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change in Frequency of Headache Days
Measure Description	Mean change from baseline in frequency (number) of headache days during the 28 day period ending with Week 24. Headache day defined as a calendar day [00:00 to 23:59] for which the patient reported >= 4 continuous hours of headache.
Time Frame	Baseline, Week 24
Safety Issue?	No

Analysis Population Description

Intent to Treat

Reporting Groups

	Description
Botulinum Toxin Type A	Two treatment sessions in the double-blind phase and three treatment sessions in the open-label extension phase. Total minimum dose is 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas with the total maximum dose of 195 U with 39 head/neck injections.
Placebo (Saline)	Two treatment sessions in the double-blind phase. Total minimum dose in 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas and the total maximum dose is 195 U with 39 head/ neck injections.

Measured Values

	Botulinum Toxin Type A	Placebo (Saline)
Number of Participants Analyzed	347	358
Change in Frequency of Headache Days [units: Headache Days] Mean (Standard Deviation)		
Baseline	19.9 (3.63)	19.7 (3.65)
Change from Baseline at Week 24	-9.0 (6.54)	-6.7 (6.67)

2. Secondary Outcome Measure:

Measure Title	Change in Total Cumulative Hours of Headache Occurring on Headache Days
Measure Description	Mean change from baseline in total cumulative hours of headache occurring on headache days during the 28 day period ending with Week 24. Headache day defined as a calendar day [00:00 to 23:59] when the patient reported >= 4 continuous hours of headache.
Time Frame	Baseline, Week 24
Safety Issue?	No

Analysis Population Description
Intent to Treat

Reporting Groups

	Description
Botulinum Toxin Type A	Two treatment sessions in the double-blind phase and three treatment sessions in the open-label extension phase. Total minimum dose is 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas with the total maximum dose of 195 U with 39 head/neck injections.

	Description
Placebo (Saline)	Two treatment sessions in the double-blind phase. Total minimum dose in 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas and the total maximum dose is 195 U with 39 head/neck injections.

Measured Values

	Botulinum Toxin Type A	Placebo (Saline)
Number of Participants Analyzed	347	358
Change in Total Cumulative Hours of Headache Occurring on Headache Days [units: Hours] Mean (Standard Deviation)		
Baseline	296.18 (121.043)	287.20 (118.089)
Change from Baseline at Week 24	-132.41 (130.216)	-90.01 (133.758)

3. Secondary Outcome Measure:

Measure Title	Change in Frequency of Moderate/Severe Headache Days
Measure Description	Mean change from baseline in frequency (number) of moderate/severe headache days during the 28 day period ending with Week 24. Those calendar days with >= 4 continuous hours of headache were selected. As per the patient diary, all headache episodes occurring during those days with a maximum severity of moderate or severe were counted.
Time Frame	Baseline, Week 24
Safety Issue?	No

Analysis Population Description

Intent to Treat

Reporting Groups

	Description
Botulinum Toxin Type A	Two treatment sessions in the double-blind phase and three treatment sessions in the open-label extension phase. Total minimum dose is 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas with the total maximum dose of 195 U with 39 head/neck injections.
Placebo (Saline)	Two treatment sessions in the double-blind phase. Total minimum dose in 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas and the total maximum dose is 195 U with 39 head/neck injections.

Measured Values

	Botulinum Toxin Type A	Placebo (Saline)
Number of Participants Analyzed	347	358
Change in Frequency of Moderate/Severe Headache Days [units: Moderate/Severe Headache Days] Mean (Standard Deviation)		
Baseline	18.1 (4.03)	17.7 (4.26)
Change from Baseline at Week 24	-8.3 (6.37)	-5.8 (6.59)

4. Secondary Outcome Measure:

Measure Title	Change in Frequency of Migraine/Probable Migraine Headache Days
Measure Description	Mean change from baseline in frequency (number) of migraine/probable migraine headache days during the 28 day period ending with Week 24. Headache day defined as a calendar day with >= 4 continuous hours of headache meeting the ICHD-II criteria for migraine or probable migraine.
Time Frame	Baseline, Week 24
Safety Issue?	No

Analysis Population Description
Intent to Treat

Reporting Groups

	Description
Botulinum Toxin Type A	Two treatment sessions in the double-blind phase and three treatment sessions in the open-label extension phase. Total minimum dose is 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas with the total maximum dose of 195 U with 39 head/neck injections.
Placebo (Saline)	Two treatment sessions in the double-blind phase. Total minimum dose in 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas and the total maximum dose is 195 U with 39 head/neck injections.

Measured Values

	Botulinum Toxin Type A	Placebo (Saline)
Number of Participants Analyzed	347	358

	Botulinum Toxin Type A	Placebo (Saline)
Change in Frequency of Migraine/Probable Migraine Headache Days [units: Migraine/Probable Migraine Headache Days] Mean (Standard Deviation)		
Baseline	19.2 (3.94)	18.7 (4.05)
Change from Baseline at Week 24	-8.7 (6.64)	-6.3 (6.71)

5. Secondary Outcome Measure:

Measure Title	Change in Frequency of Headache Episodes
Measure Description	Mean change from baseline in frequency (number) of headache episodes during the 28 day period ending with Week 24. Headache episode defined as patient-reported headache with a start and stop time indicating that the pain lasted >= 4 continuous hours.
Time Frame	Baseline, Week 24
Safety Issue?	No

Analysis Population Description

Intent to Treat

Reporting Groups

	Description
Botulinum Toxin Type A	Two treatment sessions in the double-blind phase and three treatment sessions in the open-label extension phase. Total minimum dose is 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas with the total maximum dose of 195 U with 39 head/neck injections.
Placebo (Saline)	Two treatment sessions in the double-blind phase. Total minimum dose in 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas and the total maximum dose is 195 U with 39 head/ neck injections.

Measured Values

	Botulinum Toxin Type A	Placebo (Saline)
Number of Participants Analyzed	347	358
Change in Frequency of Headache Episodes [units: Headache Episodes] Mean (Standard Deviation)		

	Botulinum Toxin Type A	Placebo (Saline)
Baseline	12.0 (5.27)	12.7 (5.29)
Change from Baseline at Week 24	-5.3 (5.12)	-4.6 (4.84)

6. Secondary Outcome Measure:

Measure Title	Percentage of Patients With Severe HIT-6 Impact Category Scores
Measure Description	Percentage of patients with a severe (60-78) score on the Headache Impact Test (HIT-6) Questionnaire during the 28 day period, ending with Week 24. The HIT-6 consisted of 6 questions about headache and impact on the patient's health and well-being. Answers for each question ranged from 6=Never, 8=Rarely, 10=Sometimes, 11=Very Often, and 13=Always. The total scores ranged from 36-49 (Little or No Impact), 50-55 (Some Impact), 56-59 (Substantial Impact) and 60-78 (Severe Impact).
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

Intent to Treat

Reporting Groups

	Description
Botulinum Toxin Type A	Two treatment sessions in the double-blind phase and three treatment sessions in the open-label extension phase. Total minimum dose is 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas with the total maximum dose of 195 U with 39 head/neck injections.
Placebo (Saline)	Two treatment sessions in the double-blind phase. Total minimum dose in 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas and the total maximum dose is 195 U with 39 head/ neck injections.

Measured Values

	Botulinum Toxin Type A	Placebo (Saline)
Number of Participants Analyzed	347	358
Percentage of Patients With Severe HIT-6 Impact Category Scores [units: Percentage of Patients]	66.3	76.5

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	For SAEs/AEs, the Total # Participants at Risk for the Botulinum toxin type A arm includes ALL patients in the safety population who received Botulinum toxin type A in the Double-Blind and Open-Label phases. The total # Participants at Risk for the Placebo arm includes ONLY Double-blind Phase patients in the safety population who received Placebo.

Reporting Groups

	Description
Botulinum Toxin Type A	Two treatment sessions in the double-blind phase and three treatment sessions in the open-label extension phase. Total minimum dose is 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas with the total maximum dose of 195 U with 39 head/neck injections.
Placebo (Saline)	Two treatment sessions in the double-blind phase. Total minimum dose in 155 U with 31 fixed-site, fixed dose injections across seven specific head/neck muscle areas and the total maximum dose is 195 U with 39 head/neck injections.

Serious Adverse Events

	Botulinum Toxin Type A	Placebo (Saline)
	Affected/At Risk (%)	Affected/At Risk (%)
Total	33/676 (4.88%)	8/358 (2.23%)
Blood and lymphatic system disorders		
Thrombocytopenia [A] †	0/676 (0%)	1/358 (0.28%)
Cardiac disorders		
Acute coronary syndrome [A] †	1/676 (0.15%)	0/358 (0%)
Acute myocardial infarction [A] †	1/676 (0.15%)	0/358 (0%)
Pericarditis [A] †	1/676 (0.15%)	0/358 (0%)
Tachycardia [A] †	1/676 (0.15%)	0/358 (0%)
Gastrointestinal disorders		
Colitis [A] †	1/676 (0.15%)	0/358 (0%)

	Botulinum Toxin Type A	Placebo (Saline)
	Affected/At Risk (%)	Affected/At Risk (%)
Colitis ischaemic [A] †	1/676 (0.15%)	0/358 (0%)
Gastric ulcer haemorrhage [A] †	1/676 (0.15%)	0/358 (0%)
General disorders		
Non-cardiac chest pain [A] †	1/676 (0.15%)	0/358 (0%)
Hepatobiliary disorders		
Cholelithiasis [A] †	0/676 (0%)	1/358 (0.28%)
Infections and infestations		
Gastroenteritis [A] †	0/676 (0%)	1/358 (0.28%)
Kidney infection [A] †	1/676 (0.15%)	0/358 (0%)
Pharyngitis streptococcal [A] †	0/676 (0%)	1/358 (0.28%)
Pneumonia [A] †	3/676 (0.44%)	1/358 (0.28%)
Sepsis [A] †	0/676 (0%)	1/358 (0.28%)
Upper respiratory tract infection bacterial [A] †	0/676 (0%)	1/358 (0.28%)
Metabolism and nutrition disorders		
Hypokalaemia [A] †	1/676 (0.15%)	0/358 (0%)
Musculoskeletal and connective tissue disorders		
Back pain [A] *	1/676 (0.15%)	0/358 (0%)
Intervertebral disc protrusion [A] †	0/676 (0%)	1/358 (0.28%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Benign colonic neoplasm [A] †	1/676 (0.15%)	0/358 (0%)
Brain neoplasm malignant [A] †	1/676 (0.15%)	0/358 (0%)
Breast cancer [A] †	3/676 (0.44%)	0/358 (0%)
Malignant melanoma [A] †	1/676 (0.15%)	0/358 (0%)

	Botulinum Toxin Type A	Placebo (Saline)
	Affected/At Risk (%)	Affected/At Risk (%)
Malignant melanoma in situ [A] †	1/676 (0.15%)	0/358 (0%)
Papillary thyroid cancer [A] †	0/676 (0%)	1/358 (0.28%)
Squamous cell carcinoma [A] †	1/676 (0.15%)	0/358 (0%)
Uterine leiomyoma [A] †	2/676 (0.3%)	0/358 (0%)
Nervous system disorders		
Convulsion [A] *	1/676 (0.15%)	0/358 (0%)
Migraine [A] *	4/676 (0.59%)	1/358 (0.28%)
Pregnancy, puerperium and perinatal conditions		
Abortion spontaneous [A] †	1/676 (0.15%)	0/358 (0%)
Psychiatric disorders		
Conversion disorder [A] †	1/676 (0.15%)	0/358 (0%)
Depression [A] †	2/676 (0.3%)	0/358 (0%)
Stress [A] *	1/676 (0.15%)	0/358 (0%)
Renal and urinary disorders		
Calculus ureteric [A] †	1/676 (0.15%)	0/358 (0%)
Reproductive system and breast disorders		
Endometriosis [A] †	0/676 (0%)	1/358 (0.28%)
Respiratory, thoracic and mediastinal disorders		
Hypoxia [A] †	1/676 (0.15%)	0/358 (0%)
Pulmonary sarcoidosis [A] †	0/676 (0%)	1/358 (0.28%)
Sleep apnoea syndrome [A] †	1/676 (0.15%)	0/358 (0%)
Vascular disorders		
Hypertensive crisis [A] †	1/676 (0.15%)	0/358 (0%)

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (11.0)

Other Adverse Events

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

	Botulinum Toxin Type A	Placebo (Saline)
	Affected/At Risk (%)	Affected/At Risk (%)
Total	195/676 (28.85%)	34/358 (9.5%)
Infections and infestations		
Nasopharyngitis [A] †	47/676 (6.95%)	14/358 (3.91%)
Sinusitis [A] †	40/676 (5.92%)	10/358 (2.79%)
Musculoskeletal and connective tissue disorders		
Muscular weakness [A] *	47/676 (6.95%)	2/358 (0.56%)
Neck pain [A] *	61/676 (9.02%)	8/358 (2.23%)

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (11.0)

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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