ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 07/15/2014

ClinicalTrials.gov ID: NCT01518257

Study Identification

Unique Protocol ID:	191622-102
Brief Title:	Safety and Efficacy Study of Botulinum Toxin Type A as Treatment for Osteoarthritis Knee Pain
Official Title:	
Secondary IDs:	

Study Status

Record Verification:	July 2014
Overall Status:	Completed
Study Start:	January 2012
Primary Completion:	January 2013 [Actual]
Study Completion:	January 2013 [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: 12/09/2011 Board Name: Den Videnskabsetiske Komité Board Affiliation: Region Nordjylland Phone: 96 35 10 41 Email: vek@rn.dk
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	Denmark: Danish Medicines Agency

Study Description

Brief Summary:	This study will evaluate the efficacy and safety of a single intra-articular (IA) injection of botulinum toxin Type A compared with placebo as treatment for osteoarthritis (OA) knee pain.
Detailed Description:	

Conditions

Conditions:	Osteoarthritis
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 1/Phase 2
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Double Blind (Subject, Investigator)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	121 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: botulinum toxin Type A A single 200U (2 mL) dose of botulinum toxin Type A injected into the intra-articular space of the study knee on Day 1.	Biological/Vaccine: botulinum toxin Type A A single 200U (2 mL) dose of botulinum toxin Type A injected into the intra-articular space of the study knee on Day 1. Other Names: • BOTOX®
Placebo Comparator: Placebo A single 2 mL dose of Normal Saline (placebo) injected into the intra-articular space of the study knee on Day 1.	Drug: Normal Saline A single 2 mL dose of Normal Saline (placebo) injected into the intra-articular space of the study knee on Day 1.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 40 Years

Maximum Age: 75 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Painful osteoarthritis in the study knee
- Able to walk without assistive walking devices, able to perform usual daily activities, and agree to maintain similar activity level throughout the study

Exclusion Criteria:

- Chronic pain conditions other than knee osteoarthritis
- Presence of bursitis, meniscus tear, ligament tear, or significant injury to the study knee within 1 year
- Surgery to the study knee within 24 weeks
- Treatment with hyaluronic acid in the study knee within 24 weeks
- Treatment with corticosteroids in the study knee within 12 weeks
- Diagnosis of myasthenia gravis, Eaton-Lambert syndrome, or amyotrophic lateral sclerosis
- Previous treatment with botulinum toxin of any serotype for any reason

Contacts/Locations

Study Officials: Medical Director
Study Director
Allergan, Inc

Locations: Denmark
Aalborg, Denmark

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Botulinum Toxin Type A	A single 200U (2 mL) dose of botulinum toxin Type A injected into the intra-articular space of the study knee on Day 1.
Placebo	A single 2 mL dose of Normal Saline (placebo) injected into the intra-articular space of the study knee on Day 1.

Overall Study

	Botulinum Toxin Type A	Placebo
Started	61	60
Completed	59	60
Not Completed	2	0
Lost to Follow-up	1	0
Other Miscellaneous Reason	1	0

Baseline Characteristics

Reporting Groups

	Description
Botulinum Toxin Type A	A single 200U (2 mL) dose of botulinum toxin Type A injected into the intra-articular space of the study knee on Day 1.
Placebo	A single 2 mL dose of Normal Saline (placebo) injected into the intra-articular space of the study knee on Day 1.

Baseline Measures

	Botulinum Toxin Type A	Placebo	Total
Number of Participants	61	60	121
Age, Customized [units: Participants]			
40 to 64 Years	30	31	61
≥ 65 Years	31	29	60
Gender, Male/Female [units: Participants]			
Female	32	30	62
Male	29	30	59

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change From Baseline in the Average Daily Worst Pain Intensity Score at Week 4
Measure Description	The patient rated their daily worst pain intensity in the study knee using an 11-point scale where: 0=no pain to 10=worst pain possible. The daily scores over the previous 14-day period were averaged. A negative change from Baseline indicated improvement.
Time Frame	Baseline, Week 4
Safety Issue?	No

Analysis Population Description

Safety population included all treated participants based on the actual treatment received.

Reporting Groups

	Description
Botulinum Toxin Type A	A single 200U (2 mL) dose of botulinum toxin Type A injected into the intra-articular space of the study knee on Day 1.
Placebo	A single 2 mL dose of Normal Saline (placebo) injected into the intra-articular space of the study knee on Day 1.

Measured Values

	Botulinum Toxin Type A	Placebo
Number of Participants Analyzed	61	60
Change From Baseline in the Average Daily Worst Pain Intensity Score at Week 4 [units: Score on a scale] Mean (Standard Deviation)		
Baseline	6.4 (1.09)	6.5 (1.28)
Change from Baseline at Week 4	-1.8 (1.66)	-1.8 (1.87)

2. Primary Outcome Measure:

Measure Title	Change From Baseline in the Average Daily Worst Pain Intensity Score at Week 8
Measure Description	The patient rated their daily worst pain intensity in the study knee using an 11-point scale where: 0=no pain to 10=worst pain possible. The daily scores over the previous 14-day period were averaged. A negative change from Baseline indicated improvement.
Time Frame	Baseline, Week 8
Safety Issue?	No

Analysis Population Description

Safety population included all treated participants based on the actual treatment received.

Reporting Groups

	Description
Botulinum Toxin Type A	A single 200U (2 mL) dose of botulinum toxin Type A injected into the intra-articular space of the study knee on Day 1.
Placebo	A single 2 mL dose of Normal Saline (placebo) injected into the intra-articular space of the study knee on Day 1.

Measured Values

	Botulinum Toxin Type A	Placebo
Number of Participants Analyzed	61	60
Change From Baseline in the Average Daily Worst Pain Intensity Score at Week 8 [units: Score on a scale] Mean (Standard Deviation)		
Baseline	6.4 (1.09)	6.5 (1.28)
Change from Baseline at Week 8	-2.2 (1.96)	-2.3 (2.15)

3. Primary Outcome Measure:

Measure Title	Change From Baseline in the Average Daily Worst Pain Intensity Score at Week 12
Measure Description	The patient rated their daily worst pain intensity in the study knee using an 11-point scale where: 0=no pain to 10=worst pain possible. The daily scores over the previous 14-day period were averaged. A negative change from Baseline indicated improvement.
Time Frame	Baseline, Week 12
Safety Issue?	No

Analysis Population Description

Safety population included all treated participants based on the actual treatment received.

Reporting Groups

	Description
Botulinum Toxin Type A	A single 200U (2 mL) dose of botulinum toxin Type A injected into the intra-articular space of the study knee on Day 1.
Placebo	A single 2 mL dose of Normal Saline (placebo) injected into the intra-articular space of the study knee on Day 1.

Measured Values

	Botulinum Toxin Type A	Placebo
Number of Participants Analyzed	61	60
Change From Baseline in the Average Daily Worst Pain Intensity Score at Week 12 [units: Score on a scale]		

	Botulinum Toxin Type A	Placebo
Mean (Standard Deviation)		
Baseline	6.4 (1.09)	6.5 (1.28)
Change from Baseline at Week 12	-2.2 (1.97)	-2.5 (2.24)

4. Secondary Outcome Measure:

Measure Title	Change From Baseline in Western Ontario and McMaster Universities Arthritis (WOMAC™) Total Index Score
Measure Description	The WOMAC Total Index Score consisted of 24 components rated on a scale of 0 to 10. The Total Index Score included the WOMAC Pain Score (5 questions about pain where: 0=no pain to 10=extreme pain), the WOMAC Physical Function score (17 questions about the difficulty of daily activities where: 0=no difficulty to 10=extreme difficulty) and the WOMAC Stiffness Score (2 questions about stiffness where: 0=no stiffness to 10=extreme stiffness) for a total possible Index Score of 0 (best) to 240 (worst). A negative change from Baseline indicated improvement.
Time Frame	Baseline, Week 8
Safety Issue?	No

Analysis Population Description

Safety population included all treated participants based on the actual treatment received.

Reporting Groups

	Description
Botulinum Toxin Type A	A single 200U (2 mL) dose of botulinum toxin Type A injected into the intra-articular space of the study knee on Day 1.
Placebo	A single 2 mL dose of Normal Saline (placebo) injected into the intra-articular space of the study knee on Day 1.

Measured Values

	Botulinum Toxin Type A	Placebo
Number of Participants Analyzed	61	60
Change From Baseline in Western Ontario and McMaster Universities Arthritis (WOMAC™) Total Index Score [units: Score on a scale] Mean (Standard Deviation)		
Baseline	104.5 (36.53)	107.6 (37.44)

	Botulinum Toxin Type A	Placebo
Change from Baseline at Week 8 (n=59,59)	-46.5 (35.21)	-43.8 (47.25)

5. Secondary Outcome Measure:

Measure Title	Change From Baseline in WOMAC Pain Score
Measure Description	The WOMAC Pain Score included 5 questions about pain where: 0=no pain to 10=extreme pain for a total possible score of 0 (best) to 50 (worst). A negative change from Baseline indicated improvement.
Time Frame	Baseline, Week 8
Safety Issue?	No

Analysis Population Description

Safety population included all treated participants based on the actual treatment received.

Reporting Groups

	Description
Botulinum Toxin Type A	A single 200U (2 mL) dose of botulinum toxin Type A injected into the intra-articular space of the study knee on Day 1.
Placebo	A single 2 mL dose of Normal Saline (placebo) injected into the intra-articular space of the study knee on Day 1.

Measured Values

	Botulinum Toxin Type A	Placebo
Number of Participants Analyzed	61	60
Change From Baseline in WOMAC Pain Score [units: Score on a scale] Mean (Standard Deviation)		
Baseline	23.9 (6.76)	24.3 (7.01)
Change from Baseline at Week 8 (n=59,59)	-10.7 (7.27)	-11.0 (9.75)

6. Secondary Outcome Measure:

Measure Title	Change From Baseline in WOMAC Physical Function Score

Measure Description	The WOMAC Physical Function Score included 17 questions about the difficulty of daily activities where: 0=no difficulty to 10=extreme difficulty for a total possible score of 0 (best) to 170 (worst). A negative change from Baseline indicated improvement.
Time Frame	Baseline, Week 8
Safety Issue?	No

Analysis Population Description

Safety population included all treated participants based on the actual treatment received.

Reporting Groups

	Description
Botulinum Toxin Type A	A single 200U (2 mL) dose of botulinum toxin Type A injected into the intra-articular space of the study knee on Day 1.
Placebo	A single 2 mL dose of Normal Saline (placebo) injected into the intra-articular space of the study knee on Day 1.

Measured Values

	Botulinum Toxin Type A	Placebo
Number of Participants Analyzed	61	60
Change From Baseline in WOMAC Physical Function Score [units: Score on a scale] Mean (Standard Deviation)		
Baseline	71.0 (28.43)	73.3 (29.77)
Change from Baseline at Week 8 (n=59,59)	-31.7 (26.41)	-28.6 (35.26)

7. Secondary Outcome Measure:

Measure Title	Patient Global Impression of Change Score
Measure Description	The participants rated the change in their health status since enrollment using a 7-point scale where: +3=very much improved, +2=much improved, +1=minimally improved, 0=no change, -1=minimally worse, -2=much worse and -3=very much worse. Negative scores indicated worsening and positive scores indicated improvement.
Time Frame	Week 8
Safety Issue?	No

Analysis Population Description

Participants from the Safety population (all treated participants based on the actual treatment received) with data available for this outcome measure.

Reporting Groups

	Description
Botulinum Toxin Type A	A single 200U (2 mL) dose of botulinum toxin Type A injected into the intra-articular space of the study knee on Day 1.
Placebo	A single 2 mL dose of Normal Saline (placebo) injected into the intra-articular space of the study knee on Day 1.

Measured Values

	Botulinum Toxin Type A	Placebo
Number of Participants Analyzed	59	59
Patient Global Impression of Change Score [units: Score on a scale] Mean (Standard Deviation)	1.3 (1.28)	1.0 (1.38)

8. Post-Hoc Outcome Measure:

Measure Title	Change From Baseline in the Average Daily Worst Pain Intensity Score in the Nociceptive Pain Group
Measure Description	The patient rated their daily worst pain intensity in the study knee using an 11-point scale where: 0=no pain to 10=worst pain possible. The daily scores over the previous 14-day period were averaged. A negative change from Baseline indicated improvement.
Time Frame	Baseline, Weeks 4, 8 and 12
Safety Issue?	No

Analysis Population Description

Participants from the Safety population (all treated participants based on the actual treatment received) in a subgroup of patients with nociceptive pain (pain that is caused by nerves that react to injury or damage) at Baseline.

Reporting Groups

	Description
Botulinum Toxin Type A	A single 200U (2 mL) dose of botulinum toxin Type A injected into the intra-articular space of the study knee on Day 1.
Placebo	A single 2 mL dose of Normal Saline (placebo) injected into the intra-articular space of the study knee on Day 1.

Measured Values

	Botulinum Toxin Type A	Placebo
Number of Participants Analyzed	36	32
Change From Baseline in the Average Daily Worst Pain Intensity Score in the Nociceptive Pain Group [units: Score on a scale] Mean (Standard Deviation)		
Baseline	6.4 (1.01)	6.4 (1.35)
Change from Baseline at Week 4	-1.9 (1.56)	-1.5 (1.58)
Change from Baseline at Week 8	-2.6 (2.01)	-1.8 (2.01)
Change from Baseline at Week 12	-2.6 (1.79)	-2.0 (2.27)

9. Post-Hoc Outcome Measure:

Measure Title	Change From Baseline in WOMAC Pain Score in the Nociceptive Pain Group
Measure Description	The WOMAC Pain Score included 5 questions about pain where: 0=no pain to 10=extreme pain for a total possible score of 0 (best) to 50 (worst). A negative change from Baseline indicated improvement.
Time Frame	Baseline, Week 8
Safety Issue?	No

Analysis Population Description

Participants from the Safety population (all treated participants based on the actual treatment received) in a subgroup of patients with nociceptive pain (pain that is caused by nerves that react to injury or damage) at Baseline.

Reporting Groups

	Description
Botulinum Toxin Type A	A single 200U (2 mL) dose of botulinum toxin Type A injected into the intra-articular space of the study knee on Day 1.
Placebo	A single 2 mL dose of Normal Saline (placebo) injected into the intra-articular space of the study knee on Day 1.

Measured Values

	Botulinum Toxin Type A	Placebo
Number of Participants Analyzed	36	32

	Botulinum Toxin Type A	Placebo
Change From Baseline in WOMAC Pain Score in the Nociceptive Pain Group [units: Score on a scale] Mean (Standard Deviation)		
Baseline	22.7 (5.95)	22.9 (6.98)
Change from Baseline at Week 8 (n=35,31)	-11.0 (7.09)	-7.5 (9.00)

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
Botulinum Toxin Type A	A single 200U (2 mL) dose of botulinum toxin Type A injected into the intra-articular space of the study knee on Day 1.
Placebo	A single 2 mL dose of Normal Saline (placebo) injected into the intra-articular space of the study knee on Day 1.

Serious Adverse Events

	Botulinum Toxin Type A	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Total	1/61 (1.64%)	0/60 (0%)
Nervous system disorders		
Cerebrovascular accident [A] †	1/61 (1.64%)	0/60 (0%)

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

Other Adverse Events

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

	Botulinum Toxin Type A	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Total	7/61 (11.48%)	14/60 (23.33%)
Infections and infestations		
Nasopharyngitis [A] †	1/61 (1.64%)	5/60 (8.33%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] *	3/61 (4.92%)	4/60 (6.67%)
Osteoarthritis [A] †	3/61 (4.92%)	5/60 (8.33%)

† Indicates events were collected by systematic assessment.

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA (15.1)

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 30 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,
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