ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 09/27/2013

ClinicalTrials.gov ID: NCT01189747

Study Identification

Unique Protocol ID:	191622-098
Brief Title:	Safety and Efficacy Study of Botulinum Toxin Type A for the Treatment of Crow's Feet Lines
Official Title:	
Secondary IDs:	

Study Status

Record Verification:	September 2013
Overall Status:	Completed
Study Start:	October 2010
Primary Completion:	April 2011 [Actual]
Study Completion:	July 2011 [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: BB-IND 8142 Serial Number: Has Expanded Access? No
Review Board:	Approval Status: Board Name: Board Affiliation: Phone: Email:
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	This study will evaluate the safety and efficacy of botulinum toxin Type A compared to placebo for the treatment of Crow's Feet Lines (Lateral Canthal Rhytides).
Detailed Description:	

Conditions

Conditions:	Lateral Canthus Rhytides Crow's Feet Lines
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: 446 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: onabotulinumtoxinA 24 units onabotulinumtoxinA (botulinum toxin Type A) total dose injected into bilateral Crow's Feet Line areas on Day 1.	Biological/Vaccine: onabotulinumtoxinA 24 units onabotulinumtoxinA (botulinum toxin Type A) total dose injected into bilateral Crow's Feet Line areas on Day 1 Other Names: • BOTOX® • BOTOX® Cosmetic • onabotulinumtoxinA
Placebo Comparator: placebo (normal saline) normal saline injected into bilateral Crow's Feet Line areas on Day 1.	Drug: normal saline Injected into bilateral Crow's Feet Line areas on Day 1

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Moderate to severe Crow's Feet Lines
- Have adequate vision without the use of eyeglasses to assess facial wrinkles in a mirror (contact lenses OK)

Exclusion Criteria:

- Current or previous botulinum toxin treatment of any serotype
- Facial laser or light treatment, microdermabrasion or superficial peels within 3 months
- Oral retinoid therapy within 1 year
- Prior facial cosmetic surgery (eg, periorbital surgery, facial lift, brow lift, eye lift, or eyebrow surgery)
- Diagnosis of myasthenia gravis, Eaton-Lambert syndrome, amyotrophic lateral sclerosis

Contacts/Locations

Study Officials: Medical Director
Study Director
Allergan, Inc.

Locations: United States, California
Newport Beach, California, United States

Canada, British Columbia
Vancouver, British Columbia, Canada

Belgium
Aalst, Belgium

United Kingdom
London, England, United Kingdom

Sutton Coldfield, England, United Kingdom

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
onabotulinumtoxinA	24 units onabotulinumtoxinA (botulinum toxin Type A) total dose injected into bilateral Crow's Feet Line areas on Day 1.
Placebo (Normal Saline)	normal saline injected into bilateral Crow's Feet Line areas on Day 1.

Overall Study

	onabotulinumtoxinA	Placebo (Normal Saline)
Started	222	224
Completed	210	206
Not Completed	12	18

Baseline Characteristics

Reporting Groups

	Description
onabotulinumtoxinA	24 units onabotulinumtoxinA (botulinum toxin Type A) total dose injected into bilateral Crow's Feet Line areas on Day 1.
Placebo (Normal Saline)	normal saline injected into bilateral Crow's Feet Line areas on Day 1.

Baseline Measures

	onabotulinumtoxinA	Placebo (Normal Saline)	Total
Number of Participants	222	224	446
Age, Customized [units: Participants]			
< 45 Years	82	101	183
45 to 65 Years	135	118	253
> 65 Years	5	5	10
Gender, Male/Female [units: Participants]			
Female	193	192	385
Male	29	32	61
CFL Severity as Assessed by Investigator [1] [units: Participants]			
Moderate	109	112	221
Severe	112	111	223
No data available	1	1	2

[1] Crow’s Feet Line (CFL) severity as assessed at Baseline by the investigator using the 4-point Facial Wrinkle Scale (FWS) at maximum smile.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Responders Based on Composite Facial Wrinkle Scale Assessment of Crow's Feet Line Severity at Maximum Smile
Measure Description	The composite facial wrinkle scale assessment is based on both the Investigator and Subject Facial Wrinkle scales at Day 30. The Investigator assessed the severity of the patient's Crow's Feet Lines at maximum smile using the 4-point Facial Wrinkle Scale: 0=none, 1=mild, 2=moderate or 3=severe and the patient assessed the severity of their Crow's Feet Lines at maximum smile using the same 4-point Facial Wrinkle Scale. A responder is defined as a participant with a ≥ 2-grade improvement from Baseline.
Time Frame	Baseline, Day 30
Safety Issue?	No

Analysis Population Description

Intent-to-treat population included all randomized participants. Participants with missing values are considered non-responders.

Reporting Groups

	Description
onabotulinumtoxinA	24 units onabotulinumtoxinA (botulinum toxin Type A) total dose injected into bilateral Crow's Feet Line areas on Day 1.
Placebo (Normal Saline)	normal saline injected into bilateral Crow's Feet Line areas on Day 1.

Measured Values

	onabotulinumtoxinA	Placebo (Normal Saline)
Number of Participants Analyzed	222	223
Percentage of Responders Based on Composite Facial Wrinkle Scale Assessment of Crow's Feet Line Severity at Maximum Smile [units: Percentage of participants]	25.7	1.3

2. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving a Grade of None or Mild at Maximum Smile Based on the Investigator's Facial Wrinkle Scale Assessment of the Severity of Crow's Feet Lines
Measure Description	The Investigator assessed the severity of the patient's Crow's Feet lines at maximum smile using the 4-point Facial Wrinkle Scale: 0=none, 1=mild, 2=moderate or 3=severe. The percentage of participants with a score of none or mild at Day 30 is reported.
Time Frame	Day 30
Safety Issue?	No

Analysis Population Description

Intent-to-treat population included all randomized participants.

Reporting Groups

	Description
onabotulinumtoxinA	24 units onabotulinumtoxinA (botulinum toxin Type A) total dose injected into bilateral Crow's Feet Line areas on Day 1.
Placebo (Normal Saline)	normal saline injected into bilateral Crow's Feet Line areas on Day 1.

Measured Values

	onabotulinumtoxinA	Placebo (Normal Saline)
Number of Participants Analyzed	222	223
Percentage of Participants Achieving a Grade of None or Mild at Maximum Smile Based on the Investigator's Facial Wrinkle Scale Assessment of the Severity of Crow's Feet Lines [units: Percentage of participants]	66.7	6.7

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a ≥ 1-Grade Improvement From Baseline by Investigator Facial Wrinkle Scale Assessment of the Severity of Crow's Feet Lines at Maximum Smile
Measure Description	The Investigator assessed the severity of the patient's Crow's Feet Lines at maximum smile using the 4-point Facial Wrinkle Scale: 0=none, 1=mild, 2=moderate or 3=severe. The percentage of participants with a ≥ 1-grade improvement from Baseline at Day 30 is reported.
Time Frame	Baseline, Day 30

Safety Issue?	No

Analysis Population Description

Intent-to-treat population included all randomized participants.

Reporting Groups

	Description
onabotulinumtoxinA	24 units onabotulinumtoxinA (botulinum toxin Type A) total dose injected into bilateral Crow's Feet Line areas on Day 1.
Placebo (Normal Saline)	normal saline injected into bilateral Crow's Feet Line areas on Day 1.

Measured Values

	onabotulinumtoxinA	Placebo (Normal Saline)
Number of Participants Analyzed	222	223
Percentage of Participants With a ≥ 1-Grade Improvement From Baseline by Investigator Facial Wrinkle Scale Assessment of the Severity of Crow's Feet Lines at Maximum Smile [units: Percentage of participants]	87.4	12.1

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a ≥ 1-Grade Improvement From Baseline by Investigator Facial Wrinkle Scale Assessment of the Severity of Crow's Feet Lines at Rest
Measure Description	The Investigator assessed the severity of the patient's Crow's Feet Lines at rest using the 4-point Facial Wrinkle Scale: 0=none, 1=mild, 2=moderate or 3=severe. The percentage of participants with a ≥ 1-grade improvement from Baseline at Day 30 is reported.
Time Frame	Baseline, Day 30
Safety Issue?	No

Analysis Population Description

Intent-to-treat participants included all randomized participants. Only participants who were rated at least mild at Baseline are included in the analyses.

Reporting Groups

	Description
onabotulinumtoxinA	24 units onabotulinumtoxinA (botulinum toxin Type A) total dose injected into bilateral Crow's Feet Line areas on Day 1.
Placebo (Normal Saline)	normal saline injected into bilateral Crow's Feet Line areas on Day 1.

Measured Values

	onabotulinumtoxinA	Placebo (Normal Saline)
Number of Participants Analyzed	214	215
Percentage of Participants With a ≥ 1-Grade Improvement From Baseline by Investigator Facial Wrinkle Scale Assessment of the Severity of Crow's Feet Lines at Rest [units: Percentage of participants]	67.3	13.5

5. Secondary Outcome Measure:

Measure Title	Subject Global Assessment of Change in Crow's Feet Lines (SGA-CFL) Score
Measure Description	Patients rated the change in their Crow's Feet Lines using the SGA-CFL 7-point scale: 1=very much improved, 2=much improved, 3=minimally improved, 4=no change, 5=minimally worse, 6=much worse or 7=very much worse at Day 30. Lower scores indicate improvement.
Time Frame	Day 30
Safety Issue?	No

Analysis Population Description

Intent-to-treat population included all randomized participants.

Reporting Groups

	Description
onabotulinumtoxinA	24 units onabotulinumtoxinA (botulinum toxin Type A) total dose injected into bilateral Crow's Feet Line areas on Day 1.
Placebo (Normal Saline)	normal saline injected into bilateral Crow's Feet Line areas on Day 1.

Measured Values

	onabotulinumtoxinA	Placebo (Normal Saline)
Number of Participants Analyzed	222	223
Subject Global Assessment of Change in Crow's Feet Lines (SGA-CFL) Score [units: Score on a scale] Mean (Standard Deviation)	2.2 (1.06)	3.8 (0.67)

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants Who Judged Themselves in a Younger Self-Perception of Age Category Than at Baseline
Measure Description	Participants were considered to judge themselves younger if the category change was from “look my current age” at Baseline to “look younger” at Day 30 or from “look older” at Baseline to “look my current age/younger” at Day 30.
Time Frame	Baseline, Day 30
Safety Issue?	No

Analysis Population Description

Intent-to-treat population included all randomized participants. Only those participants who rated themselves as "look my current age" or "look older" at Baseline are included in the analyses.

Reporting Groups

	Description
onabotulinumtoxinA	24 units onabotulinumtoxinA (botulinum toxin Type A) total dose injected into bilateral Crow's Feet Line areas on Day 1.
Placebo (Normal Saline)	normal saline injected into bilateral Crow's Feet Line areas on Day 1.

Measured Values

	onabotulinumtoxinA	Placebo (Normal Saline)
Number of Participants Analyzed	183	185
Percentage of Participants Who Judged Themselves in a Younger Self-Perception of Age Category Than at Baseline [units: Percentage of participants]	45.4	10.8

7. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a ≥ 2-point Improvement From Baseline for Facial Line Outcomes Questionnaire (FLO-11) Item 2 at Day 30
Measure Description	The percentage of FLO-11 Item #2 responders, defined as participants with a ≥ 2-point improvement in FLO-11 score from Baseline for FLO-11 Question #2: “When I look in the mirror, my facial lines make me look older than I want to look.” The FLO-11 questionnaire is comprised of 11 items that assess the subject's perceptions about specific aspects of their facial lines for the previous 7 days. Each question is scored on an 11-point scale (0=not at all, 5=somewhat, 10=very much).
Time Frame	Baseline, Day 30
Safety Issue?	No

Analysis Population Description

Intent-to-treat population consisted of all randomized participants. Only subjects with Baseline scores ≥ 2 were included.

Reporting Groups

	Description
onabotulinumtoxinA	24 units onabotulinumtoxinA (botulinum toxin Type A) total dose injected into bilateral Crow's Feet Line areas on Day 1.
Placebo (Normal Saline)	normal saline injected into bilateral Crow's Feet Line areas on Day 1.

Measured Values

	onabotulinumtoxinA	Placebo (Normal Saline)
Number of Participants Analyzed	213	211
Percentage of Participants With a ≥ 2-point Improvement From Baseline for Facial Line Outcomes Questionnaire (FLO-11) Item 2 at Day 30 [units: Percentage of participants]	70.0	28.4

8. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a ≥ 2-point Improvement From Baseline for Facial Line Outcomes Questionnaire (FLO-11) Item 5 at Day 30
Measure Description	The percentage of FLO-11 Item #5 responders, defined as participants with a ≥ 2-point improvement in FLO-11 score from Baseline for FLO-11 Question #5: “My facial lines make me look less attractive than I want to look.” The FLO-11 questionnaire is comprised of 11 items that assess the subject's perceptions about specific aspects of their facial lines for the previous 7 days. Each question is scored on an 11-point scale (0=not at all, 5=somewhat, 10=very much).

Time Frame	Baseline, Day 30
Safety Issue?	No

Analysis Population Description

Intent-to-treat population consisted of all randomized participants. Only subjects with Baseline scores ≥ 2 were included.

Reporting Groups

	Description
onabotulinumtoxinA	24 units onabotulinumtoxinA (botulinum toxin Type A) total dose injected into bilateral Crow's Feet Line areas on Day 1.
Placebo (Normal Saline)	normal saline injected into bilateral Crow's Feet Line areas on Day 1.

Measured Values

	onabotulinumtoxinA	Placebo (Normal Saline)
Number of Participants Analyzed	202	202
Percentage of Participants With a ≥ 2-point Improvement From Baseline for Facial Line Outcomes Questionnaire (FLO-11) Item 5 at Day 30 [units: Percentage of participants]	66.8	22.8

9. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a ≥ 3-point Improvement From Baseline for Facial Line Outcomes Questionnaire (FLO-11) Item 8 at Day 30
Measure Description	The percentage of FLO-11 Item #8 responders, defined as participants with a ≥ 3-point improvement in FLO-11 score from baseline for FLO-11 Question #8: “My facial lines make me look tired” The FLO-11 questionnaire is comprised of 11 items that assess the subject's perceptions about specific aspects of their facial lines for the previous 7 days. Each question is scored on an 11-point scale (0=not at all, 5=somewhat, 10=very much).
Time Frame	Baseline, Day 30
Safety Issue?	No

Analysis Population Description

Intent-to-treat population consisted of all randomized participants. Only subjects with Baseline scores ≥ 3 were included.

Reporting Groups

	Description
onabotulinumtoxinA	24 units onabotulinumtoxinA (botulinum toxin Type A) total dose injected into bilateral Crow's Feet Line areas on Day 1.
Placebo (Normal Saline)	normal saline injected into bilateral Crow's Feet Line areas on Day 1.

Measured Values

	onabotulinumtoxinA	Placebo (Normal Saline)
Number of Participants Analyzed	199	203
Percentage of Participants With a ≥ 3-point Improvement From Baseline for Facial Line Outcomes Questionnaire (FLO-11) Item 8 at Day 30 [units: Percentage of participants]	55.8	16.3

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	The safety population (all treated participants) was used to calculate the number of participants at risk for Serious Adverse Events and Adverse Events.

Reporting Groups

	Description
onabotulinumtoxinA	24 units onabotulinumtoxinA (botulinum toxin Type A) total dose injected into bilateral Crow's Feet Line areas on Day 1.
Placebo (Normal Saline)	normal saline injected into bilateral Crow's Feet Line areas on Day 1.

Serious Adverse Events

	onabotulinumtoxinA	Placebo (Normal Saline)
	Affected/At Risk (%)	Affected/At Risk (%)
Total	6/220 (2.73%)	3/224 (1.34%)
Cardiac disorders		

	onabotulinumtoxinA	Placebo (Normal Saline)
	Affected/At Risk (%)	Affected/At Risk (%)
Coronary artery disease [A] †	1/220 (0.45%)	0/224 (0%)
Myocardial infarction [A] †	1/220 (0.45%)	0/224 (0%)
Hepatobiliary disorders		
Cholangitis [A] †	1/220 (0.45%)	0/224 (0%)
Infections and infestations		
Bursitis infective [A] †	1/220 (0.45%)	0/224 (0%)
Musculoskeletal and connective tissue disorders		
Invertebral disc disorder [A] †	0/220 (0%)	1/224 (0.45%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Basal cell carcinoma [A] †	1/220 (0.45%)	0/224 (0%)
Breast cancer [A] †	1/220 (0.45%)	0/224 (0%)
Intraductal papilloma of breast [A] †	0/220 (0%)	1/224 (0.45%)
Pregnancy, puerperium and perinatal conditions		
Abortion [A] *	1/220 (0.45%)	0/224 (0%)
Vascular disorders		
Femoral artery occlusion [A] †	0/220 (0%)	1/224 (0.45%)

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA 14.0

Other Adverse Events

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

	onabotulinumtoxinA	Placebo (Normal Saline)
	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/220 (0%)	0/224 (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:

Name/Official Title: Therapeutic Area Head,
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