



Clinical trial results: An Exploratory Study of the Safety and Efficacy of BOTOX® for the Treatment of Premature Ejaculation

Summary

EudraCT number	2013-001650-94
Trial protocol	GB
Global end of trial date	15 August 2017

Results information

Result version number	v1 (current)
This version publication date	25 August 2018
First version publication date	25 August 2018

Trial information

Trial identification

Sponsor protocol code	191622-133
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01917006
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergan
Sponsor organisation address	2525 Dupont Dr, Irvine, United States, 92612
Public contact	Clinical Trials Registry Team, Allergan, 001 8772778566, IR-CTRegistration@Allergan.com
Scientific contact	Therapeutic Area Head, Allergan, 001 714-246-4500, IR-CTRegistration@Allergan.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 August 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	15 August 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary study objectives were to explore the safety and efficacy of a range of doses of OnabotulinumtoxinA for the treatment of premature ejaculation in male participants.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 August 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 17
Country: Number of subjects enrolled	United States: 42
Worldwide total number of subjects	59
EEA total number of subjects	17

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	59
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants received a single treatment of either placebo or OnabotulinumtoxinA (Doses 1, 2, 3, 4, 5, 6), delivered bilaterally to the bulbospongiosus muscle in randomized-treatment period. Participants who completed 12 weeks of randomized period were eligible to receive second injection with OnabotulinumtoxinA Dose 2 in Open-label Period.

Pre-assignment period milestones

Number of subjects started	59
Number of subjects completed	57

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Not Included in mITT Population: 2
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Period 1

Period 1 title	Randomized-treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive? Yes

Arm title OnabotulinumtoxinA Dose 1

Arm description:

OnabotulinumtoxinA Dose 1 injected into specified muscle per protocol on Day 1.

Arm type	Experimental
Investigational medicinal product name	BOTOX®
Investigational medicinal product code	
Other name	Botulinum Toxin Type A
Pharmaceutical forms	Powder for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received a single treatment of OnabotulinumtoxinA Dose 1 delivered bilaterally to the bulbospongiosus muscle (BSM).

Arm title OnabotulinumtoxinA Dose 2

Arm description:

OnabotulinumtoxinA Dose 2 injected into specified muscle per protocol on Day 1. Participants were eligible for another treatment after 12 weeks.

Arm type	Experimental
Investigational medicinal product name	BOTOX®
Investigational medicinal product code	
Other name	Botulinum Toxin Type A
Pharmaceutical forms	Powder for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received a single treatment of OnabotulinumtoxinA Dose 2 delivered bilaterally to the BSM.

Arm title	OnabotulinumtoxinA Dose 3
Arm description: OnabotulinumtoxinA Dose 3 injected into specified muscle per protocol on Day 1.	
Arm type	Experimental
Investigational medicinal product name	BOTOX®
Investigational medicinal product code	
Other name	Botulinum Toxin Type A
Pharmaceutical forms	Powder for injection
Routes of administration	Intramuscular use
Dosage and administration details: Participants received a single treatment of OnabotulinumtoxinA Dose 3 delivered bilaterally to the BSM.	
Arm title	OnabotulinumtoxinA Dose 4
Arm description: OnabotulinumtoxinA Dose 4 injected into specified muscle per protocol on Day 1.	
Arm type	Experimental
Investigational medicinal product name	BOTOX®
Investigational medicinal product code	
Other name	Botulinum Toxin Type A
Pharmaceutical forms	Powder for injection
Routes of administration	Intramuscular use
Dosage and administration details: Participants received a single treatment of OnabotulinumtoxinA Dose 4 U delivered bilaterally to the BSM.	
Arm title	OnabotulinumtoxinA Dose 5
Arm description: OnabotulinumtoxinA Dose 5 injected into specified muscle per protocol on Day 1.	
Arm type	Experimental
Investigational medicinal product name	BOTOX®
Investigational medicinal product code	
Other name	Botulinum Toxin Type A
Pharmaceutical forms	Powder for injection
Routes of administration	Intramuscular use
Dosage and administration details: Participants received a single treatment of OnabotulinumtoxinA Dose 5 delivered bilaterally to the BSM.	
Arm title	OnabotulinumtoxinA Dose 6
Arm description: OnabotulinumtoxinA Dose 6 injected into specified muscle per protocol on Day 1.	
Arm type	Experimental
Investigational medicinal product name	BOTOX®
Investigational medicinal product code	
Other name	Botulinum Toxin Type A
Pharmaceutical forms	Powder for injection
Routes of administration	Intramuscular use
Dosage and administration details: Participants received a single treatment of OnabotulinumtoxinA Dose 6 delivered bilaterally to the BSM.	
Arm title	Placebo
Arm description: Placebo (normal saline) injected into specified muscle per protocol on Day 1.	
Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received a single treatment of Placebo delivered bilaterally to the BSM.

Number of subjects in period 1 ^[1]	OnabotulinumtoxinA Dose 1	OnabotulinumtoxinA Dose 2	OnabotulinumtoxinA Dose 3
	Started	5	7
Completed	3	7	8
Not completed	2	0	0
Lost to follow-up	1	-	-
Other Miscellaneous Reasons	-	-	-
Protocol deviation	1	-	-

Number of subjects in period 1 ^[1]	OnabotulinumtoxinA Dose 4	OnabotulinumtoxinA Dose 5	OnabotulinumtoxinA Dose 6
	Started	7	8
Completed	7	8	7
Not completed	0	0	0
Lost to follow-up	-	-	-
Other Miscellaneous Reasons	-	-	-
Protocol deviation	-	-	-

Number of subjects in period 1 ^[1]	Placebo
	Started
Completed	14
Not completed	1
Lost to follow-up	-
Other Miscellaneous Reasons	1
Protocol deviation	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Baseline characteristics are based on the mITT population and excludes 2 participants.

Period 2

Period 2 title	Open-label Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Open-label Period: OnabotulinumtoxinA Dose 2
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Arm description:

Participants who completed 12 weeks of randomized period were eligible to receive a second injection with active drug in the Open-label Period.

Arm type	Experimental
Investigational medicinal product name	BOTOX®
Investigational medicinal product code	
Other name	Botulinum Toxin Type A
Pharmaceutical forms	Powder for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received a single treatment of OnabotulinumtoxinA Dose 2 delivered bilaterally to the BSM.

Number of subjects in period 2^[2]	Open-label Period: OnabotulinumtoxinA Dose 2
Started	8
Completed	6
Not completed	2
Adverse Events	1
Lost to follow-up	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Only 8 participants were enrolled in the Open-Label Period.

Baseline characteristics

Reporting groups

Reporting group title	OnabotulinumtoxinA Dose 1
Reporting group description: OnabotulinumtoxinA Dose 1 injected into specified muscle per protocol on Day 1.	
Reporting group title	OnabotulinumtoxinA Dose 2
Reporting group description: OnabotulinumtoxinA Dose 2 injected into specified muscle per protocol on Day 1. Participants were eligible for another treatment after 12 weeks.	
Reporting group title	OnabotulinumtoxinA Dose 3
Reporting group description: OnabotulinumtoxinA Dose 3 injected into specified muscle per protocol on Day 1.	
Reporting group title	OnabotulinumtoxinA Dose 4
Reporting group description: OnabotulinumtoxinA Dose 4 injected into specified muscle per protocol on Day 1.	
Reporting group title	OnabotulinumtoxinA Dose 5
Reporting group description: OnabotulinumtoxinA Dose 5 injected into specified muscle per protocol on Day 1.	
Reporting group title	OnabotulinumtoxinA Dose 6
Reporting group description: OnabotulinumtoxinA Dose 6 injected into specified muscle per protocol on Day 1.	
Reporting group title	Placebo
Reporting group description: Placebo (normal saline) injected into specified muscle per protocol on Day 1.	

Reporting group values	OnabotulinumtoxinA Dose 1	OnabotulinumtoxinA Dose 2	OnabotulinumtoxinA Dose 3
Number of subjects	5	7	8
Age categorical Units: Subjects			
Adults (18-64 years)	5	7	8
Age Continuous Units: years			
arithmetic mean	41.2	41.9	39.1
standard deviation	± 10.83	± 11.65	± 5.62
Sex: Female, Male Units: Subjects			
Female	0	0	0
Male	5	7	8
Race/Ethnicity, Customized Units: Subjects			
Caucasian	3	4	5
Black	1	2	1
Asian	0	1	0
Hispanic	1	0	0
Other	0	0	2

Reporting group values	OnabotulinumtoxinA Dose 4	OnabotulinumtoxinA Dose 5	OnabotulinumtoxinA Dose 6
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Number of subjects	7	8	7
Age categorical			
Units: Subjects			
Adults (18-64 years)	7	8	7
Age Continuous			
Units: years			
arithmetic mean	39.3	40.1	39.9
standard deviation	± 9.05	± 6.53	± 5.96
Sex: Female, Male			
Units: Subjects			
Female	0	0	0
Male	7	8	7
Race/Ethnicity, Customized			
Units: Subjects			
Caucasian	5	5	6
Black	1	1	0
Asian	1	1	0
Hispanic	0	1	1
Other	0	0	0

Reporting group values	Placebo	Total	
Number of subjects	15	57	
Age categorical			
Units: Subjects			
Adults (18-64 years)	15	57	
Age Continuous			
Units: years			
arithmetic mean	41.0	-	
standard deviation	± 6.08	-	
Sex: Female, Male			
Units: Subjects			
Female	0	0	
Male	15	57	
Race/Ethnicity, Customized			
Units: Subjects			
Caucasian	9	37	
Black	3	9	
Asian	1	4	
Hispanic	2	5	
Other	0	2	

End points

End points reporting groups

Reporting group title	OnabotulinumtoxinA Dose 1
Reporting group description:	OnabotulinumtoxinA Dose 1 injected into specified muscle per protocol on Day 1.
Reporting group title	OnabotulinumtoxinA Dose 2
Reporting group description:	OnabotulinumtoxinA Dose 2 injected into specified muscle per protocol on Day 1. Participants were eligible for another treatment after 12 weeks.
Reporting group title	OnabotulinumtoxinA Dose 3
Reporting group description:	OnabotulinumtoxinA Dose 3 injected into specified muscle per protocol on Day 1.
Reporting group title	OnabotulinumtoxinA Dose 4
Reporting group description:	OnabotulinumtoxinA Dose 4 injected into specified muscle per protocol on Day 1.
Reporting group title	OnabotulinumtoxinA Dose 5
Reporting group description:	OnabotulinumtoxinA Dose 5 injected into specified muscle per protocol on Day 1.
Reporting group title	OnabotulinumtoxinA Dose 6
Reporting group description:	OnabotulinumtoxinA Dose 6 injected into specified muscle per protocol on Day 1.
Reporting group title	Placebo
Reporting group description:	Placebo (normal saline) injected into specified muscle per protocol on Day 1.
Reporting group title	Open-label Period: OnabotulinumtoxinA Dose 2
Reporting group description:	Participants who completed 12 weeks of randomized period were eligible to receive a second injection with active drug in the Open-label Period.

Primary: Change from Baseline in Geometric Mean Intravaginal Ejaculatory Latency Time (IELT)

End point title	Change from Baseline in Geometric Mean Intravaginal Ejaculatory Latency Time (IELT)
End point description:	<p>IELT, the time from vaginal penetration to ejaculation, was measured by a stopwatch and was recorded in the sexual intercourse diary (SID). The Logarithm Value of the Geometric Mean of each individual participant's IELT recorded in the SID up to each time point was calculated. The mean and standard deviation (SD) of log-transformed geometric mean IELTs are then calculated for each treatment group. An Analysis of Covariance (ANCOVA) Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate was used for analyses. A positive change from Baseline indicates improvement.</p> <p>The modified intent-to-treat (mITT) population included all randomized participants who received study treatment and had post-baseline intravaginal ejaculatory latency time (IELT) data available based on the dose actually received by the participant. Here, "n" is the number of participants with available data at the given time-point.</p>
End point type	Primary
End point timeframe:	Baseline (Day 1) to Week 12

End point values	Onabotulinumt oxinA Dose 1	Onabotulinumt oxinA Dose 2	Onabotulinumt oxinA Dose 3	Onabotulinumt oxinA Dose 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	8	7
Units: seconds				
arithmetic mean (standard deviation)				
Baseline(n=5,6,8,7,8,7,15)	3.57 (± 0.283)	3.50 (± 0.631)	3.46 (± 0.371)	3.52 (± 0.531)
Change from Baseline to Week 12(n=5,6,8,7,8,7,15)	0.55 (± 1.037)	0.69 (± 1.426)	0.05 (± 0.856)	0.30 (± 0.472)

End point values	Onabotulinumt oxinA Dose 5	Onabotulinumt oxinA Dose 6	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	7	15	
Units: seconds				
arithmetic mean (standard deviation)				
Baseline(n=5,6,8,7,8,7,15)	3.53 (± 0.475)	3.54 (± 0.505)	3.46 (± 0.610)	
Change from Baseline to Week 12(n=5,6,8,7,8,7,15)	0.31 (± 0.525)	0.59 (± 0.719)	0.44 (± 0.615)	

Statistical analyses

Statistical analysis title	OnabotulinumtoxinA Dose 1 versus (vs) Placebo
Comparison groups	OnabotulinumtoxinA Dose 1 v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.393 ^[1]
Method	ANCOVA

Notes:

[1] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from analysis of covariance (ANCOVA) Model with treatment as fixed effect and baseline geometric mean IELT as covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 2 vs Placebo
Comparison groups	OnabotulinumtoxinA Dose 2 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.263 ^[2]
Method	ANCOVA

Notes:

[2] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 3 vs Placebo
Comparison groups	OnabotulinumtoxinA Dose 3 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.861 ^[3]
Method	ANCOVA

Notes:

[3] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 4 vs Placebo
Comparison groups	OnabotulinumtoxinA Dose 4 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.647 ^[4]
Method	ANCOVA

Notes:

[4] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 5 vs Placebo
Comparison groups	OnabotulinumtoxinA Dose 5 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.645 ^[5]
Method	ANCOVA

Notes:

[5] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 6 vs Placebo
Comparison groups	OnabotulinumtoxinA Dose 6 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.343 ^[6]
Method	ANCOVA

Notes:

[6] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Secondary: Change from Baseline in Average IELT

End point title	Change from Baseline in Average IELT
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End point description:

IELT, the time from vaginal penetration to ejaculation, was measured by a stopwatch and was recorded in the SID. The average of each individual participant's IELT recorded in the SID up to each time point was calculated. The mean and SD of average IELTs were then calculated for each treatment group. An ANCOVA Model with treatment as the fixed effect and baseline average mean IELT as the covariate was used for analyses. A positive change from Baseline indicates improvement.

The mITT population included all randomized participants who received study treatment and had post-baseline IELTS data available based on the dose actually received by the participants. Here "n" is the number of participants with available data at the given time-point.

End point type	Secondary
End point timeframe:	
Baseline (Day 1) to Weeks 2, 4, 6, 8, 10, and 12	

End point values	Onabotulinumt oxinA Dose 1	Onabotulinumt oxinA Dose 2	Onabotulinumt oxinA Dose 3	Onabotulinumt oxinA Dose 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	8	7
Units: seconds				
arithmetic mean (standard deviation)				
Baseline(n=5,6,8,7,8,7,15)	37.25 (± 10.518)	39.42 (± 21.504)	34.41 (± 10.194)	38.00 (± 16.008)
Change from Baseline to Week 2(n=5,6,8,7,8,7,14)	66.25 (± 101.132)	180.31 (± 317.657)	24.73 (± 59.725)	34.87 (± 74.842)
Change from Baseline to Week 4(n=5,6,8,7,8,7,14)	61.94 (± 100.446)	176.71 (± 367.665)	24.06 (± 59.472)	35.00 (± 73.475)
Change from Baseline to Week 6(n=5,6,8,7,8,7,14)	61.42 (± 100.446)	183.44 (± 374.404)	20.75 (± 55.850)	36.95 (± 71.996)
Change from Baseline to Week 8(n=5,6,8,7,8,7,14)	59.55 (± 100.896)	176.59 (± 349.777)	17.08 (± 44.158)	37.69 (± 71.873)
Change from Baseline to Week 10(n=5,6,8,7,8,7,15)	56.13 (± 101.447)	170.65 (± 331.039)	15.55 (± 39.149)	37.45 (± 71.782)
Change from Baseline to Week 12(n=5,6,8,7,8,7,15)	53.65 (± 102.527)	152.74 (± 295.219)	12.95 (± 30.930)	28.32 (± 48.965)

End point values	Onabotulinumt oxinA Dose 5	Onabotulinumt oxinA Dose 6	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	7	15	
Units: seconds				
arithmetic mean (standard deviation)				
Baseline(n=5,6,8,7,8,7,15)	40.88 (± 16.435)	38.75 (± 15.596)	37.92 (± 16.656)	
Change from Baseline to Week 2(n=5,6,8,7,8,7,14)	28.04 (± 31.298)	55.77 (± 65.549)	11.25 (± 23.985)	
Change from Baseline to Week 4(n=5,6,8,7,8,7,14)	28.46 (± 36.881)	64.97 (± 67.471)	29.30 (± 69.073)	
Change from Baseline to Week 6(n=5,6,8,7,8,7,14)	29.35 (± 39.334)	64.49 (± 66.546)	47.62 (± 89.847)	
Change from Baseline to Week 8(n=5,6,8,7,8,7,14)	29.48 (± 44.505)	65.19 (± 65.612)	65.57 (± 128.470)	
Change from Baseline to Week 10(n=5,6,8,7,8,7,15)	27.49 (± 45.365)	63.91 (± 67.725)	68.26 (± 146.330)	
Change from Baseline to Week 12(n=5,6,8,7,8,7,15)	27.51 (± 48.720)	66.01 (± 71.489)	68.49 (± 151.680)	

Statistical analyses

Statistical analysis title	OnabotulinumtoxinA Dose 1 vs Placebo at Week 2
Comparison groups	OnabotulinumtoxinA Dose 1 v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.184 ^[7]
Method	ANCOVA

Notes:

[7] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 2 vs Placebo at Week 2
Comparison groups	OnabotulinumtoxinA Dose 2 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 ^[8]
Method	ANCOVA

Notes:

[8] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 3 vs Placebo at Week 2
Comparison groups	OnabotulinumtoxinA Dose 3 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.404 ^[9]
Method	ANCOVA

Notes:

[9] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 4 vs Placebo at Week 2
Comparison groups	OnabotulinumtoxinA Dose 4 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.328 ^[10]
Method	ANCOVA

Notes:

[10] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 5 vs Placebo at Week 2
Comparison groups	OnabotulinumtoxinA Dose 5 v Placebo

Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.362 ^[11]
Method	ANCOVA

Notes:

[11] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 6 vs Placebo at Week 2
Comparison groups	OnabotulinumtoxinA Dose 6 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.203 ^[12]
Method	ANCOVA

Notes:

[12] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 1 vs Placebo at Week 4
Comparison groups	OnabotulinumtoxinA Dose 1 v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.322 ^[13]
Method	ANCOVA

Notes:

[13] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 2 vs Placebo at Week 4
Comparison groups	OnabotulinumtoxinA Dose 2 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015 ^[14]
Method	ANCOVA

Notes:

[14] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 3 vs Placebo at Week 4
Comparison groups	OnabotulinumtoxinA Dose 3 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.541 ^[15]
Method	ANCOVA

Notes:

[15] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 4 vs Placebo at Week 4
Comparison groups	OnabotulinumtoxinA Dose 4 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.459 ^[16]
Method	ANCOVA

Notes:

[16] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 5 vs Placebo at Week 4
Comparison groups	OnabotulinumtoxinA Dose 5 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.491 ^[17]
Method	ANCOVA

Notes:

[17] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 6 vs Placebo at Week 4
Comparison groups	OnabotulinumtoxinA Dose 6 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.281 ^[18]
Method	ANCOVA

Notes:

[18] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 1 vs Placebo at Week 6
Comparison groups	OnabotulinumtoxinA Dose 1 v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.424 ^[19]
Method	ANCOVA

Notes:

[19] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 2 vs Placebo at Week 6
Comparison groups	OnabotulinumtoxinA Dose 2 v Placebo

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.026 ^[20]
Method	ANCOVA

Notes:

[20] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 3 vs Placebo at Week 6
Comparison groups	OnabotulinumtoxinA Dose 3 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.67 ^[21]
Method	ANCOVA

Notes:

[21] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 4 vs Placebo at Week 6
Comparison groups	OnabotulinumtoxinA Dose 4 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.561 ^[22]
Method	ANCOVA

Notes:

[22] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 5 vs Placebo at Week 6
Comparison groups	OnabotulinumtoxinA Dose 5 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.604 ^[23]
Method	ANCOVA

Notes:

[23] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 6 vs Placebo at Week 6
Comparison groups	OnabotulinumtoxinA Dose 6 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.394 ^[24]
Method	ANCOVA

Notes:

[24] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 1 vs Placebo at Week 8
Comparison groups	OnabotulinumtoxinA Dose 1 v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.532 ^[25]
Method	ANCOVA

Notes:

[25] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 2 vs Placebo at Week 8
Comparison groups	OnabotulinumtoxinA Dose 2 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.058 ^[26]
Method	ANCOVA

Notes:

[26] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 3 vs Placebo at Week 8
Comparison groups	OnabotulinumtoxinA Dose 3 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.778 ^[27]
Method	ANCOVA

Notes:

[27] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 4 vs Placebo at Week 8
Comparison groups	OnabotulinumtoxinA Dose 4 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.662 ^[28]
Method	ANCOVA

Notes:

[28] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 5 vs Placebo at Week 8
Comparison groups	OnabotulinumtoxinA Dose 5 v Placebo

Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.712 ^[29]
Method	ANCOVA

Notes:

[29] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 6 vs Placebo at Week 8
Comparison groups	OnabotulinumtoxinA Dose 6 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.501 ^[30]
Method	ANCOVA

Notes:

[30] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 1 vs Placebo at Week 10
Comparison groups	OnabotulinumtoxinA Dose 1 v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.565 ^[31]
Method	ANCOVA

Notes:

[31] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 2 vs Placebo at Week 10
Comparison groups	OnabotulinumtoxinA Dose 2 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.071 ^[32]
Method	ANCOVA

Notes:

[32] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 3 vs Placebo at Week 10
Comparison groups	OnabotulinumtoxinA Dose 3 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.799 ^[33]
Method	ANCOVA

Notes:

[33] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 4 vs Placebo at Week 10
Comparison groups	OnabotulinumtoxinA Dose 4 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.681 ^[34]
Method	ANCOVA

Notes:

[34] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 5 vs Placebo at Week 10
Comparison groups	OnabotulinumtoxinA Dose 5 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.741 ^[35]
Method	ANCOVA

Notes:

[35] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 6 vs Placebo at Week 10
Comparison groups	OnabotulinumtoxinA Dose 6 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.526 ^[36]
Method	ANCOVA

Notes:

[36] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 1 vs Placebo at Week 12
Comparison groups	OnabotulinumtoxinA Dose 1 v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.584 ^[37]
Method	ANCOVA

Notes:

[37] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 2 vs Placebo at Week 12
Comparison groups	OnabotulinumtoxinA Dose 2 v Placebo

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.101 ^[38]
Method	ANCOVA

Notes:

[38] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 3 vs Placebo at Week 12
Comparison groups	OnabotulinumtoxinA Dose 3 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.823 ^[39]
Method	ANCOVA

Notes:

[39] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 4 vs Placebo at Week 12
Comparison groups	OnabotulinumtoxinA Dose 4 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.741 ^[40]
Method	ANCOVA

Notes:

[40] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 5 vs Placebo at Week 12
Comparison groups	OnabotulinumtoxinA Dose 5 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.756 ^[41]
Method	ANCOVA

Notes:

[41] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 6 vs Placebo at Week 12
Comparison groups	OnabotulinumtoxinA Dose 6 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.517 ^[42]
Method	ANCOVA

Notes:

[42] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline average IELT as the covariate.

Secondary: Change from Baseline in Geometric Mean IELT

End point title	Change from Baseline in Geometric Mean IELT
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End point description:

IELT, the time from vaginal penetration to ejaculation, was measured by a stopwatch and was recorded in the SID. The Logarithm Value of the Geometric Mean of each individual participant's IELT recorded in the SID up to each time point was calculated. The mean and SD of log-transformed geometric mean IELTs were then calculated for each treatment group. An ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate was used for analyses. A positive change from Baseline indicates improvement.

The mITT population included all randomized participants who received study treatment and had post-baseline IELT data available based on the dose actually received by the participant. Here "n" is the number of participants with available data at the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) to Weeks 2, 4, 6, 8, and 10

End point values	Onabotulinumt oxinA Dose 1	Onabotulinumt oxinA Dose 2	Onabotulinumt oxinA Dose 3	Onabotulinumt oxinA Dose 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	8	7
Units: seconds				
arithmetic mean (standard deviation)				
Baseline(n=5,6,8,7,8,7,15)	3.57 (± 0.283)	3.50 (± 0.631)	3.46 (± 0.371)	3.52 (± 0.531)
Change at Week 2(n=5,6,8,7,8,7,14)	0.76 (± 1.014)	0.95 (± 1.497)	0.26 (± 0.677)	0.34 (± 0.690)
Change at Week 4(n=5,6,8,7,8,7,14)	0.70 (± 1.000)	0.77 (± 1.505)	0.18 (± 0.879)	0.33 (± 0.616)
Change at Week 6(n=5,6,8,7,8,7,14)	0.70 (± 0.999)	0.83 (± 1.513)	0.08 (± 0.971)	0.36 (± 0.629)
Change at Week 8(n=5,6,8,7,8,7,14)	0.67 (± 1.007)	0.79 (± 1.525)	0.05 (± 0.968)	0.37 (± 0.627)
Change at Week 10(n=5,6,8,7,8,7,15)	0.60 (± 1.009)	0.80 (± 1.503)	0.07 (± 0.905)	0.37 (± 0.624)

End point values	Onabotulinumt oxinA Dose 5	Onabotulinumt oxinA Dose 6	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	7	15	
Units: seconds				
arithmetic mean (standard deviation)				
Baseline(n=5,6,8,7,8,7,15)	3.53 (± 0.475)	3.54 (± 0.505)	3.46 (± 0.610)	
Change at Week 2(n=5,6,8,7,8,7,14)	0.47 (± 0.604)	0.62 (± 0.623)	0.19 (± 0.486)	
Change at Week 4(n=5,6,8,7,8,7,14)	0.38 (± 0.481)	0.61 (± 0.618)	0.22 (± 0.627)	
Change at Week 6(n=5,6,8,7,8,7,14)	0.36 (± 0.483)	0.59 (± 0.722)	0.36 (± 0.524)	
Change at Week 8(n=5,6,8,7,8,7,14)	0.36 (± 0.522)	0.61 (± 0.682)	0.44 (± 0.567)	
Change at Week 10(n=5,6,8,7,8,7,15)	0.32 (± 0.512)	0.56 (± 0.727)	0.44 (± 0.603)	

Statistical analyses

Statistical analysis title	OnabotulinumtoxinA Dose 1 vs Placebo at Week 2
Comparison groups	OnabotulinumtoxinA Dose 1 v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.079 ^[43]
Method	ANCOVA

Notes:

[43] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 2 vs Placebo at Week 2
Comparison groups	OnabotulinumtoxinA Dose 2 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.025 ^[44]
Method	ANCOVA

Notes:

[44] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 3 vs Placebo at Week 2
Comparison groups	OnabotulinumtoxinA Dose 3 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.417 ^[45]
Method	ANCOVA

Notes:

[45] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 4 vs Placebo at Week 2
Comparison groups	OnabotulinumtoxinA Dose 4 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.33 ^[46]
Method	ANCOVA

Notes:

[46] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 5 vs Placebo at Week 2
Comparison groups	OnabotulinumtoxinA Dose 5 v Placebo

Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.199 ^[47]
Method	ANCOVA

Notes:

[47] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 6 vs Placebo at Week 2
Comparison groups	OnabotulinumtoxinA Dose 6 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.113 ^[48]
Method	ANCOVA

Notes:

[48] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 1 vs Placebo at Week 4
Comparison groups	OnabotulinumtoxinA Dose 1 v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.127 ^[49]
Method	ANCOVA

Notes:

[49] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 2 vs Placebo at Week 4
Comparison groups	OnabotulinumtoxinA Dose 2 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.087 ^[50]
Method	ANCOVA

Notes:

[50] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 3 vs Placebo at Week 4
Comparison groups	OnabotulinumtoxinA Dose 3 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.543 ^[51]
Method	ANCOVA

Notes:

[51] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 4 vs Placebo at Week 4
Comparison groups	OnabotulinumtoxinA Dose 4 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.377 ^[52]
Method	ANCOVA

Notes:

[52] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 5 vs Placebo at Week 4
Comparison groups	OnabotulinumtoxinA Dose 5 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.321 ^[53]
Method	ANCOVA

Notes:

[53] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 6 vs Placebo at Week 4
Comparison groups	OnabotulinumtoxinA Dose 6 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.149 ^[54]
Method	ANCOVA

Notes:

[54] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 1 vs Placebo at Week 6
Comparison groups	OnabotulinumtoxinA Dose 1 v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.215 ^[55]
Method	ANCOVA

Notes:

[55] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 2 vs Placebo at Week 6
Comparison groups	OnabotulinumtoxinA Dose 2 v Placebo

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.126 ^[56]
Method	ANCOVA

Notes:

[56] - A one-sided p-value of mean difference vs placebo for each active BOTOX dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 3 vs Placebo at Week 6
Comparison groups	OnabotulinumtoxinA Dose 3 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.774 ^[57]
Method	ANCOVA

Notes:

[57] - A one-sided p-value of mean difference vs placebo for each active BOTOX dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 4 vs Placebo at Week 6
Comparison groups	OnabotulinumtoxinA Dose 4 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.495 ^[58]
Method	ANCOVA

Notes:

[58] - A one-sided p-value of mean difference vs placebo for each active BOTOX dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 5 vs Placebo at Week 6
Comparison groups	OnabotulinumtoxinA Dose 5 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.495 ^[59]
Method	ANCOVA

Notes:

[59] - A one-sided p-value of mean difference vs placebo for each active BOTOX dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 6 vs Placebo at Week 6
Comparison groups	OnabotulinumtoxinA Dose 6 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.274 ^[60]
Method	ANCOVA

Notes:

[60] - A one-sided p-value of mean difference vs placebo for each active BOTOX dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 1 vs Placebo at Week 8
Comparison groups	OnabotulinumtoxinA Dose 1 v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.308 ^[61]
Method	ANCOVA

Notes:

[61] - A one-sided p-value of mean difference vs placebo for each active BOTOX dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 2 vs Placebo at Week 8
Comparison groups	OnabotulinumtoxinA Dose 2 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.205 ^[62]
Method	ANCOVA

Notes:

[62] - A one-sided p-value of mean difference vs placebo for each active BOTOX dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 3 vs Placebo at Week 8
Comparison groups	OnabotulinumtoxinA Dose 3 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.849 ^[63]
Method	ANCOVA

Notes:

[63] - A one-sided p-value of mean difference vs placebo for each active BOTOX dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 4 vs Placebo at Week 8
Comparison groups	OnabotulinumtoxinA Dose 4 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.571 ^[64]
Method	ANCOVA

Notes:

[64] - A one-sided p-value of mean difference vs placebo for each active BOTOX dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 5 vs Placebo at Week 8
Comparison groups	OnabotulinumtoxinA Dose 5 v Placebo

Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.592 ^[65]
Method	ANCOVA

Notes:

[65] - A one-sided p-value of mean difference vs placebo for each active BOTOX dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 6 vs Placebo at Week 8
Comparison groups	OnabotulinumtoxinA Dose 6 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.34 ^[66]
Method	ANCOVA

Notes:

[66] - A one-sided p-value of mean difference vs placebo for each active BOTOX dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 1 vs Placebo at Week 10
Comparison groups	OnabotulinumtoxinA Dose 1 v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.36 ^[67]
Method	ANCOVA

Notes:

[67] - A one-sided p-value of mean difference vs placebo for each active BOTOX dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 2 vs Placebo at Week 10
Comparison groups	OnabotulinumtoxinA Dose 2 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.192 ^[68]
Method	ANCOVA

Notes:

[68] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 3 vs Placebo at Week 10
Comparison groups	OnabotulinumtoxinA Dose 3 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.843 ^[69]
Method	ANCOVA

Notes:

[69] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 4 vs Placebo at Week 10
Comparison groups	OnabotulinumtoxinA Dose 4 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.572 ^[70]
Method	ANCOVA

Notes:

[70] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 5 vs Placebo at Week 10
Comparison groups	OnabotulinumtoxinA Dose 5 v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.628 ^[71]
Method	ANCOVA

Notes:

[71] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Statistical analysis title	OnabotulinumtoxinA Dose 6 vs Placebo at Week 10
Comparison groups	OnabotulinumtoxinA Dose 6 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.38 ^[72]
Method	ANCOVA

Notes:

[72] - A one-sided p-value of mean difference vs placebo for each active OnabotulinumtoxinA dose level is calculated from the ANCOVA Model with treatment as the fixed effect and baseline geometric mean IELT as the covariate.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose and for at least 28 days after the last dose of study medication (Up to 26 Weeks in the Randomized-treatment Period and Up to 17 Weeks in the Open-Label Period)

Adverse event reporting additional description:

A treatment-emergent adverse event (TEAE) was an adverse event with onset on or after the initiation of study treatment or an adverse event with onset prior to study treatment that worsened in severity or became serious after the initiation of study treatment.

Safety Population included all treated participants.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	OnabotulinumtoxinA Dose 1
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Reporting group description:

OnabotulinumtoxinA Dose 1 injected into specified muscle per protocol on Day 1.

Reporting group title	OnabotulinumtoxinA Dose 2
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Reporting group description:

OnabotulinumtoxinA Dose 2 injected into specified muscle per protocol on Day 1.

Reporting group title	OnabotulinumtoxinA Dose 3
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Reporting group description:

OnabotulinumtoxinA Dose 3 injected into specified muscle per protocol on Day 1.

Reporting group title	OnabotulinumtoxinA Dose 4
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Reporting group description:

OnabotulinumtoxinA Dose 4 injected into specified muscle per protocol on Day 1.

Reporting group title	OnabotulinumtoxinA Dose 6
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Reporting group description:

OnabotulinumtoxinA Dose 6 injected into specified muscle per protocol on Day 1.

Reporting group title	OnabotulinumtoxinA Dose 5
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Reporting group description:

OnabotulinumtoxinA Dose 5 injected into specified muscle per protocol on Day 1.

Reporting group title	Placebo
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Reporting group description:

Placebo (normal saline) injected into specified muscle per protocol on Day 1.

Reporting group title	OnabotulinumtoxinA Dose 2 (Open-label Period)
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Reporting group description:

Participants who completed 12 weeks of randomized period were eligible to receive a second injection with active drug in the Open-label Period.

Serious adverse events	OnabotulinumtoxinA Dose 1	OnabotulinumtoxinA Dose 2	OnabotulinumtoxinA Dose 3
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	OnabotulinumtoxinA Dose 4	OnabotulinumtoxinA Dose 6	OnabotulinumtoxinA Dose 5
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Placebo	OnabotulinumtoxinA Dose 2 (Open-label Period)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	OnabotulinumtoxinA Dose 1	OnabotulinumtoxinA Dose 2	OnabotulinumtoxinA Dose 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 5 (60.00%)	2 / 7 (28.57%)	1 / 8 (12.50%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injection site paraesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injection site pruritus			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Reproductive system and breast disorders			
Ejaculation disorder subjects affected / exposed occurrences (all)	3 / 5 (60.00%) 6	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Epididymal tenderness subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Perineal pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Pruritus genital subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Erectile dysfunction subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Ejaculation failure subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Sinus congestion subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Psychiatric disorders			

Enuresis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Psychogenic erectile dysfunction subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Investigations Semen volume decreased subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Heart rate irregular subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Injury, poisoning and procedural complications Joint injury subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Penis injury subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Concussion subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Contusion subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Road traffic accident subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0

Nervous system disorders			
Headache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Loss of consciousness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Memory impairment			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Abnormal faeces			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dyshidrotic eczema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Skin odour abnormal subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Rosacea subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Renal and urinary disorders			
Dysuria subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 7 (14.29%) 1	0 / 8 (0.00%) 0
Terminal dribbling subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 7 (14.29%) 1	0 / 8 (0.00%) 0
Urine odour abnormal subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Endocrine disorders			
Hypogonadism subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Muscle spasms subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Arthralgia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	0 / 8 (0.00%) 0
Infections and infestations			
Influenza subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 7 (14.29%) 1	0 / 8 (0.00%) 0
Upper respiratory tract infection			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	OnabotulinumtoxinA Dose 4	OnabotulinumtoxinA Dose 6	OnabotulinumtoxinA Dose 5
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)	4 / 8 (50.00%)	3 / 8 (37.50%)
Vascular disorders			
Hypertension			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Chills			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Injection site paraesthesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injection site pruritus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Ejaculation disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Epididymal tenderness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Perineal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pruritus genital			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Erectile dysfunction			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Ejaculation failure			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Sinus congestion subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 8 (12.50%) 1	0 / 8 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Psychiatric disorders Enuresis subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Psychogenic erectile dysfunction subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Investigations Semen volume decreased subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	1 / 8 (12.50%) 1
Heart rate irregular subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Injury, poisoning and procedural complications Joint injury subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Penis injury subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0

Concussion subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Contusion subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Road traffic accident subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 8 (12.50%) 2	0 / 8 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Loss of consciousness subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Memory impairment subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	1 / 8 (12.50%) 1
Abdominal pain lower subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	1 / 8 (12.50%) 1

Constipation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Abnormal faeces			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dyshidrotic eczema			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Skin odour abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rosacea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Terminal dribbling			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urine odour abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypogonadism			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Gastroenteritis subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Placebo	OnabotulinumtoxinA Dose 2 (Open-label Period)	
Total subjects affected by non-serious adverse events subjects affected / exposed	12 / 15 (80.00%)	3 / 8 (37.50%)	
Vascular disorders Hypertension subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions Injection site pain subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Chills subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Injection site paraesthesia subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Injection site pruritus subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders Ejaculation disorder subjects affected / exposed	2 / 15 (13.33%)	0 / 8 (0.00%)	
occurrences (all)	3	0	
Epididymal tenderness subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Perineal pain			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	
Pruritus genital subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 8 (12.50%) 1	
Erectile dysfunction subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	
Ejaculation failure subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders			
Sinus congestion subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	
Cough subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Dyspnoea subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Psychiatric disorders			
Enuresis subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	
Psychogenic erectile dysfunction subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Investigations			
Semen volume decreased subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	
Blood creatine phosphokinase increased			

subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2	0 / 8 (0.00%) 0	
Heart rate irregular subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Injury, poisoning and procedural complications			
Joint injury subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	
Penis injury subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	
Concussion subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Contusion subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Road traffic accident subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Cardiac disorders			
Angina pectoris subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	3 / 15 (20.00%) 4	0 / 8 (0.00%) 0	
Dizziness subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Loss of consciousness subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Memory impairment			

subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Abdominal pain lower subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Abnormal faeces subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 1 / 15 (6.67%) 1 1 / 15 (6.67%) 1	0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0	
Skin and subcutaneous tissue disorders Dyshidrotic eczema subjects affected / exposed occurrences (all) Skin odour abnormal subjects affected / exposed occurrences (all) Rosacea subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0 1 / 15 (6.67%) 2 0 / 15 (0.00%) 0	0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 1 / 8 (12.50%) 1	
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) Terminal dribbling	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	
Urine odour abnormal subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Endocrine disorders Hypogonadism subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 8 (12.50%) 1	
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 2	0 / 8 (0.00%) 0	
Muscle spasms subjects affected / exposed occurrences (all)	3 / 15 (20.00%) 3	0 / 8 (0.00%) 0	
Arthralgia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Infections and infestations Influenza subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	
Rhinitis subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 15 (20.00%) 3	0 / 8 (0.00%) 0	
Pharyngitis streptococcal subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	
Sinusitis			

subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Conjunctivitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Ear infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis viral			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 April 2015	Amendment 1 • The first amendment of the protocol was implemented prior to enrollment for Cohort 5 • This amendment incorporated collection and analysis for an additional exploratory efficacy endpoint • Using an ultrasound, various measurements of participants bulbospongiosus muscle (BSM) were taken prior to treatment and at the Week 4 visit • The statistical analysis plan (SAP) was amended to include an analysis of these measurements, which was descriptive in nature • The collection and analysis of the BSM were only undertaken with participants in Cohort 5 and subsequently excluded in Amendment 2 • Additionally, after the Data Review Committee's (DRC's) review of safety data from the first 6 participants in Cohort 5, it was decided to reduce the dosage for subsequent participants enrolled into the active treatment arm of Cohort 5. The active dose was reduced from OnabotulinumtoxinA Dose 1 down to OnabotulinumtoxinA Dose 2. Since authority to do so was granted to the DRC in both the original study protocol as well as DRC charter, a protocol amendment was not required • Other than inclusion of an additional treatment arm, this decision implied no material change to the planned statistical analysis. Consequently, a SAP amendment was not needed.
15 July 2016	Amendment 2 • The second amendment to the protocol occurred prior to the start of Cohort 6 • This amendment stipulated an increase in the number of participants enrolled into Cohort 6 from 10 to 24 as well as changing the dosage of the active treatment from OnabotulinumtoxinA Dose A to OnabotulinumtoxinA Dose 2 • Additionally, participants in Cohort 6 had the option to enter a 12-week open-label extension period • As mentioned earlier, the BSM measurements included in Amendment 1 were removed for Amendment 2 • The SAP was amended to incorporate analysis for the open-label period that was descriptive in nature.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
01 February 2015	The study was on an enrollment hold due to a major protocol amendment and adding the Dose 2 dose. The hold was not mandated by Food and Drug Administration (FDA), but was necessary to program our interactive web response system (IWRS) and Electronic Data Capture (EDC) systems to account for the major changes. The hold went from Sept 2015 to May of 2016.	-

Notes:

Limitations and caveats

None reported