Clinical trial results:
Long-term Extension Study of BOTOX® in the Treatment of Urinary Incontinence Due to Neurogenic Detrusor Overactivity in Patients 5 to 17 Years of Age

Summary

EudraCT number	2012-004898-30
Trial protocol	BE CZ AT IT DE PL FR
Global end of trial date	03 October 2019

Results information

Result version number	v1 (current)
This version publication date	19 April 2020
First version publication date	19 April 2020

Trial information

Trial identification

Sponsor protocol code	191622-121

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01852058
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergan plc
Sponsor organisation address	1st Floor, Marlow International, The Parkway, Marlow Buckinghamshire, United Kingdom, SL7 1YL
Public contact	Clinical Trials Registry Team, Allergan plc, 001 8772778566, IR-CTRegistration@allergan.com
Scientific contact	Therapeutic Area, Head, Allergan plc, 001 862-261-7000, 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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 October 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial is to evaluate the long-term safety and efficacy of onabotulinumtoxinA (botulinum toxin Type A; BOTOX®) for the treatment of urinary incontinence due to neurogenic detrusor overactivity in participants who successfully completed Study 191622-120 (NCT01852045).

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	11 January 2014
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	Belgium: 13
Country: Number of subjects enrolled	Czech Republic: 5
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Poland: 22
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Turkey: 2
Country: Number of subjects enrolled	United States: 35
Worldwide total number of subjects	95
EEA total number of subjects	56

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)	47
Adolescents (12-17 years)	48
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants who successfully completed Study 191622-120 (NCT01852045) were enrolled in this study and were followed for up to an additional 60 weeks.

Pre-assignment

Screening details:

Data from the participant's participation in this extension Study 191622-121 (121) were integrated with the corresponding
participant's data from the preceding Study 191622-120 (120).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	OnabotulinumtoxinA 50 U

Arm description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Arm type	Experimental
Investigational medicinal product name	OnabotulinumtoxinA
Investigational medicinal product code	
Other name	BOTOX® botulinum toxin Type A
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

OnabotulinumtoxinA injected into the detrusor wall. Treatments were administered as needed with a minimum of a 12-week interval between doses.

Arm title	OnabotulinumtoxinA 100 U

Arm description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Arm type	Experimental
Investigational medicinal product name	OnabotulinumtoxinA
Investigational medicinal product code	
Other name	BOTOX® botulinum toxin Type A
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

OnabotulinumtoxinA injected into the detrusor wall. Treatments were administered as needed with a minimum of a 12-week interval between doses.

Arm title	OnabotulinumtoxinA 200 U

Arm description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Arm type	Experimental
Investigational medicinal product name	OnabotulinumtoxinA
Investigational medicinal product code	
Other name	BOTOX® botulinum toxin Type A
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

OnabotulinumtoxinA injected into the detrusor wall. Treatments were administered as needed with a minimum of a 12-week interval between doses.

Number of subjects in period 1	OnabotulinumtoxinA 50 U	OnabotulinumtoxinA 100 U	OnabotulinumtoxinA 200 U
Started	31	39	25
Completed	22	36	17
Not completed	9	3	8
Adverse event, non-fatal	1	-	-
Protocol Deviation	1	-	-
Withdrawal by Subject	3	1	1
Lost to follow-up	2	-	-
Reason not Specified	1	2	6
Lack of efficacy	1	-	1

Baseline characteristics

Reporting groups	
Reporting group title	OnabotulinumtoxinA 50 U
Reporting group description:	
Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).	
Reporting group title	OnabotulinumtoxinA 100 U
Reporting group description:	
Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).	
Reporting group title	OnabotulinumtoxinA 200 U
Reporting group description:	
Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).	

Reporting group values	OnabotulinumtoxinA 50 U	OnabotulinumtoxinA 100 U	OnabotulinumtoxinA 200 U
Number of subjects	31	39	25
Age categorical Units: Subjects			
Children (2-11 years)	15	22	10
Adolescents (12-17 years)	16	17	15
Age Continuous Units: years			
arithmetic mean	11.7	10.8	11.7
standard deviation	± 3.49	± 3.36	± 3.22
Sex: Female, Male Units: participants			
Female	17	14	13
Male	14	25	12
Race/Ethnicity, Customized Units: Subjects			
White	22	28	18
Black or African American	6	3	2
Asian	1	2	0
Hispanic	1	3	3
Other	1	3	2

Reporting group values	Total		
Number of subjects	95		
Age categorical Units: Subjects			
Children (2-11 years)	47		

Adolescents (12-17 years)	48		

Age Continuous Units: years arithmetic mean standard deviation	- -		
Sex: Female, Male Units: participants			
Female	44		
Male	51		
Race/Ethnicity, Customized Units: Subjects			
White	68		
Black or African American	11		
Asian	3		
Hispanic	7		
Other	6		

End points

End points reporting groups

Reporting group title	OnabotulinumtoxinA 50 U

Reporting group description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Reporting group title	OnabotulinumtoxinA 100 U

Reporting group description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Reporting group title	OnabotulinumtoxinA 200 U

Reporting group description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 50 U
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 100 U
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 200 U
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 50 U
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 100 U
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 200 U
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 50 U
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Following treatment with onabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) intramuscular injection into the detrusor wall in Study 120, participants were eligible for retreatments in this study as needed with a minimum 12-week interval between doses for a maximum of 3 retreatments. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 50 U (Treatment Cycle 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 1. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 100 U (Treatment Cycle 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 1. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 200 U (Treatment Cycle 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 1. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 50 U (Treatment Cycle 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 2. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 100 U (Treatment Cycle 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 2. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 200 U (Treatment Cycle 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 2. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 50 U (Treatment Cycle 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 3. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 100 U (Treatment Cycle 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 3. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 200 U (Treatment Cycle 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 3. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 50 U (Treatment Cycle 4)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 4. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 100 U (Treatment Cycle 4)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 4. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Subject analysis set title	OnabotulinumtoxinA 200 U (Treatment Cycle 4)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

OnabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 4. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Primary: Change From Study Baseline in the Daily Normalized Daytime Average Number of Urinary Incontinence Episodes in Treatment Cycle 1

End point title	Change From Study Baseline in the Daily Normalized Daytime Average Number of Urinary Incontinence Episodes in Treatment Cycle 1[1]

End point description:

Urinary incontinence was defined as involuntary loss of urine as recorded by the participant in a bladder diary during 2 consecutive days in the week prior to the study visit (normalized to a 12 hour daytime period). Daytime is defined as the time between waking up to start the day and going to bed to sleep for the night. The number of daily daytime incontinence episodes were averaged during the 2-day period. A negative change from Baseline indicates improvement. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into the extension study who received at least 1 BOTOX treatment over the course of the total evaluation period, starting from their first treatment in Study 120. 'n' is the number of participants with evaluable data at the given time point.

End point type	Primary

End point timeframe:

Study Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 1

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not available

End point values	Onabotulinumtoxin A 50 U (Treatment Cycle 1)	Onabotulinumtoxin A 100 U (Treatment Cycle 1)	Onabotulinumtoxin A 200 U (Treatment Cycle 1)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	31	39	25	
Units: urinary incontinence episodes per day				
arithmetic mean (standard deviation)				
Baseline (n= 31, 39, 25)	2.66 (± 0.876)	2.97 (± 1.135)	3.99 (± 5.492)	
Change from Baseline to Week 6 (n= 30, 36, 23)	-1.19 (± 1.156)	-1.39 (± 1.585)	-2.19 (± 5.738)	

Statistical analyses

No statistical analyses for this end point

Primary: Change From Study Baseline in the Daily Normalized Daytime Average Number of Urinary Incontinence Episodes in Treatment Cycle 2

End point title	Change From Study Baseline in the Daily Normalized Daytime Average Number of Urinary Incontinence Episodes in Treatment Cycle 2[2]

End point description:

Urinary incontinence was defined as involuntary loss of urine as recorded by the participant in a bladder diary during 2 consecutive days in the week prior to the study visit (normalized to a 12 hour daytime period). Daytime is defined as the time between waking up to start the day and going to bed to sleep for the night. The number of daily daytime incontinence episodes were averaged during the 2-day period. A negative change from Baseline indicates improvement. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into the extension study who received at least 1 BOTOX treatment over the course of the total evaluation period, starting from their first treatment in Study 120. 'n' is the number of participants with evaluable data at the given time point.

End point type	Primary

End point timeframe:

Study Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 2

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not available

End point values	Onabotulinumtoxin A 50 U (Treatment Cycle 2)	Onabotulinumtoxin A 100 U (Treatment Cycle 2)	Onabotulinumtoxin A 200 U (Treatment Cycle 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	45	36	
Units: urinary incontinence episodes per day				
arithmetic mean (standard deviation)				
Baseline (n=9, 45, 36)	2.57 (± 0.937)	2.80 (± 0.915)	3.83 (± 4.623)	
Change from Baseline to Week 6 (n=6, 44, 34)	-1.07 (± 2.092)	-1.70 (± 1.331)	-1.64 (± 1.906)	

Statistical analyses

No statistical analyses for this end point

Primary: Change From Study Baseline in the Daily Normalized Daytime Average Number of Urinary Incontinence Episodes in Treatment Cycle 3

End point title	Change From Study Baseline in the Daily Normalized Daytime Average Number of Urinary Incontinence Episodes in Treatment Cycle 3[3]

End point description:

Urinary incontinence was defined as involuntary loss of urine as recorded by the participant in a bladder diary during 2 consecutive days in the week prior to the study visit (normalized to a 12 hour daytime period). Daytime is defined as the time between waking up to start the day and going to bed to sleep for the night. The number of daily daytime incontinence episodes were averaged during the 2-day period. A negative change from Baseline indicates improvement. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into the extension study who received at least 1 BOTOX treatment over the course of the total evaluation period, starting from their first treatment in Study 120. 'n' is the number of participants with evaluable data at the given time point.

End point type	Primary

End point timeframe:

Study Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 3

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not available

End point values	Onabotulinumtoxin A 50 U (Treatment Cycle 3)	Onabotulinumtoxin A 100 U (Treatment Cycle 3)	Onabotulinumtoxin A 200 U (Treatment Cycle 3)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	16	34	
Units: urinary incontinence episodes per day				
arithmetic mean (standard deviation)				
Baseline (n=5, 16, 34)	2.48 (± 0.228)	2.94 (± 0.923)	3.80 (± 4.678)	
Change from Baseline to Week 6 (n=5, 16, 33)	-1.92 (± 0.858)	-1.73 (± 1.057)	-2.74 (± 4.833)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment Emergent Adverse Events (TEAEs) and Serious Treatment Emergent Adverse Events (STEAEs)

End point title	Number of Participants with Treatment Emergent Adverse Events (TEAEs) and Serious Treatment Emergent Adverse Events (STEAEs)

End point description:

Adverse event:any untoward medical occurrence in patient or clinical investigation participant administered pharmaceutical product,which does not necessarily have causal relationship with treatment.It can therefore be any unfavorable and unintended sign(including abnormal laboratory finding),symptom,or disease temporally associated with use of medicinal(investigational)product,whether or not related to medicinal product.Serious AE(SAE):any AE resulted in death,inpatient hospitalization/prolongation of existing hospitalization,persistent or significant disability/incapacity,life threatening,congenital anomaly/birth defect or important medical event.TEAE/STEAE:any new AE/worsening of existing condition after initiation of treatment.Data summarized under respective treatments participants received in corresponding treatment cycles.BOTOX-treated Population:all participants enrolled into Study121,received >=1BOTOX treatment during total evaluation period,from first treatment in Study120.

End point type	Secondary

End point timeframe:

First injection on Day 1 in Study 120 through completion of Study 121 (Up to 108 weeks)

End point values	OnabotulinumtoxinA 50 U (Treatment Cycle 1)	OnabotulinumtoxinA 100 U (Treatment Cycle 1)	OnabotulinumtoxinA 200 U (Treatment Cycle 1)	OnabotulinumtoxinA 50 U (Treatment Cycle 2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	39	25	9
Units: participants				
TEAEs	23	31	19	7
STEAEs	2	3	1	0

End point values	OnabotulinumtoxinA 100 U (Treatment Cycle 2)	OnabotulinumtoxinA 200 U (Treatment Cycle 2)	OnabotulinumtoxinA 50 U (Treatment Cycle 3)	OnabotulinumtoxinA 100 U (Treatment Cycle 3)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	45	36	5	16
Units: participants				
TEAEs	34	31	4	10
STEAEs	5	6	0	1

End point values	Onabotulinumtoxin A 200 U (Treatment Cycle 3)	Onabotulinumtoxin A 50 U (Treatment Cycle 4)	Onabotulinumtoxin A 100 U (Treatment Cycle 4)	Onabotulinumtoxin A 200 U (Treatment Cycle 4)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	34	3	4	4
Units: participants				
TEAEs	21	3	2	4
STEAEs	2	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with ≥ 50%, ≥ 75%, ≥ 90%, and ≥ 100% Reduction from Baseline in the Number of Normalized Daytime Urinary Incontinence Episodes in Treatment Cycle 1

End point title	Percentage of Participants with ≥ 50%, ≥ 75%, ≥ 90%, and ≥ 100% Reduction from Baseline in the Number of Normalized Daytime Urinary Incontinence Episodes in Treatment Cycle 1

End point description:

Urinary incontinence was defined as involuntary loss of urine as recorded by the participant in a bladder diary during 2 consecutive days in the week prior to the study visit (normalized to a 12 hour daytime period). Daytime is defined as the time between waking up to start the day and going to bed to sleep for the night. The number of daily incontinence episodes were averaged during the 2-day period. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received at least 1 BOTOX treatment over the course of total evaluation period, starting from their first treatment in Study 120. Number analysed is the number of participants with evaluable data for the specific category.

End point type	Secondary

End point timeframe:

Study Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 1

End point values	Onabotulinumtoxin A 50 U (Treatment Cycle 1)	Onabotulinumtoxin A 100 U (Treatment Cycle 1)	Onabotulinumtoxin A 200 U (Treatment Cycle 1)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	36	23	
Units: percentage of participants				
number (confidence interval 95%)				
≥50% Reduction from Baseline to Week 6	53.3 (34.33 to 71.66)	55.6 (38.10 to 72.06)	52.2 (30.59 to 73.18)	
≥75% Reduction from Baseline to Week 6	30.0 (14.73 to 49.40)	41.7 (25.51 to 59.24)	39.1 (19.71 to 61.46)	
≥90% Reduction from Baseline to Week 6	26.7 (12.28 to 45.89)	30.6 (16.35 to 48.11)	30.4 (13.21 to 52.92)	

≥100% Reduction from Baseline to Week 6	26.7 (12.28 to 45.89)	27.8 (14.20 to 45.19)	26.1 (10.23 to 48.41)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with ≥ 50%, ≥ 75%, ≥ 90%, and ≥ 100% Reduction from Baseline in the Number of Normalized Daytime Urinary Incontinence Episodes in Treatment Cycle 2

End point title	Percentage of Participants with ≥ 50%, ≥ 75%, ≥ 90%, and ≥ 100% Reduction from Baseline in the Number of Normalized Daytime Urinary Incontinence Episodes in Treatment Cycle 2

End point description:

Urinary incontinence was defined as involuntary loss of urine as recorded by the participant in a bladder diary during 2 consecutive days in the week prior to the study visit (normalized to a 12 hour daytime period). Daytime is defined as the time between waking up to start the day and going to bed to sleep for the night. The number of daily incontinence episodes were averaged during the 2-day period. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received at least 1 BOTOX treatment over the course of total evaluation period, starting from their first treatment in Study 120. Number analysed is the number of participants with evaluable data for the specific category.

End point type	Secondary

End point timeframe:

Study Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 2

End point values	Onabotulinumtoxin A 50 U (Treatment Cycle 2)	Onabotulinumtoxin A 100 U (Treatment Cycle 2)	Onabotulinumtoxin A 200 U (Treatment Cycle 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	44	34	
Units: percentage of participants				
number (confidence interval 95%)				
≥50% Reduction from Baseline to Week 6	66.7 (22.28 to 95.67)	65.9 (50.08 to 79.51)	58.8 (40.70 to 75.35)	
≥75% Reduction from Baseline to Week 6	50.0 (11.81 to 88.19)	43.2 (28.35 to 58.97)	47.1 (29.78 to 64.87)	
≥90% Reduction from Baseline to Week 6	50.0 (11.81 to 88.19)	27.3 (14.96 to 42.79)	41.2 (24.65 to 59.30)	
≥100% Reduction from Baseline to Week 6	50.0 (11.81 to 88.19)	25.0 (13.19 to 40.34)	38.2 (22.17 to 56.44)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with ≥ 50%, ≥ 75%, ≥ 90%, and ≥ 100% Reduction from Baseline in the Number of Normalized Daytime Urinary Incontinence Episodes in Treatment Cycle 3

End point title	Percentage of Participants with ≥ 50%, ≥ 75%, ≥ 90%, and ≥ 100% Reduction from Baseline in the Number of Normalized Daytime Urinary Incontinence Episodes in Treatment Cycle 3

End point description:

Urinary incontinence was defined as involuntary loss of urine as recorded by the participant in a bladder diary during 2 consecutive days in the week prior to the study visit (normalized to a 12 hour daytime period). Daytime is defined as the time between waking up to start the day and going to bed to sleep for the night. The number of daily incontinence episodes were averaged during the 2-day period. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received at least 1 BOTOX treatment over the course of total evaluation period, starting from their first treatment in Study 120. Number analysed is the number of participants with evaluable data for the specific category.

End point type	Secondary

End point timeframe:

Study Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 3

End point values	OnabotulinumtoxinA 50 U (Treatment Cycle 3)	OnabotulinumtoxinA 100 U (Treatment Cycle 3)	OnabotulinumtoxinA 200 U (Treatment Cycle 3)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	16	33	
Units: percentage of participants				
number (confidence interval 95%)				
≥50% Reduction from Baseline at Week 6	60.0 (14.66 to 94.73)	75.0 (47.62 to 92.73)	69.7 (51.29 to 84.41)	
≥75% Reduction from Baseline at Week 6	60.0 (14.66 to 94.73)	37.5 (15.20 to 64.57)	39.4 (22.91 to 57.86)	
≥90% Reduction from Baseline at Week 6	60.0 (14.66 to 94.73)	18.8 (4.05 to 45.65)	33.3 (17.96 to 51.83)	
≥100% Reduction from Baseline at Week 6	60.0 (14.66 to 94.73)	18.8 (4.05 to 45.65)	30.3 (15.59 to 48.71)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Average Urine Volume at First Morning Catheterization in Treatment Cycle 1

End point title	Change from Baseline in Average Urine Volume at First Morning Catheterization in Treatment Cycle 1

End point description:

The change in urine volume at first morning catherization was recorded by the participant in a bladder diary in the 2 consecutive days during the week prior to the study visit. The daily values were averaged during the 2-day period. A positive change from Baseline indicates improvement. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received >=1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. Overall number of participants analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 1

End point values	OnabotulinumtoxinA 50 U (Treatment Cycle 1)	OnabotulinumtoxinA 100 U (Treatment Cycle 1)	OnabotulinumtoxinA 200 U (Treatment Cycle 1)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	36	21	
Units: mL				
arithmetic mean (standard deviation)	14.68 (± 88.146)	39.88 (± 72.787)	96.90 (± 120.429)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Average Urine Volume at First Morning Catheterization in Treatment Cycle 2

End point title	Change from Baseline in Average Urine Volume at First Morning Catheterization in Treatment Cycle 2

End point description:

The change in urine volume at first morning catherization was recorded by the participant in a bladder diary in the 2 consecutive days during the week prior to the study visit. The daily values were averaged during the 2-day period. A positive change from Baseline indicates improvement. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received >=1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. Overall number of participants analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 2

End point values	OnabotulinumtoxinA 50 U (Treatment Cycle 2)	OnabotulinumtoxinA 100 U (Treatment Cycle 2)	OnabotulinumtoxinA 200 U (Treatment Cycle 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	43	31	
Units: mL				
arithmetic mean (standard deviation)	7.92 (± 148.597)	79.53 (± 106.794)	35.34 (± 98.209)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Average Urine Volume at First Morning Catheterization in Treatment Cycle 3

End point title	Change from Baseline in Average Urine Volume at First Morning Catheterization in Treatment Cycle 3

End point description:

The change in urine volume at first morning catherization was recorded by the participant in a bladder diary in the 2 consecutive days during the week prior to the study visit. The daily values were averaged during the 2-day period. A positive change from Baseline indicates improvement. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received >=1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. Overall number of participants analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline (Prior to Day 1 in Study 120) to 2 consecutive days in the week prior to Week 6 in Treatment Cycle 3

End point values	OnabotulinumtoxinA 50 U (Treatment Cycle 3)	OnabotulinumtoxinA 100 U (Treatment Cycle 3)	OnabotulinumtoxinA 200 U (Treatment Cycle 3)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	10	31	
Units: mL				
arithmetic mean (standard deviation)	58.50 (± 22.749)	57.86 (± 74.762)	92.39 (± 147.322)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Night Time Urinary Incontinence in Treatment Cycle 1

End point title	Percentage of Participants with Night Time Urinary Incontinence in Treatment Cycle 1

End point description:

Urinary incontinence was defined as involuntary loss of urine. Night time urinary incontinence was recorded by the participant on the bladder diary as a presence or absence of urinary leakage upon waking, for 2 consecutive days in the week prior to the week 6 visit. Night time was defined as the time between going to bed to sleep for the night and waking up to start the day. The percentage of participants with night time urinary incontinence is presented in categories 0, 1, and 2 nights. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received >= 1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. 'n' is the number of participants with data available for analyses at the given time point.

End point type	Secondary

End point timeframe:

Baseline (Prior to Day 1 in Study 120) and 2 consecutive days in the week prior to Week 6 in Treatment Cycle 1

End point values	Onabotulinumtoxin A 50 U (Treatment Cycle 1)	Onabotulinumtoxin A 100 U (Treatment Cycle 1)	Onabotulinumtoxin A 200 U (Treatment Cycle 1)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	31	39	25	
Units: percentage of participants				
number (not applicable)				
0 Nights of Incontinence at Baseline (n=31,39,23)	0.0	15.4	4.3	
0 Nights of Incontinence at Week 6 (n=30,37,24)	30.0	37.8	25.0	
1 Night of Incontinence at Baseline (n=31,39,23)	12.9	2.6	17.4	
1 Night of Incontinence at Week 6 (n=30,37,24)	20.0	16.2	29.2	
2 Nights of Incontinence at Baseline (n=31,39,23)	87.1	82.1	78.3	
2 Nights of Incontinence at Week 6 (n=30,37,24)	50.0	45.9	45.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Night Time Urinary Incontinence in Treatment Cycle 2

End point title	Percentage of Participants with Night Time Urinary Incontinence in Treatment Cycle 2

End point description:

Urinary incontinence was defined as involuntary loss of urine. Night time urinary incontinence was recorded by the participant on the bladder diary as a presence or absence of urinary leakage upon waking, for 2 consecutive days in the week prior to the week 6 visit. Night time was defined as the time between going to bed to sleep for the night and waking up to start the day. The percentage of participants with night time urinary incontinence is presented in categories 0, 1, and 2 nights. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received >= 1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. 'n' is the number of participants with data available for analyses at the given time point.

End point type	Secondary

End point timeframe:

Baseline (Prior to Day 1 in Study 120) and 2 consecutive days in the week prior to Week 6 in Treatment Cycle 2

End point values	Onabotulinumtoxin A 50 U (Treatment Cycle 2)	Onabotulinumtoxin A 100 U (Treatment Cycle 2)	Onabotulinumtoxin A 200 U (Treatment Cycle 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	45	36	
Units: percentage of participants				
number (not applicable)				
0 Nights of Incontinence at Baseline (n=9, 45, 34)	0.0	8.9	5.9	
0 Nights of Incontinence at Week 6 (n=6, 44, 34)	66.7	34.1	23.5	
1 Night of Incontinence at Baseline (n=9, 45, 34)	22.2	6.7	8.8	
1 Night of Incontinence at Week 6 (n=6, 44, 34)	16.7	22.7	8.8	
2 Nights of Incontinence at Baseline (n=9, 45, 34)	77.8	84.4	85.3	
2 Nights of Incontinence at Week 6 (n=6, 44, 34)	16.7	43.2	67.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Night Time Urinary Incontinence in Treatment Cycle 3

End point title	Percentage of Participants with Night Time Urinary Incontinence in Treatment Cycle 3

End point description:

Urinary incontinence was defined as involuntary loss of urine. Night time urinary incontinence was recorded by the participant on the bladder diary as a presence or absence of urinary leakage upon waking, for 2 consecutive days in the week prior to the week 6 visit. Night time was defined as the time between going to bed to sleep for the night and waking up to start the day. The percentage of participants with night time urinary incontinence is presented in categories 0, 1, and 2 nights. Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received >= 1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. 'n' is the number of participants with data available for analyses at the given time point.

End point type	Secondary

End point timeframe:

Baseline (Prior to Day 1 in Study 120) and 2 consecutive days in the week prior to Week 6 in Treatment Cycle 3

End point values	Onabotulinumtoxin A 50 U (Treatment Cycle 3)	Onabotulinumtoxin A 100 U (Treatment Cycle 3)	Onabotulinumtoxin A 200 U (Treatment Cycle 3)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	16	34	
Units: percentage of participants				
number (not applicable)				

0 Nights of Incontinence at Baseline (n=5, 16, 34)	0.0	12.5	5.9	
0 Nights of Incontinence at Week 6 (n=5, 16, 33)	20.0	31.3	21.2	
1 Night of Incontinence at Baseline (n=5, 16, 34)	0.0	0.0	5.9	
1 Night of Incontinence at Week 6 (n=5, 16, 33)	40.0	12.5	27.3	
2 Nights of Incontinence at Baseline (n=5, 16, 34)	100.0	87.5	88.2	
2 Nights of Incontinence at Week 6 (n=5, 16, 33)	40.0	56.3	51.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Average Time to Participant's Request for Retreatment

End point title	Average Time to Participant's Request for Retreatment

End point description:

Time to request for re-treatment is the time in weeks between last injection and request for next injection, regardless of fulfillment of the re-treatment criteria. Data are summarized under the respective treatments that participants received across entire study. Data is reported for only participants that had at least one request for retreatment while on a specified BOTOX dose. BOTOX-treated Population included all participants enrolled into extension study who received >=1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. Overall number of participants analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

First injection on Day 1 in Study 120 through to the date of completion of Study 121 (Up to 108 weeks)

End point values	Onabotulinumtoxin A 50 U	Onabotulinumtoxin A 100 U	Onabotulinumtoxin A 200 U	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	53	35	
Units: weeks				
median (full range (min-max))	24.55 (11.9 to 89.7)	24.64 (11.7 to 73.3)	25.43 (11.1 to 78.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Average Time to Participant's Qualification for Retreatment

End point title	Average Time to Participant's Qualification for Retreatment

End point description:

The criteria for qualification of retreatment included 1) Participant/parent/caregiver requests retreatment; 2) Participant has a total of at least 2 daytime urinary incontinence episodes over the 2-day bladder diary collection period; 3) At least 12 weeks has elapsed since treatment 1 and 4)

Participant has not experienced a serious treatment-related adverse event at any time. Data are summarized under the respective treatments that participants received across entire study. Data is reported for only participants that had at least one request for retreatment while on a specified BOTOX dose. BOTOX-treated Population included all participants enrolled into extension study who received >=1 BOTOX treatment over course of total evaluation period, starting from their first treatment in Study 120. Overall number of participants analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

First injection on Day 1 in Study 120 through to the date of completion of Study 121 (Up to 108 weeks)

End point values	Onabotulinumtoxin A 200 U	Onabotulinumtoxin A 100 U	Onabotulinumtoxin A 50 U	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	25	53	29	
Units: weeks				
median (confidence interval 95%)	26.29 (11.1 to 78.9)	25.43 (11.7 to 76.1)	25.38 (11.9 to 84.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Positive Response on Modified Treatment Benefit Scale (TBS) in Treatment Cycle 1

End point title	Percentage of Participants with Positive Response on Modified Treatment Benefit Scale (TBS) in Treatment Cycle 1

End point description:

The Modified TBS is a single-item scale which assesses the participant's condition (urinary problems, urinary incontinence) on a 4-point scale where 1 = greatly improved; 2 = improved; 3 = not changed; and 4 = worsened. A participant was considered to have a positive treatment response if they responded to the TBS question as either "greatly improved" or "improved". Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received >=1 BOTOX treatment over course of total evaluation period,starting from their first treatment in Study 120. Overall number of participants analysed is number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Week 6 in Treatment Cycle 1

End point values	Onabotulinumtoxin A 50 U (Treatment Cycle 1)	Onabotulinumtoxin A 100 U (Treatment Cycle 1)	Onabotulinumtoxin A 200 U (Treatment Cycle 1)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	35	24	
Units: percentage of participants				
number (confidence interval 95%)	80.0 (61.43 to 92.29)	80.0 (63.06 to 91.56)	75.0 (53.29 to 90.23)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Positive Response on Modified Treatment Benefit Scale (TBS) in Treatment Cycle 2

End point title	Percentage of Participants with Positive Response on Modified Treatment Benefit Scale (TBS) in Treatment Cycle 2

End point description:

The Modified TBS is a single-item scale which assesses the participant's condition (urinary problems, urinary incontinence) on a 4-point scale where 1 = greatly improved; 2 = improved; 3 = not changed; and 4 = worsened. A participant was considered to have a positive treatment response if they responded to the TBS question as either "greatly improved" or "improved". Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-treated Population included all participants enrolled into extension study who received >=1 BOTOX treatment over course of total evaluation period,starting from their first treatment in Study 120. Overall number of participants analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Week 6 in Treatment Cycle 2

End point values	Onabotulinumtoxin A 50 U (Treatment Cycle 2)	Onabotulinumtoxin A 100 U (Treatment Cycle 2)	Onabotulinumtoxin A 200 U (Treatment Cycle 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	42	30	
Units: percentage of participants				
number (confidence interval 95%)	75.0 (34.91 to 96.81)	97.6 (87.43 to 99.94)	83.3 (65.28 to 94.36)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Positive Response on Modified Treatment Benefit Scale (TBS) in Treatment Cycle 3

End point title	Percentage of Participants with Positive Response on Modified Treatment Benefit Scale (TBS) in Treatment Cycle 3

End point description:

The Modified TBS is a single-item scale which assesses the participant's condition (urinary problems, urinary incontinence) on a 4-point scale where 1 = greatly improved; 2 = improved; 3 = not changed; and 4 = worsened. A participant was considered to have a positive treatment response if they responded to the TBS question as either "greatly improved" or "improved". Data are summarized under the respective treatments that participants received in the corresponding treatment cycle. BOTOX-

treated Population included all participants enrolled into extension study who received >=1 BOTOX treatment over course of total evaluation period,starting from their first treatment in Study 120. Overall number of participants analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Week 6 in Treatment Cycle 3

End point values	OnabotulinumtoxinA 50 U (Treatment Cycle 3)	OnabotulinumtoxinA 100 U (Treatment Cycle 3)	OnabotulinumtoxinA 200 U (Treatment Cycle 3)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	15	33	
Units: percentage of participants				
number (confidence interval 95%)	100 (47.82 to 100.00)	80.0 (51.91 to 95.67)	84.8 (68.10 to 94.89)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First injection on Day 1 in Study 120 through the completion of Study 121 (Up to 108 Weeks)

Adverse event reporting additional description:

BOTOX-treated Population included all participants enrolled into the extension study who received at least 1 BOTOX treatment over the course of the total evaluation period, starting from their first treatment in Study 191622-120. Data are summarized under the respective treatments that participants received in the corresponding treatment cycles.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	OnabotulinumtoxinA 100 U (Treatment Cycle 1)

Reporting group description:

OnabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 1. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Reporting group title	OnabotulinumtoxinA 50 U (Treatment Cycle 1)

Reporting group description:

OnabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 1. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Reporting group title	OnabotulinumtoxinA 200 U (Treatment Cycle 1)

Reporting group description:

OnabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 1. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Reporting group title	OnabotulinumtoxinA 50 U (Treatment Cycle 2)

Reporting group description:

OnabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 2. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Reporting group title	OnabotulinumtoxinA 100 U (Treatment Cycle 2)

Reporting group description:

OnabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 2. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Reporting group title	OnabotulinumtoxinA 200 U (Treatment Cycle 2)

Reporting group description:

OnabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 2. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Reporting group title	OnabotulinumtoxinA 50 U (Treatment Cycle 3)

Reporting group description:

OnabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 3. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).

Reporting group title	OnabotulinumtoxinA 100 U (Treatment Cycle 3)
Reporting group description:	
OnabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 3. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).	

Reporting group title	OnabotulinumtoxinA 200 U (Treatment Cycle 3)
Reporting group description:	
OnabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 3. Participants were eligible for retreatment after Week 12 if qualified. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).	

Reporting group title	OnabotulinumtoxinA 50 U (Treatment Cycle 4)
Reporting group description:	
OnabotulinumtoxinA (botulinum toxin Type A) 50 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 4. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).	

Reporting group title	OnabotulinumtoxinA 100 U (Treatment Cycle 4)
Reporting group description:	
OnabotulinumtoxinA (botulinum toxin Type A) 100 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 4. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).	

Reporting group title	OnabotulinumtoxinA 200 U (Treatment Cycle 4)
Reporting group description:	
OnabotulinumtoxinA (botulinum toxin Type A) 200 U (not to exceed 6 U/kg) injected into the detrusor wall on Day 1 in Treatment Cycle 4. Blinded dose increases (one level) were allowed based on clinical response from cycle to cycle (not to exceed 6 U/kg).	

Serious adverse events	OnabotulinumtoxinA 100 U (Treatment Cycle 1)	OnabotulinumtoxinA 50 U (Treatment Cycle 1)	OnabotulinumtoxinA 200 U (Treatment Cycle 1)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 39 (7.69%)	2 / 31 (6.45%)	1 / 25 (4.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Arteriovenous fistula thrombosis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 31 (3.23%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			

subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hydrocephalus			
subjects affected / exposed	1 / 39 (2.56%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip deformity			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			

subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 39 (5.13%)	1 / 31 (3.23%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis viral			
subjects affected / exposed	1 / 39 (2.56%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial diarrhoea			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device malfunction			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	OnabotulinumtoxinA 50 U (Treatment Cycle 2)	OnabotulinumtoxinA 100 U (Treatment Cycle 2)	OnabotulinumtoxinA 200 U (Treatment Cycle 2)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	5 / 45 (11.11%)	6 / 36 (16.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Arteriovenous fistula thrombosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hydrocephalus			

subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip deformity			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			

subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	2 / 36 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis viral			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 9 (0.00%)	2 / 45 (4.44%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial diarrhoea			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			

subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device malfunction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	OnabotulinumtoxinA 50 U (Treatment Cycle 3)	OnabotulinumtoxinA 100 U (Treatment Cycle 3)	OnabotulinumtoxinA 200 U (Treatment Cycle 3)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	1 / 16 (6.25%)	2 / 34 (5.88%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Arteriovenous fistula thrombosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hydrocephalus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			

subjects affected / exposed	0 / 5 (0.00%)	1 / 16 (6.25%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip deformity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	2 / 34 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis viral			

subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device malfunction			

subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	OnabotulinumtoxinA 50 U (Treatment Cycle 4)	OnabotulinumtoxinA 100 U (Treatment Cycle 4)	OnabotulinumtoxinA 200 U (Treatment Cycle 4)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Arteriovenous fistula thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hydrocephalus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Psoriasis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip deformity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis viral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bacterial diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device malfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	OnabotulinumtoxinA 100 U (Treatment Cycle 1)	OnabotulinumtoxinA 50 U (Treatment Cycle 1)	OnabotulinumtoxinA 200 U (Treatment Cycle 1)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 39 (79.49%)	21 / 31 (67.74%)	16 / 25 (64.00%)
Investigations			
Blood urine present			
subjects affected / exposed	2 / 39 (5.13%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Protein urine present			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Eschar			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 39 (0.00%)	1 / 31 (3.23%)	0 / 25 (0.00%)
occurrences (all)	0	2	0
Skin laceration			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 39 (17.95%)	2 / 31 (6.45%)	2 / 25 (8.00%)
occurrences (all)	15	2	4
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	5 / 39 (12.82%)	1 / 31 (3.23%)	0 / 25 (0.00%)
occurrences (all)	7	1	0
Suprapubic pain			
subjects affected / exposed	0 / 39 (0.00%)	2 / 31 (6.45%)	1 / 25 (4.00%)
occurrences (all)	0	2	1
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	2 / 39 (5.13%)	2 / 31 (6.45%)	2 / 25 (8.00%)
occurrences (all)	8	3	2
Abdominal pain			
subjects affected / exposed	1 / 39 (2.56%)	2 / 31 (6.45%)	1 / 25 (4.00%)
occurrences (all)	1	2	2
Nausea			
subjects affected / exposed	0 / 39 (0.00%)	2 / 31 (6.45%)	0 / 25 (0.00%)
occurrences (all)	0	2	0
Vomiting			
subjects affected / exposed	2 / 39 (5.13%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Constipation			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Testicular retraction			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea	Additional description: Number of participants at risk in the OnabotulinumtoxinA 200 U (Treatment Cycle 2) arm group is based on the female population.		
subjects affected / exposed[1]	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 39 (2.56%)	2 / 31 (6.45%)	0 / 25 (0.00%)
occurrences (all)	1	3	0
Oropharyngeal pain			
subjects affected / exposed	2 / 39 (5.13%)	0 / 31 (0.00%)	1 / 25 (4.00%)
occurrences (all)	2	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 39 (0.00%)	1 / 31 (3.23%)	0 / 25 (0.00%)
occurrences (all)	0	1	0

Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 39 (2.56%)	2 / 31 (6.45%)	1 / 25 (4.00%)
occurrences (all)	1	3	1
Rash			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Leukocyturia			
subjects affected / exposed	3 / 39 (7.69%)	1 / 31 (3.23%)	3 / 25 (12.00%)
occurrences (all)	3	2	4
Haematuria			
subjects affected / exposed	1 / 39 (2.56%)	1 / 31 (3.23%)	1 / 25 (4.00%)
occurrences (all)	1	1	1
Hydronephrosis			
subjects affected / exposed	0 / 39 (0.00%)	2 / 31 (6.45%)	0 / 25 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 39 (5.13%)	1 / 31 (3.23%)	0 / 25 (0.00%)
occurrences (all)	2	1	0
Neck pain			
subjects affected / exposed	1 / 39 (2.56%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	13 / 39 (33.33%)	9 / 31 (29.03%)	5 / 25 (20.00%)
occurrences (all)	22	12	7
Bacteriuria			
subjects affected / exposed	7 / 39 (17.95%)	5 / 31 (16.13%)	5 / 25 (20.00%)
occurrences (all)	12	10	10
Pharyngitis			
subjects affected / exposed	4 / 39 (10.26%)	3 / 31 (9.68%)	0 / 25 (0.00%)
occurrences (all)	4	3	0
Nasopharyngitis			

subjects affected / exposed	1 / 39 (2.56%)	0 / 31 (0.00%)	4 / 25 (16.00%)
occurrences (all)	1	0	4
Gastroenteritis			
subjects affected / exposed	3 / 39 (7.69%)	1 / 31 (3.23%)	0 / 25 (0.00%)
occurrences (all)	3	2	0
Bronchitis			
subjects affected / exposed	3 / 39 (7.69%)	0 / 31 (0.00%)	1 / 25 (4.00%)
occurrences (all)	3	0	1
Cystitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Viral infection			
subjects affected / exposed	1 / 39 (2.56%)	1 / 31 (3.23%)	0 / 25 (0.00%)
occurrences (all)	1	1	0
Tinea capitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 31 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 39 (0.00%)	2 / 31 (6.45%)	1 / 25 (4.00%)
occurrences (all)	0	2	1
Asymptomatic bacteriuria			
subjects affected / exposed	2 / 39 (5.13%)	1 / 31 (3.23%)	0 / 25 (0.00%)
occurrences (all)	2	1	0
Influenza			
subjects affected / exposed	2 / 39 (5.13%)	0 / 31 (0.00%)	1 / 25 (4.00%)
occurrences (all)	2	0	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 39 (5.13%)	0 / 31 (0.00%)	1 / 25 (4.00%)
occurrences (all)	3	0	1

Non-serious adverse events	OnabotulinumtoxinA 50 U (Treatment Cycle 2)	OnabotulinumtoxinA 100 U (Treatment Cycle 2)	OnabotulinumtoxinA 200 U (Treatment Cycle 2)
Total subjects affected by non-serious adverse events			

subjects affected / exposed	7 / 9 (77.78%)	32 / 45 (71.11%)	27 / 36 (75.00%)
Investigations			
Blood urine present			
subjects affected / exposed	2 / 9 (22.22%)	4 / 45 (8.89%)	2 / 36 (5.56%)
occurrences (all)	2	4	2
Protein urine present			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Eschar			
subjects affected / exposed	1 / 9 (11.11%)	0 / 45 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Foot fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 9 (11.11%)	3 / 45 (6.67%)	2 / 36 (5.56%)
occurrences (all)	1	3	2
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 9 (0.00%)	6 / 45 (13.33%)	3 / 36 (8.33%)
occurrences (all)	0	9	3
Suprapubic pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 9 (11.11%)	2 / 45 (4.44%)	3 / 36 (8.33%)
occurrences (all)	1	2	3
Abdominal pain			

subjects affected / exposed	1 / 9 (11.11%)	3 / 45 (6.67%)	1 / 36 (2.78%)
occurrences (all)	1	3	1
Nausea			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	2 / 9 (22.22%)	2 / 45 (4.44%)	0 / 36 (0.00%)
occurrences (all)	2	4	0
Constipation			
subjects affected / exposed	0 / 9 (0.00%)	3 / 45 (6.67%)	0 / 36 (0.00%)
occurrences (all)	0	3	0
Reproductive system and breast disorders			
Testicular retraction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea	Additional description: Number of participants at risk in the OnabotulinumtoxinA 200 U (Treatment Cycle 2) arm group is based on the female population.		
subjects affected / exposed[1]	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	1 / 36 (2.78%)
occurrences (all)	0	1	1
Oropharyngeal pain			
subjects affected / exposed	0 / 9 (0.00%)	5 / 45 (11.11%)	0 / 36 (0.00%)
occurrences (all)	0	5	0
Rhinorrhoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Nasal congestion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0

Rash			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Leukocyturia			
subjects affected / exposed	2 / 9 (22.22%)	1 / 45 (2.22%)	3 / 36 (8.33%)
occurrences (all)	2	1	4
Haematuria			
subjects affected / exposed	1 / 9 (11.11%)	1 / 45 (2.22%)	0 / 36 (0.00%)
occurrences (all)	1	1	0
Hydronephrosis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 45 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 9 (11.11%)	22 / 45 (48.89%)	6 / 36 (16.67%)
occurrences (all)	1	33	8
Bacteriuria			
subjects affected / exposed	1 / 9 (11.11%)	9 / 45 (20.00%)	2 / 36 (5.56%)
occurrences (all)	1	15	3
Pharyngitis			
subjects affected / exposed	0 / 9 (0.00%)	3 / 45 (6.67%)	2 / 36 (5.56%)
occurrences (all)	0	3	2
Nasopharyngitis			
subjects affected / exposed	0 / 9 (0.00%)	2 / 45 (4.44%)	3 / 36 (8.33%)
occurrences (all)	0	2	3
Gastroenteritis			
subjects affected / exposed	2 / 9 (22.22%)	2 / 45 (4.44%)	0 / 36 (0.00%)
occurrences (all)	3	2	0

Bronchitis			
subjects affected / exposed	1 / 9 (11.11%)	1 / 45 (2.22%)	0 / 36 (0.00%)
occurrences (all)	1	1	0
Cystitis			
subjects affected / exposed	1 / 9 (11.11%)	1 / 45 (2.22%)	0 / 36 (0.00%)
occurrences (all)	1	1	0
Gastroenteritis viral			
subjects affected / exposed	1 / 9 (11.11%)	1 / 45 (2.22%)	0 / 36 (0.00%)
occurrences (all)	1	1	0
Viral infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Tinea capitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 45 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 9 (0.00%)	2 / 45 (4.44%)	0 / 36 (0.00%)
occurrences (all)	0	4	0
Asymptomatic bacteriuria			
subjects affected / exposed	1 / 9 (11.11%)	1 / 45 (2.22%)	0 / 36 (0.00%)
occurrences (all)	1	1	0
Influenza			
subjects affected / exposed	0 / 9 (0.00%)	4 / 45 (8.89%)	1 / 36 (2.78%)
occurrences (all)	0	4	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	2 / 45 (4.44%)	2 / 36 (5.56%)
occurrences (all)	0	4	3

Non-serious adverse events	OnabotulinumtoxinA 50 U (Treatment Cycle 3)	OnabotulinumtoxinA 100 U (Treatment Cycle 3)	OnabotulinumtoxinA 200 U (Treatment Cycle 3)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 5 (80.00%)	10 / 16 (62.50%)	19 / 34 (55.88%)
Investigations			
Blood urine present			
subjects affected / exposed	2 / 5 (40.00%)	1 / 16 (6.25%)	5 / 34 (14.71%)
occurrences (all)	2	1	5
Protein urine present			

subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Eschar			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 5 (0.00%)	1 / 16 (6.25%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	0 / 5 (0.00%)	1 / 16 (6.25%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 5 (40.00%)	0 / 16 (0.00%)	1 / 34 (2.94%)
occurrences (all)	2	0	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	3 / 34 (8.82%)
occurrences (all)	0	0	3
Suprapubic pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1

Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 16 (6.25%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Testicular retraction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea	Additional description: Number of participants at risk in the OnabotulinumtoxinA 200 U (Treatment Cycle 2) arm group is based on the female population.		
subjects affected / exposed[1]	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 16 (6.25%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 5 (0.00%)	1 / 16 (6.25%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			

Leukocyturia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Hydronephrosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	4 / 16 (25.00%)	6 / 34 (17.65%)
occurrences (all)	0	6	7
Bacteriuria			
subjects affected / exposed	0 / 5 (0.00%)	3 / 16 (18.75%)	4 / 34 (11.76%)
occurrences (all)	0	3	8
Pharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 16 (6.25%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 16 (6.25%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Bronchitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Cystitis			

subjects affected / exposed	0 / 5 (0.00%)	1 / 16 (6.25%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis viral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Tinea capitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Asymptomatic bacteriuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 16 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	OnabotulinumtoxinA 50 U (Treatment Cycle 4)	OnabotulinumtoxinA 100 U (Treatment Cycle 4)	OnabotulinumtoxinA 200 U (Treatment Cycle 4)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	2 / 4 (50.00%)	4 / 4 (100.00%)
Investigations			
Blood urine present			
subjects affected / exposed	2 / 3 (66.67%)	2 / 4 (50.00%)	2 / 4 (50.00%)
occurrences (all)	2	2	2
Protein urine present			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Procedural pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eschar			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Suprapubic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Constipation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Testicular retraction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Dysmenorrhoea	Additional description: Number of participants at risk in the OnabotulinumtoxinA 200 U (Treatment Cycle 2) arm group is based on the female population.		
subjects affected / exposed[1]	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Leukocyturia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Haematuria			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Bacteriuria			
subjects affected / exposed	2 / 3 (66.67%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tinea capitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Asymptomatic bacteriuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Number of subjects exposed in the OnabotulinumtoxinA 200 U (Treatment Cycle 2) arm group is based on the female population.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 October 2013	Amendment 1 - The following changes were implemented with Amendment 1: Provided clarifications and guidance to investigators regarding entry criteria, study procedures, and prohibited medications/treatments. In addition, the following procedures were added to the protocol: • Addition of renal function assessment [estimated glomerular filtration rate (eGFR)] • Added form for collecting 'Reason for Requesting Retreatment' at week 12 and later.
05 May 2016	Amendment 2 - The following changes were implemented with Amendment 1: Modified the inclusion criteria to change the minimum age to 5 years old from 8 years old and to include dosing information for a younger patient population. In addition, an update was made to the criteria which the investigator should consider when determining if a patient had a urinary track infection (UTI). According to the protocol, an adverse event of UTI was defined as 'a symptomatic UTI that required treatment in the opinion of the investigator'. The protocol also indicated that if urinalysis/culture results were reported which, in the opinion of the investigator, were considered clinically significant but did not fulfill the definition of UTI, the findings were to be recorded as adverse events (e.g., bacteriuria, leukocyturia). In addition, the investigator was required to describe the criteria used for qualifying 'leukocyturia' as an adverse event.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported