Clinical trial results:
Prospective, open-label, non-randomized, single-arm, multi-center dose titration study to investigate the safety and efficacy of NT 201 in subjects deemed to require total body doses of 800 U of NT 201 during the course of the study for the treatment of upper and lower limb spasticity of the same body side due to cerebral causes

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2010-020886-26
Trial protocol	DE ES PT IT
Global end of trial date	12 September 2014

Results information

Result version number	v1
This version publication date	16 July 2016
First version publication date	16 July 2016

Trial information

Trial identification

Sponsor protocol code	MRZ60201_3053_1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01603459
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merz Pharmaceuticals GmbH
Sponsor organisation address	Eckenheimer Landstrasse 100, Frankfurt/M, Germany, 60318
Public contact	Public Disclosure Manager, Merz Pharmaceuticals GmbH, clinicaltrials@merz.de
Scientific contact	Public Disclosure Manager, Merz Pharmaceuticals GmbH, clinicaltrials@merz.de

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 September 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 September 2014
Global end of trial reached?	Yes
Global end of trial date	12 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to determine whether injections with increasing doses (up to 800 units) of Botulinum toxin type A into muscles of the leg and/or arm are safe and effective in treating patients with spasticity on one body side due to cerebral causes.

Protection of trial subjects:

High medical and ethical standards were followed in accordance with Good Clinical Practice and other applicable regulations. In addition, an independent data monitoring committee was in charge of monitoring patient safety while the study was ongoing.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 May 2012
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	Canada: 3
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Germany: 45
Country: Number of subjects enrolled	Italy: 33
Country: Number of subjects enrolled	Norway: 7
Country: Number of subjects enrolled	Portugal: 18
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	United States: 18
Worldwide total number of subjects	155
EEA total number of subjects	134

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	115
From 65 to 84 years	40
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The clinical study was conducted at 30 sites located in Canada, France, Germany, Italy, Norway, Portugal, Spain, and the United States of America.

Pre-assignment

Screening details:

A total of 193 subjects were screened for the study, of which 155 were enrolled into the study. All enrolled subjects were treated with study drug according to the study protocol.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	IncobotulinumtoxinA (Xeomin) (up to 800 Units)

Arm description:

IncobotulinumtoxinA (Xeomin, also known as "NT 201" or "Botulinum toxin type A (150 kiloDalton), free from complexing proteins") (active ingredient: Clostridium Botulinum neurotoxin Type A free from complexing proteins) powder for solution for injection.
IncobotulinumtoxinA: Subjects to receive up to 3 injection cycle, with the dose titrated from 400 units to up to 800 units.
For each injection session: Solution prepared by reconstitution of powder with 0.9% Sodium Chloride (NaCl), 400-800 units, volume 2.0 mL per 100 units;
Mode of administration: Intramuscular injection.

Arm type	Experimental
Investigational medicinal product name	NT 201
Investigational medicinal product code	NT 201
Other name	Xeomin
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects to receive Intramuscular injection of solution prepared by reconstitution of powder with 0.9% Sodium Chloride (NaCl), 400-800 units, volume 2.0 mL per 100 units.

Number of subjects in period 1	IncobotulinumtoxinA (Xeomin) (up to 800 Units)
Started	155
Completed	137
Not completed	18
Consent withdrawn by subject	5
Adverse event, non-fatal	5
Non-compliance	1
Lost to follow-up	3
Predefined discontinuation criteria	3

Administrative reason	1

Baseline characteristics

Reporting groups	
Reporting group title	IncobotulinumtoxinA (Xeomin) (up to 800 Units)

Reporting group description:

IncobotulinumtoxinA (Xeomin, also known as "NT 201" or "Botulinum toxin type A (150 kiloDalton), free from complexing proteins") (active ingredient: Clostridium Botulinum neurotoxin Type A free from complexing proteins) powder for solution for injection.
IncobotulinumtoxinA: Subjects to receive up to 3 injection cycle, with the dose titrated from 400 units to up to 800 units.
For each injection session: Solution prepared by reconstitution of powder with 0.9% Sodium Chloride (NaCl), 400-800 units, volume 2.0 mL per 100 units;
Mode of administration: Intramuscular injection.

Reporting group values	IncobotulinumtoxinA (Xeomin) (up to 800 Units)	Total	
Number of subjects	155	155	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	115	115	
From 65-84 years	40	40	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	53.7		
standard deviation	± 13.1	-	
Gender, Male/Female Units: participants			
Female	51	51	
Male	104	104	

End points

End points reporting groups

Reporting group title	IncobotulinumtoxinA (Xeomin) (up to 800 Units)
Reporting group description:	
IncobotulinumtoxinA (Xeomin, also known as "NT 201" or "Botulinum toxin type A (150 kiloDalton), free from complexing proteins") (active ingredient: Clostridium Botulinum neurotoxin Type A free from complexing proteins) powder for solution for injection. IncobotulinumtoxinA: Subjects to receive up to 3 injection cycle, with the dose titrated from 400 units to up to 800 units. For each injection session: Solution prepared by reconstitution of powder with 0.9% Sodium Chloride (NaCl), 400-800 units, volume 2.0 mL per 100 units; Mode of administration: Intramuscular injection.	
Subject analysis set title	IncobotulinumtoxinA (Xeomin): Injection Cycle 1
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects to receive IncobotulinumtoxinA fixed total body dose of 400 units Intramuscular injection.	
Subject analysis set title	IncobotulinumtoxinA (Xeomin): Injection Cycle 2
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects to receive IncobotulinumtoxinA fixed total body dose of 600 units Intramuscular injection.	
Subject analysis set title	IncobotulinumtoxinA (Xeomin): Injection Cycle 3
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects to receive IncobotulinumtoxinA total body dose of 800 units Intramuscular injection.	
Subject analysis set title	IncobotulinumtoxinA (Xeomin): Injection Cycle 1 Baseline Visit
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects to receive IncobotulinumtoxinA fixed total body dose of 400 units Intramuscular injection.	
Subject analysis set title	IncobotulinumtoxinA(Xeomin): Injection Cycle 1 Control Visit 1
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects to receive IncobotulinumtoxinA fixed total body dose of 400 units Intramuscular injection.	
Subject analysis set title	IncobotulinumtoxinA (Xeomin): Injection Cycle 2 Baseline Visit
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects to receive IncobotulinumtoxinA fixed total body dose of 600 units Intramuscular injection.	
Subject analysis set title	IncobotulinumtoxinA(Xeomin): Injection Cycle 2 Control Visit 1
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects to receive IncobotulinumtoxinA fixed total body dose of 600 units Intramuscular injection.	
Subject analysis set title	IncobotulinumtoxinA (Xeomin): Injection Cycle 3 Baseline Visit
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects to receive IncobotulinumtoxinA total body dose of 800 units Intramuscular injection.	
Subject analysis set title	IncobotulinumtoxinA(Xeomin): Injection Cycle 3 Control Visit 1
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects to receive IncobotulinumtoxinA total body dose of 800 units Intramuscular injection.	

Primary: Occurrence of Treatment-Emergent Adverse Events (AEs), AEs of Special Interest (AESIs), and Serious AEs (SAEs) by Injection Cycle, Overall and Related to the Administration of Study Medication

End point title	Occurrence of Treatment-Emergent Adverse Events (AEs), AEs of Special Interest (AESIs), and Serious AEs (SAEs) by Injection Cycle, Overall and Related to the Administration of Study Medication[1]

End point description:

Treatment-emergent Adverse Events (TEASs) are events observed from the time point of first injection until 16 weeks after last injection. Values reported here refer to the number of subjects affected.

End point type	Primary

End point timeframe:

From baseline to week 36-48

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: No inferential statistical analyses were performed.

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	155	152	140	
Units: subjects				
Any TEAE	56	57	36	
Any related TEAE	7	8	4	
Any TEAE of special interest	6	8	7	
Any related TEAE of special interest	2	4	3	
Any serious TEAE	4	11	3	
Any related serious TEAE	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Investigator’s Global Assessment of Tolerability in subjects

End point title	Investigator’s Global Assessment of Tolerability in subjects[2]

End point description:

A 4-point Likert scale was used with the ratings 1 = very good, 2 = good, 3 = moderate, and 4 = poor.

End point type	Primary

End point timeframe:

Up to Week 48

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: No inferential statistical analyses were performed.

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	155	152	140	
Units: subjects				
Very good	121	111	117	
Good	29	26	20	
Moderate	3	3	1	
Poor	0	2	0	
Missing	2	10	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Ashworth Scale (AS) Scores of the Target Joint Selected at Study Baseline Visit

End point title	Ashworth Scale (AS) Scores of the Target Joint Selected at Study Baseline Visit

End point description:

The AS is a well known and commonly used scale in clinical trials with spasticity. It was considered to be the best clinical tool for measuring resistance to movement. It was used to categorize the severity of spasticity by judging resistance to passive movement. It is a 5-point scale that ranges from 0 (=no increase in tone) to 4 (=limb rigid in flexion or extension).

End point type	Secondary

End point timeframe:

From Cycle Baseline to Week 4 of Each Cycle

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1 Baseline Visit	IncobotulinumtoxinA(Xeomin) : Injection Cycle 1 Control Visit 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2 Baseline Visit	IncobotulinumtoxinA(Xeomin) : Injection Cycle 2 Control Visit 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	154	154	151	148
Units: units on a scale				
arithmetic mean (standard deviation)	3 (± 0.7)	2.1 (± 0.9)	2.7 (± 0.7)	2 (± 0.9)

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 3 Baseline Visit	IncobotulinumtoxinA(Xeomin) : Injection Cycle 3 Control Visit 1		

Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	140	138		
Units: units on a scale				
arithmetic mean (standard deviation)	2.6 (± 0.8)	1.7 (± 1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Ashworth Scale (AS) Score of the Target Joint Selected at Study Baseline Visit From Injection Cycle Baseline Visits to Respective Control Visits

End point title	Change of Ashworth Scale (AS) Score of the Target Joint Selected at Study Baseline Visit From Injection Cycle Baseline Visits to Respective Control Visits

End point description:

The AS is a well known and commonly used scale in clinical trials with spasticity. It was considered to be the best clinical tool for measuring resistance to movement. It was used to categorize the severity of spasticity by judging resistance to passive movement. It is a 5-point scale that ranges from 0 (=no increase in tone) to 4 (=limb rigid in flexion or extension).

End point type	Secondary

End point timeframe:

From Cycle Baseline to Week 4 of Each Cycle

End point values	Incobotulinumtoxin A (Xeomin): Injection Cycle 1	Incobotulinumtoxin A (Xeomin): Injection Cycle 2	Incobotulinumtoxin A (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	154	148	138	
Units: units on a scale				
arithmetic mean (standard deviation)	-0.8 (± 0.9)	-0.8 (± 0.8)	-0.9 (± 0.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Ashworth Scale (AS) Score of the Target Joint Selected at Study Baseline Visit From Study Baseline Visit to Control Visits of Injection Cycles

End point title	Change of Ashworth Scale (AS) Score of the Target Joint Selected at Study Baseline Visit From Study Baseline Visit to Control Visits of Injection Cycles

End point description:

The AS is a well known and commonly used scale in clinical trials with spasticity. It was considered to be the best clinical tool for measuring resistance to movement. It was used to categorize the severity of spasticity by judging resistance to passive movement. It is a 5-point scale that ranges from 0 (=no increase in tone) to 4 (=limb rigid in flexion or extension).

End point type	Secondary

End point timeframe:

From Study Baseline to Week 4, 16-20 and 28-36

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	154	148	138	
Units: units on a scale				
arithmetic mean (standard deviation)	-0.8 (± 0.9)	-1 (± 0.9)	-1.3 (± 1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Ashworth Scale (AS) Score of the Target Joint Selected at Study Baseline Visit from Study Baseline Visit to Injection Cycle Baseline Visits and End of Study Visit

End point title	Change of Ashworth Scale (AS) Score of the Target Joint Selected at Study Baseline Visit from Study Baseline Visit to Injection Cycle Baseline Visits and End of Study Visit

End point description:

The AS is a well known and commonly used scale in clinical trials with spasticity. It was considered to be the best clinical tool for measuring resistance to movement. It was used to categorize the severity of spasticity by judging resistance to passive movement. It is a 5-point scale that ranges from 0 (=no increase in tone) to 4 (=limb rigid in flexion or extension).

End point type	Secondary

End point timeframe:

From Study Baseline to Week 12-16, 24-32 and 36-48

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	151	140	137	
Units: units on a scale				
arithmetic mean (standard deviation)	-0.2 (± 0.7)	-0.3 (± 0.8)	-0.7 (± 0.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Ashworth Scale (AS) Scores of Every Joint Affected by Clinical Patterns of Spasticity

End point title	Ashworth Scale (AS) Scores of Every Joint Affected by Clinical Patterns of Spasticity

End point description:

Clinical pattern treated at corresponding cycle of the same body side as the selected target joint. The AS is a well known and commonly used scale in clinical trials with spasticity. It was considered to be the best clinical tool for measuring resistance to movement. It was used to categorize the severity of spasticity by judging resistance to passive movement. It is a 5-point scale that ranges from 0 (=no increase in tone) to 4 (=limb rigid in flexion or extension). Internally rotated/extended/adducted shoulder (n= 52, 52, 69, 68, 84, 83). Here, "n" is number of subjects analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

From Cycle Baseline to Week 4 of Each Cycle

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1 Baseline Visit	IncobotulinumtoxinA(Xeomin) : Injection Cycle 1 Control Visit 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2 Baseline Visit	IncobotulinumtoxinA(Xeomin) : Injection Cycle 2 Control Visit 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	155	155	152	152
Units: units on a scale				
arithmetic mean (standard deviation)				
Internally rotated/extended/adducted shoulder	2.7 (± 0.6)	2.2 (± 0.8)	2.5 (± 0.8)	2 (± 0.9)
Flexed elbow (n= 117, 117, 122, 121, 124, 122)	2.6 (± 0.7)	1.9 (± 0.9)	2.4 (± 0.7)	1.7 (± 0.9)
Extended elbow (n= 11, 11, 16, 15, 19, 19)	2.7 (± 0.5)	1.8 (± 0.9)	2.5 (± 0.6)	2.1 (± 0.7)
Pronated forearm (n= 37, 37, 50, 50, 48, 47)	2.7 (± 0.7)	1.6 (± 0.9)	2.4 (± 0.8)	1.7 (± 1)
Flexed wrist (n= 84, 84, 87, 85, 91, 90)	2.7 (± 0.8)	1.8 (± 1)	2.4 (± 0.9)	1.5 (± 1)
Clenched fist (n= 96, 96, 110, 108, 110, 108)	2.9 (± 0.7)	2 (± 0.9)	2.7 (± 0.8)	1.8 (± 0.9)
Thumb in palm (n= 53, 53, 63, 61, 65, 63)	2.4 (± 0.9)	1.5 (± 1.1)	2.3 (± 0.9)	1.4 (± 1)
Flexed hip (n= 0, 0, 0, 0, 6, 5)	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Adducted thigh (n= 4, 4, 7, 7, 7, 7)	1.8 (± 0.5)	1.5 (± 0.6)	2 (± 1.2)	1.9 (± 0.9)
Internally rotated hip (n= 1, 1, 2, 2, 3, 3)	3 (± 99999)	2 (± 99999)	2 (± 1.4)	2 (± 1.4)
Flexed knee (n= 12, 12, 24, 23, 32, 32)	2.4 (± 0.7)	2 (± 0.7)	2.4 (± 0.6)	1.8 (± 0.7)
Extended knee (n= 11, 11, 22, 21, 27, 26)	2.6 (± 0.7)	2.3 (± 0.9)	2.1 (± 0.8)	1.8 (± 0.9)
Pes equinovarus (n= 88, 88, 117, 115, 122, 120)	2.8 (± 0.7)	2.1 (± 0.9)	2.6 (± 0.8)	1.9 (± 1)
Pes equinovalgus (n= 5, 5, 10, 10, 8, 8)	2.8 (± 0.4)	2.4 (± 1.3)	2.6 (± 0.8)	1.9 (± 0.7)
Extended hallux (n= 10, 10, 10, 10, 20, 19)	1.7 (± 1.1)	0.9 (± 0.7)	1.8 (± 0.8)	0.9 (± 0.7)
Flexed toes (n= 27, 27, 34, 34, 45, 45)	1.8 (± 0.9)	1.3 (± 0.8)	1.6 (± 0.9)	1.1 (± 0.8)

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 3 Baseline Visit	IncobotulinumtoxinA(Xeomin) : Injection Cycle 3 Control Visit 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	140	140		
Units: units on a scale				
arithmetic mean (standard deviation)				
Internally rotated/extended/adducted shoulder	2.5 (± 0.8)	1.9 (± 0.9)		
Flexed elbow (n= 117, 117, 122, 121, 124, 122)	2.4 (± 0.8)	1.4 (± 0.9)		
Extended elbow (n= 11, 11, 16, 15, 19, 19)	2.6 (± 0.6)	1.7 (± 0.8)		
Pronated forearm (n= 37, 37, 50, 50, 48, 47)	2.5 (± 0.7)	1.4 (± 0.8)		
Flexed wrist (n= 84, 84, 87, 85, 91, 90)	2.4 (± 0.8)	1.4 (± 1)		
Clenched fist (n= 96, 96, 110, 108, 110, 108)	2.5 (± 0.7)	1.5 (± 0.9)		
Thumb in palm (n= 53, 53, 63, 61, 65, 63)	2.2 (± 0.8)	1.3 (± 1)		
Flexed hip (n= 0, 0, 0, 0, 6, 5)	1.8 (± 0.8)	1.4 (± 0.9)		
Adducted thigh (n= 4, 4, 7, 7, 7, 7)	2.3 (± 0.8)	2 (± 0.6)		
Internally rotated hip (n= 1, 1, 2, 2, 3, 3)	2.7 (± 0.6)	1.7 (± 0.6)		
Flexed knee (n= 12, 12, 24, 23, 32, 32)	2.5 (± 0.7)	1.8 (± 1)		
Extended knee (n= 11, 11, 22, 21, 27, 26)	2.2 (± 0.8)	1.5 (± 0.8)		
Pes equinovarus (n= 88, 88, 117, 115, 122, 120)	2.5 (± 0.8)	1.6 (± 0.9)		
Pes equinovalgus (n= 5, 5, 10, 10, 8, 8)	2.3 (± 0.9)	2 (± 1.1)		
Extended hallux (n= 10, 10, 10, 10, 20, 19)	1.9 (± 0.9)	1.1 (± 0.8)		
Flexed toes (n= 27, 27, 34, 34, 45, 45)	1.9 (± 0.9)	1.1 (± 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Ashworth Scale (AS) Score of Every Joint Affected by Clinical Patterns of Spasticity From Injection Cycle Baseline Visits to Respective Control Visits

End point title	Change of Ashworth Scale (AS) Score of Every Joint Affected by Clinical Patterns of Spasticity From Injection Cycle Baseline Visits to Respective Control Visits

End point description:

Clinical pattern treated at corresponding cycle of the same body side as the selected target joint. The AS is a well known and commonly used scale in clinical trials with spasticity. It was considered to be the best clinical tool for measuring resistance to movement. It was used to categorize the severity of spasticity by judging resistance to passive movement. It is a 5-point scale that ranges from 0 (=no

increase in tone) to 4 (=limb rigid in flexion or extension). Internally rotated/extended/adducted shoulder (n= 52, 68, 83). Here, "n" is number of subjects analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

From Cycle Baseline to Week 4 of Each Cycle

End point values	Incobotulinumtoxin A (Xeomin): Injection Cycle 1 Baseline Visit	Incobotulinumtoxin A (Xeomin): Injection Cycle 2 Baseline Visit	Incobotulinumtoxin A (Xeomin): Injection Cycle 3 Baseline Visit	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	155	152	140	
Units: units on a scale				
arithmetic mean (standard deviation)				
Internally rotated/extended/adducted shoulder	-0.5 (± 0.8)	-0.6 (± 0.8)	-0.5 (± 0.8)	
Flexed elbow (n= 117, 121, 122)	-0.7 (± 0.8)	-0.7 (± 0.8)	-0.9 (± 0.9)	
Extended elbow (n= 11, 15, 19)	-0.9 (± 0.8)	-0.5 (± 0.9)	-0.8 (± 0.8)	
Pronated forearm (n= 37, 50, 47)	-1.1 (± 0.6)	-0.7 (± 0.7)	-1 (± 0.8)	
Flexed wrist (n= 84, 85, 90)	-0.9 (± 0.8)	-0.9 (± 0.8)	-1 (± 0.9)	
Clenched fist (n= 96, 108, 108)	-0.9 (± 0.8)	-0.9 (± 0.8)	-1.1 (± 0.8)	
Thumb in palm (n= 53, 61, 63)	-0.9 (± 1)	-0.9 (± 1.1)	-0.9 (± 1)	
Flexed hip (n= 0, 0, 5)	0 (± 0)	0 (± 0)	-0.4 (± 0.9)	
Adducted thigh (n= 4, 7, 7)	-0.3 (± 0.5)	-0.1 (± 0.7)	-0.3 (± 0.5)	
Internally rotated hip (n= 1, 2, 3)	-1 (± 99999)	0 (± 0)	-1 (± 1)	
Flexed knee (n= 12, 23, 32)	-0.4 (± 0.5)	-0.6 (± 0.6)	-0.8 (± 0.9)	
Extended knee (n= 11, 21, 26)	-0.4 (± 0.5)	-0.4 (± 0.7)	-0.7 (± 0.9)	
Pes equinovarus (n= 88, 115, 120)	-0.7 (± 0.8)	-0.7 (± 0.8)	-0.8 (± 0.8)	
Pes equinovalgus (n= 5, 10, 8)	-0.4 (± 1.1)	-0.7 (± 0.7)	-0.3 (± 0.7)	
Extended hallux (n= 10, 10, 19)	-0.8 (± 0.9)	-0.9 (± 1)	-0.8 (± 1.3)	
Flexed toes (n= 27, 34, 45)	-0.5 (± 0.8)	-0.5 (± 0.8)	-0.8 (± 0.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Ashworth Scale (AS) Score of Every Joint Affected by Clinical Patterns of Spasticity From Study Baseline Visit to Control Visits of Injection Cycles

End point title	Change of Ashworth Scale (AS) Score of Every Joint Affected by Clinical Patterns of Spasticity From Study Baseline Visit to Control Visits of Injection Cycles

End point description:

Clinical pattern treated at corresponding cycle of the same body side as the selected target joint. The AS is a well known and commonly used scale in clinical trials with spasticity. It was considered to be the best clinical tool for measuring resistance to movement. It was used to categorize the severity of spasticity by judging resistance to passive movement. It is a 5-point scale that ranges from 0 (=no increase in tone) to 4 (=limb rigid in flexion or extension). Internally rotated/extended/adducted shoulder (n= 52, 68, 83). Here, "n" is number of subjects analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

From Study Baseline to Week 4, 16-20 and 28-36

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	155	152	140	
Units: units on a scale				
arithmetic mean (standard deviation)				
Internally rotated/extended/adducted shoulder	-0.5 (± 0.8)	-0.6 (± 0.9)	-0.5 (± 1)	
Flexed elbow (n= 117, 121, 122)	-0.7 (± 0.8)	-0.9 (± 0.8)	-1.2 (± 0.9)	
Extended elbow (n= 11, 15, 19)	-0.9 (± 0.8)	-0.7 (± 0.8)	-0.9 (± 1)	
Pronated forearm (n= 37, 50, 47)	-1.1 (± 0.6)	-1 (± 0.9)	-1.1 (± 0.9)	
Flexed wrist (n= 84, 85, 90)	-0.9 (± 0.8)	-1.1 (± 0.9)	-1.2 (± 1.1)	
Clenched fist (n= 96, 108, 108)	-0.9 (± 0.8)	-1.1 (± 0.9)	-1.4 (± 0.9)	
Thumb in palm (n= 53, 61, 63)	-0.9 (± 1)	-1 (± 1.2)	-1.1 (± 1.3)	
Flexed hip (n= 0, 0, 5)	0 (± 0)	0 (± 0)	-0.6 (± 1.5)	
Adducted thigh (n= 4, 7, 7)	-0.3 (± 0.5)	-0.1 (± 0.7)	-0.6 (± 0.8)	
Internally rotated hip (n= 1, 2, 3)	-1 (± 99999)	-0.5 (± 0.7)	-0.7 (± 1.5)	
Flexed knee (n= 12, 23, 32)	-0.4 (± 0.5)	-0.4 (± 0.8)	-0.4 (± 1.2)	
Extended knee (n= 11, 21, 26)	-0.4 (± 0.5)	-0.4 (± 0.6)	-0.6 (± 0.6)	
Pes equinovarus (n= 88, 115, 120)	-0.7 (± 0.8)	-0.8 (± 0.9)	-1.1 (± 0.9)	
Pes equinovalgus (n= 5, 10, 8)	-0.4 (± 1.1)	-0.9 (± 0.6)	-0.4 (± 0.7)	
Extended hallux (n= 10, 10, 19)	-0.8 (± 0.9)	-0.9 (± 1.1)	-0.2 (± 1.3)	
Flexed toes (n= 27, 34, 45)	-0.5 (± 0.8)	-0.5 (± 0.7)	-0.6 (± 0.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Ashworth Scale (AS) Score of Every Joint Affected by Clinical Patterns of Spasticity From Study Baseline Visit to Injection Cycle Baseline Visits and End of Study Visit

End point title	Change of Ashworth Scale (AS) Score of Every Joint Affected by Clinical Patterns of Spasticity From Study Baseline Visit to Injection Cycle Baseline Visits and End of Study Visit

End point description:

Clinical pattern treated at corresponding cycle of the same body side as the selected target joint. The AS is a well known and commonly used scale in clinical trials with spasticity. It was considered to be the best clinical tool for measuring resistance to movement. It was used to categorize the severity of spasticity by judging resistance to passive movement. It is a 5-point scale that ranges from 0 (=no increase in tone) to 4 (=limb rigid in flexion or extension). Internally rotated/extended/adducted shoulder (n= 69, 84, 82). Here, "n" is number of subjects analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

From Study Baseline to Week 12-16, 24-32 and 36-48

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	155	152	140	
Units: units on a scale				
arithmetic mean (standard deviation)				
Internally rotated/extended/adducted shoulder	0 (± 0.7)	0 (± 0.9)	-0.3 (± 0.9)	
Flexed elbow (n= 122, 124, 121)	-0.2 (± 0.7)	-0.3 (± 0.8)	-0.8 (± 0.9)	
Extended elbow (n= 16, 19, 18)	-0.2 (± 0.7)	-0.1 (± 0.9)	-0.2 (± 0.8)	
Pronated forearm (n= 50, 48, 47)	-0.3 (± 0.9)	-0.1 (± 0.7)	-0.7 (± 1)	
Flexed wrist (n= 87, 91, 89)	-0.2 (± 0.7)	-0.2 (± 1)	-0.7 (± 1)	
Clenched fist (n= 110, 110, 108)	-0.2 (± 0.7)	-0.3 (± 0.7)	-0.8 (± 0.9)	
Thumb in palm (n= 63, 65, 64)	-0.2 (± 0.9)	-0.3 (± 0.9)	-0.8 (± 1.1)	
Flexed hip (n= 0, 6, 6)	0 (± 0)	-0.2 (± 1)	-0.3 (± 1.4)	
Adducted thigh (n= 7, 7, 7)	0 (± 0)	-0.3 (± 0.5)	-0.4 (± 0.8)	
Internally rotated hip (n= 2, 3, 3)	-0.5 (± 0.7)	0.3 (± 0.6)	0 (± 1)	
Flexed knee (n= 24, 32, 32)	0.1 (± 0.9)	0.4 (± 1.2)	-0.4 (± 1.1)	
Extended knee (n= 22, 27, 25)	-0.1 (± 0.4)	0.1 (± 0.5)	-0.4 (± 0.7)	
Pes equinovarus (n= 117, 122, 119)	-0.1 (± 0.6)	-0.2 (± 0.7)	-0.7 (± 0.9)	
Pes equinovalgus (n= 10, 8, 7)	-0.2 (± 0.4)	-0.1 (± 0.6)	-0.4 (± 0.5)	
Extended hallux (n= 10, 20, 20)	0 (± 1.2)	0.6 (± 1.3)	-0.2 (± 1)	
Flexed toes (n= 34, 45, 45)	0 (± 0.7)	0.2 (± 0.7)	-0.4 (± 0.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Resistance to Passive Movement Scale (REPAS) Scores of Treated Side

End point title	Resistance to Passive Movement Scale (REPAS) Scores of Treated Side

End point description:

The REPAS is a summary 26-item test used to assess resistance to passive movement in all four limbs of the body. It provides a global evaluation of spasticity status, as well as per hemibody and per limb. 16 items describe the condition of both upper limbs, 10 that of both lower limbs. Each item is rated by using the Ashworth Scale. The sum of the values represent the REPAS score which may range from zero (no resistance for any item) to 104 (limbs rigid for all items). Here, the hemi-REPAS was evaluated, that is, the maximum value for the treated body side was 52.

End point type	Secondary

End point timeframe:

From Cycle Baseline to Week 4 of Each Cycle

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1 Baseline Visit	IncobotulinumtoxinA(Xeomin) : Injection Cycle 1 Control Visit 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2 Baseline Visit	IncobotulinumtoxinA(Xeomin) : Injection Cycle 2 Control Visit 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	155	155	152	149
Units: units on a scale				
arithmetic mean (standard deviation)	24.8 (± 6.7)	20.2 (± 7.1)	24 (± 7)	18.1 (± 7.6)

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 3 Baseline Visit	IncobotulinumtoxinA(Xeomin) : Injection Cycle 3 Control Visit 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	140	138		
Units: units on a scale				
arithmetic mean (standard deviation)	22.9 (± 7.2)	15.7 (± 7.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Resistance to Passive Movement Scale (REPAS) Score of Treated Side From Injection Cycle Baseline Visits to Respective Control Visits

End point title	Change of Resistance to Passive Movement Scale (REPAS) Score of Treated Side From Injection Cycle Baseline Visits to Respective Control Visits

End point description:

The REPAS is a summary 26-item test used to assess resistance to passive movement in all four limbs of the body. It provides a global evaluation of spasticity status, as well as per hemibody and per limb. 16 items describe the condition of both upper limbs, 10 that of both lower limbs. Each item is rated by using the Ashworth Scale. The sum of the values represent the REPAS score which may range from zero (no resistance for any item) to 104 (limbs rigid for all items).

End point type	Secondary

End point timeframe:

From Cycle Baseline to Week 4 of Each Cycle

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	155	149	138	
Units: units on a scale				
arithmetic mean (standard deviation)	-4.6 (± 3.9)	-5.9 (± 4.2)	-7.1 (± 4.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Resistance to Passive Movement Scale (REPAS) Score of Treated Side From Study Baseline Visit to Control Visits of Injection Cycles

End point title	Change of Resistance to Passive Movement Scale (REPAS) Score of Treated Side From Study Baseline Visit to Control Visits of Injection Cycles

End point description:

The REPAS is a summary 26-item test used to assess resistance to passive movement in all four limbs of the body. It provides a global evaluation of spasticity status, as well as per hemibody and per limb. 16 items describe the condition of both upper limbs, 10 that of both lower limbs. Each item is rated by using the Ashworth Scale. The sum of the values represent the REPAS score which may range from zero (no resistance for any item) to 104 (limbs rigid for all items).

End point type	Secondary

End point timeframe:

From Study Baseline to Week 4, 16-20 and 28-36

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	155	149	138	
Units: units on a scale				
arithmetic mean (standard deviation)	-4.6 (± 3.9)	-6.7 (± 4.6)	-9 (± 5.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Resistance to Passive Movement Scale (REPAS) Score of Treated Side From Study Baseline Visit to Injection Cycle Baseline Visits and End of Study Visit

End point title	Change of Resistance to Passive Movement Scale (REPAS) Score of Treated Side From Study Baseline Visit to Injection Cycle Baseline Visits and End of Study Visit

End point description:

The REPAS is a summary 26-item test used to assess resistance to passive movement in all four limbs of the body. It provides a global evaluation of spasticity status, as well as per hemibody and per limb. 16 items describe the condition of both upper limbs, 10 that of both lower limbs. Each item is rated by using the Ashworth Scale. The sum of the values represent the REPAS score which may range from zero (no resistance for any item) to 104 (limbs rigid for all items).

End point type	Secondary

End point timeframe:

From Study Baseline to Week 12-16, 24-32 and 36-48

End point values	Incobotulinumtoxin A (Xeomin): Injection Cycle 1	Incobotulinumtoxin A (Xeomin): Injection Cycle 2	Incobotulinumtoxin A (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	152	140	137	
Units: units on a scale				
arithmetic mean (standard deviation)	-0.8 (± 4.2)	-1.9 (± 4.7)	-5.5 (± 5.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Functional Ambulation Classification (FAC) Scale Scores

End point title	Functional Ambulation Classification (FAC) Scale Scores

End point description:

The FAC examines the independence and ambulation of subjects whereby supervision/physical assistance from 1 person is allowed. Subjects are classified to following categories: Level 0: no functional ambulation; Level 1: Ambulator-dependent for physical assistance (Level II); Level 2: Ambulator-dependent for physical assistance (Level I); Level 3: Ambulator-dependent for supervision; Level 4: Ambulator-independent, level surface only; Level 5: Ambulator-independent.

End point type	Secondary

End point timeframe:

From Cycle Baseline to Week 4 of Each Cycle

End point values	Incobotulinumtoxin A (Xeomin): Injection Cycle 1 Baseline Visit	Incobotulinumtoxin A(Xeomin) : Injection Cycle 1 Control Visit 1	Incobotulinumtoxin A (Xeomin): Injection Cycle 2 Baseline Visit	Incobotulinumtoxin A(Xeomin) : Injection Cycle 2 Control Visit 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	155	155	152	149
Units: units on a scale				
arithmetic mean (standard deviation)	3.5 (± 1.4)	3.7 (± 1.3)	3.7 (± 1.3)	3.8 (± 1.3)

End point values	Incobotulinumtoxin A (Xeomin): Injection Cycle 3 Baseline Visit	Incobotulinumtoxin A(Xeomin) : Injection Cycle 3 Control Visit		

		1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	140	138		
Units: units on a scale				
arithmetic mean (standard deviation)	3.8 (± 1.3)	3.9 (± 1.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Functional Ambulation Classification (FAC) Score From Injection Cycle Baseline Visits to Respective Control Visits

End point title	Change of Functional Ambulation Classification (FAC) Score From Injection Cycle Baseline Visits to Respective Control Visits

End point description:

The FAC examines the independence and ambulation of subjects whereby supervision/physical assistance from 1 person is allowed. Subjects are classified to following categories: Level 0: no functional ambulation; Level 1: Ambulator-dependent for physical assistance (Level II); Level 2: Ambulator-dependent for physical assistance (Level I); Level 3: Ambulator-dependent for supervision; Level 4: Ambulator-independent, level surface only; Level 5: Ambulator-independent.

End point type	Secondary

End point timeframe:

From Cycle Baseline to Week 4 of Each Cycle

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	155	149	138	
Units: units on a scale				
arithmetic mean (standard deviation)	0.1 (± 0.5)	0.1 (± 0.4)	0.1 (± 0.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Functional ambulation classification (FAC) Score From Study Baseline Visit to Control Visits of Injection Cycles

End point title	Change of Functional ambulation classification (FAC) Score From Study Baseline Visit to Control Visits of Injection Cycles

End point description:

The FAC examines the independence and ambulation of subjects whereby supervision/physical assistance from 1 person is allowed. Subjects are classified to following categories: Level 0: no functional ambulation; Level 1: Ambulator-dependent for physical assistance (Level II); Level 2: Ambulator-dependent for physical assistance (Level I); Level 3: Ambulator-dependent for supervision; Level 4: Ambulator-independent, level surface only; Level 5: Ambulator-independent.

End point type	Secondary

End point timeframe:

From Study Baseline to Week 4, 16-20 and 28-36

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	155	149	138	
Units: units on a scale				
arithmetic mean (standard deviation)	0.1 (± 0.5)	0.3 (± 0.6)	0.4 (± 0.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Functional Ambulation Classification (FAC) Score From Study Baseline Visit to Injection Cycle Baseline Visits and End of Study Visit

End point title	Change of Functional Ambulation Classification (FAC) Score From Study Baseline Visit to Injection Cycle Baseline Visits and End of Study Visit

End point description:

The FAC examines the independence and ambulation of subjects whereby supervision/physical assistance from 1 person is allowed. Subjects are classified to following categories: Level 0: no functional ambulation; Level 1: Ambulator-dependent for physical assistance (Level II); Level 2: Ambulator-dependent for physical assistance (Level I); Level 3: Ambulator-dependent for supervision; Level 4: Ambulator-independent, level surface only; Level 5: Ambulator-independent.

End point type	Secondary

End point timeframe:

From Study Baseline to Week 12-16, 24-32 and 36-48

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	152	140	137	
Units: units on a scale				
arithmetic mean (standard deviation)	0.2 (± 0.5)	0.3 (± 0.6)	0.4 (± 0.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Global Attainment Scale (GAS) Scores for Upper and Lower Limb, Respectively

End point title	Global Attainment Scale (GAS) Scores for Upper and Lower Limb, Respectively

End point description:

Change from respective injection cycle baseline visit. GAS measures the extent to which a subject's individual goals are achieved in the course of intervention. Subject and treating team have to identify 2 personal goals for each treated limb at each injection cycle. Investigator rates the GAS score for each injection cycle. Each goal is rated on a 5-point scale, with degree of attainment captured for each goal area: -2 = a lot less than expected; -1 = a little less than expected; 0 = expected level of achievement; +1 = a little better than expected; +2 = a lot better than expected. The GAS score at injection cycle baseline is always set as -1. Here, "n" is number of subjects analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

From Cycle Baseline Visit to Week 12-16, 24-32 and 36-48

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	140	138	135	
Units: units on a scale				
arithmetic mean (standard deviation)				
Upper limb (n= 140, 138, 135)	7.178 (± 9.254)	10.601 (± 9.211)	13.028 (± 8.765)	
Lower limb (n= 105, 126, 130)	8.222 (± 9.649)	10.914 (± 9.251)	13.579 (± 10.196)	

Statistical analyses

No statistical analyses for this end point

Secondary: Disability Assessment Scale (DAS) Scores in a Selected Principal Therapeutic Target Domain Affecting the Upper Limb

End point title	Disability Assessment Scale (DAS) Scores in a Selected Principal Therapeutic Target Domain Affecting the Upper Limb

End point description:

The Disability Assessment Scale consists of the four domains hygiene, dressing, limb position, and pain which are assessed on a 4-point scale with the values 0 (=no disability), 1 (=mild disability), 2 (=moderate disability), and 3 (=severe disability). One of the domains will be selected per injection cycle.

End point type	Secondary

End point timeframe:

From Cycle Baseline to Week 4 of Each Cycle

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1 Baseline Visit	IncobotulinumtoxinA(Xeomin): Injection Cycle 1 Control Visit 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2 Baseline Visit	IncobotulinumtoxinA(Xeomin): Injection Cycle 2 Control Visit 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	143	143	151	143
Units: units on a scale				
arithmetic mean (standard deviation)	2.6 (± 0.5)	2 (± 0.7)	2.4 (± 0.6)	1.7 (± 0.7)

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 3 Baseline Visit	IncobotulinumtoxinA(Xeomin): Injection Cycle 3 Control Visit 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	140	128		
Units: units on a scale				
arithmetic mean (standard deviation)	2.2 (± 0.6)	1.5 (± 0.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Disability Assessment Scale (DAS) Score in a Selected Principal Therapeutic Target Domain Affecting the Upper Limb From Injection Cycle Baseline Visits to Respective Control Visits

End point title	Change of Disability Assessment Scale (DAS) Score in a Selected Principal Therapeutic Target Domain Affecting the Upper Limb From Injection Cycle Baseline Visits to Respective Control Visits

End point description:

The Disability Assessment Scale consists of the four domains hygiene, dressing, limb position, and pain which are assessed on a 4-point scale with the values 0 (=no disability), 1 (=mild disability), 2 (=moderate disability), and 3 (=severe disability). One of the domains will be selected per injection cycle.

End point type	Secondary

End point timeframe:

Week 4 of Each Cycle

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	143	143	128	
Units: units on a scale				
arithmetic mean (standard deviation)	-0.6 (± 0.7)	-0.7 (± 0.7)	-0.7 (± 0.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Disability Assessment Scale (DAS) Score in a Selected Principal Therapeutic Target Domain Affecting the Upper Limb From Study Baseline Visit to Control Visits of Injection Cycles

End point title	Change of Disability Assessment Scale (DAS) Score in a Selected Principal Therapeutic Target Domain Affecting the Upper Limb From Study Baseline Visit to Control Visits of Injection Cycles

End point description:

The Disability Assessment Scale consists of the four domains hygiene, dressing, limb position, and pain which are assessed on a 4-point scale with the values 0 (=no disability), 1 (=mild disability), 2 (=moderate disability), and 3 (=severe disability). One of the domains will be selected per injection cycle.

End point type	Secondary

End point timeframe:

From Study Baseline to Week 4, 16-20 and 28-36

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	143	143	128	
Units: units on a scale				
arithmetic mean (standard deviation)	-0.6 (± 0.7)	-0.9 (± 0.8)	-1 (± 0.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Disability Assessment Scale (DAS) Score in a Selected Principal Therapeutic Target Domain Affecting the Upper Limb From Study Baseline Visit to Injection Cycle Baseline Visits and End of Study Visit

End point title	Change of Disability Assessment Scale (DAS) Score in a Selected Principal Therapeutic Target Domain Affecting the

	Upper Limb From Study Baseline Visit to Injection Cycle Baseline Visits and End of Study Visit

End point description:

The Disability Assessment Scale consists of the four domains hygiene, dressing, limb position, and pain which are assessed on a 4-point scale with the values 0 (=no disability), 1 (=mild disability), 2 (=moderate disability), and 3 (=severe disability). One of the domains will be selected per injection cycle.

End point type	Secondary

End point timeframe:

From Study Baseline to Week 12-16, 24-32 and 36-48

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	151	140	127	
Units: units on a scale				
arithmetic mean (standard deviation)	-0.2 (± 0.6)	-0.3 (± 0.7)	-0.9 (± 0.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Global Assessment of Efficacy Scores

End point title	Global Assessment of Efficacy Scores

End point description:

Investigator assessment. The global assessment of efficacy will be assessed by the investigator, the subject, and the caregiver using a 4-point Likert scale with the ratings 1 = very good, 2 = good, 3 = moderate, and 4 = poor.

End point type	Secondary

End point timeframe:

Week 12-16, 24-32 and 36-48

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	155	152	140	
Units: subjects				
number (not applicable)				
Frequency 1	7	21	38	
Frequency 2	79	89	87	
Frequency 3	63	28	11	

Frequency 4	3	3	1	
Missing	3	11	3	

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL 5-Dimensions Questionnaire (EQ-5D) Scores

End point title	EuroQoL 5-Dimensions Questionnaire (EQ-5D) Scores

End point description:

The EQ-5D is a common quality of life questionnaire to be filled out by the subject. In addition, the subject was to indicate on a visual analogue scale, ranging from 0 to 100, how good or bad their own health was on the examination day. Frequency 1= Best, 2= Intermediate, 3= Worst value.
Usual activities: Frequency 1, 2 and 3 (n= 155, 155, 152, 148, 140, 138); Pain/discomfort: Frequency 1, 2 and 3 (n= 155, 155, 152, 149, 140, 138); Anxiety/depression: Frequency 1, 2 and 3 (n= 155, 155, 152, 149, 140, 138). Here, "n" is number of subjects analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

From Cycle Baseline to Week 4 of Each Cycle

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1 Baseline Visit	IncobotulinumtoxinA(Xeomin) : Injection Cycle 1 Control Visit 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2 Baseline Visit	IncobotulinumtoxinA(Xeomin) : Injection Cycle 2 Control Visit 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	155	155	152	149
Units: subjects				
number (not applicable)				
Mobility: Frequency 1 (n=155,155,152,149,140,138)	12	27	14	24
Mobility: Frequency 2 (n=155,155,152,149,140,138)	139	125	136	122
Mobility: Frequency 3 (n=155,155,152,149,140,138)	4	3	2	3
Self-care: Frequency 1 (n=155,155,152,148,140,138)	30	31	30	24
Self-care: Frequency 2 (n=155,155,152,148,140,138)	96	100	101	104
Self-care: Frequency 3 (n=155,155,152,148,140,138)	29	24	21	20
Usual activities: Frequency 1	11	19	16	21
Usual activities: Frequency 2	113	108	119	110
Usual activities: Frequency 3	31	28	17	17
Pain/discomfort: Frequency 1	53	73	56	74
Pain/discomfort: Frequency 2	85	75	88	70
Pain/discomfort: Frequency 3	17	7	8	5
Anxiety/depression: Frequency 1	72	82	83	93
Anxiety/depression: Frequency 2	69	67	63	49

Anxiety/depression: Frequency 3	14	6	6	7

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 3 Baseline Visit	IncobotulinumtoxinA(Xeomin) : Injection Cycle 3 Control Visit 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	140	138		
Units: subjects				
number (not applicable)				
Mobility: Frequency 1 (n=155,155,152,149,140,138)	19	20		
Mobility: Frequency 2 (n=155,155,152,149,140,138)	119	116		
Mobility: Frequency 3 (n=155,155,152,149,140,138)	2	2		
Self-care: Frequency 1 (n=155,155,152,148,140,138)	24	22		
Self-care: Frequency 2 (n=155,155,152,148,140,138)	101	107		
Self-care: Frequency 3 (n=155,155,152,148,140,138)	15	9		
Usual activities: Frequency 1	15	17		
Usual activities: Frequency 2	113	111		
Usual activities: Frequency 3	12	10		
Pain/discomfort: Frequency 1	57	77		
Pain/discomfort: Frequency 2	79	58		
Pain/discomfort: Frequency 3	4	3		
Anxiety/depression: Frequency 1	78	85		
Anxiety/depression: Frequency 2	57	49		
Anxiety/depression: Frequency 3	5	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Visual Analogue Scale (VAS) of EuroQoL 5-Dimensions Questionnaire (EQ-5D) Scores

End point title	Visual Analogue Scale (VAS) of EuroQoL 5-Dimensions Questionnaire (EQ-5D) Scores

End point description:

The EQ-5D is a common quality of life questionnaire to be filled out by the subject. In addition, the subject was to indicate on a visual analogue scale, ranging from 0 to 100, how good or bad their own health was on the examination day. Frequency 1= Best, 2= Intermediate, 3= Worst value.

End point type	Secondary

End point timeframe:

From Cycle Baseline to Week 4 of Each Cycle

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1 Baseline Visit	IncobotulinumtoxinA(Xeomin): Injection Cycle 1 Control Visit 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2 Baseline Visit	IncobotulinumtoxinA(Xeomin): Injection Cycle 2 Control Visit 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	154	155	152	149
Units: units on a scale				
arithmetic mean (standard deviation)	59.9 (± 18.9)	66.7 (± 17.6)	67.2 (± 17)	69.9 (± 16.6)

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 3 Baseline Visit	IncobotulinumtoxinA(Xeomin): Injection Cycle 3 Control Visit 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	140	138		
Units: units on a scale				
arithmetic mean (standard deviation)	67.1 (± 17.9)	68.9 (± 17.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change of EuroQoL 5-dimensions questionnaire (EQ-5D) Score From Injection Cycle Baseline Visits to Respective Control Visits

End point title	Change of EuroQoL 5-dimensions questionnaire (EQ-5D) Score From Injection Cycle Baseline Visits to Respective Control Visits

End point description:

The EQ-5D is a common quality of life questionnaire to be filled out by the subject. In addition, the subject was to indicate on a visual analogue scale, ranging from 0 to 100, how good or bad their own health was on the examination day. Here, "n" is number of subjects analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

From Cycle Baseline to Week 4 of Each Cycle

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	155	149	138	
Units: units on a scale				
number (not applicable)				
Mobility: Frequency -1 (n= 155, 149, 138)	18	11	6	
Mobility: Frequency 0 (n= 155, 149, 138)	135	136	128	
Mobility: Frequency 1 (n= 155, 149, 138)	2	2	4	
Self-care: Frequency -1 (n= 155, 148, 138)	19	7	11	
Self-care: Frequency 0 (n= 155, 148, 138)	123	127	121	
Self-care: Frequency 1 (n= 155, 148, 138)	13	14	6	
Usual activities: Frequency -2 (n= 155, 148, 138)	0	0	1	
Usual activities: Frequency -1 (n= 155, 148, 138)	20	18	7	
Usual activities: Frequency 0 (n= 155, 148, 138)	126	116	126	
Usual activities: Frequency 1 (n= 155, 148, 138)	9	14	4	
Pain/discomfort: Frequency -2 (n= 155, 149, 138)	1	2	0	
Pain/discomfort: Frequency -1 (n= 155, 149, 138)	39	30	29	
Pain/discomfort: Frequency 0 (n= 155, 149, 138)	105	105	102	
Pain/discomfort: Frequency 1 (n= 155, 149, 138)	9	12	7	
Pain/discomfort: Frequency 2 (n= 155, 149, 138)	1	0	0	
Anxiety/depression:Frequency -2 (n= 155, 149, 138)	0	0	1	
Anxiety/depression:Frequency -1 (n= 155, 149, 138)	27	18	17	
Anxiety/depression: Frequency 0 (n= 155, 149, 138)	119	121	111	
Anxiety/depression: Frequency 1 (n= 155, 149, 138)	9	9	9	
Anxiety/depression: Frequency 2 (n= 155, 149, 138)	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Visual Analogue Scale of EuroQoL 5-dimensions questionnaire (EQ-5D) Score From Injection Cycle Baseline Visits to Respective Control Visits

End point title	Change in Visual Analogue Scale of EuroQoL 5-dimensions

	questionnaire (EQ-5D) Score From Injection Cycle Baseline Visits to Respective Control Visits

End point description:

The EQ-5D is a common quality of life questionnaire to be filled out by the subject. In addition, the subject was to indicate on a visual analogue scale, ranging from 0 to 100, how good or bad their own health was on the examination day.

End point type	Secondary

End point timeframe:

From Cycle Baseline to Week 4 of Each Cycle

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	154	149	138	
Units: units on a scale				
arithmetic mean (standard deviation)	6.7 (± 14.1)	2.4 (± 12.4)	1.7 (± 12.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change of EuroQoL 5-dimensions questionnaire (EQ-5D) Score From Study Baseline Visit to Control Visits of Injection Cycles

End point title	Change of EuroQoL 5-dimensions questionnaire (EQ-5D) Score From Study Baseline Visit to Control Visits of Injection Cycles

End point description:

The EQ-5D is a common quality of life questionnaire to be filled out by the subject. In addition, the subject was to indicate on a visual analogue scale, ranging from 0 to 100, how good or bad their own health was on the examination day. Here, "n" is number of subjects analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

From Study Baseline to Week 4, 16-20 and 28-36

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	155	149	138	
Units: subjects				
number (not applicable)				
Mobility: Frequency -1 (n= 155, 149, 138)	18	16	14	

Mobility: Frequency 0 (n= 155, 149, 138)	135	127	118	
Mobility: Frequency 1 (n= 155, 149, 138)	2	5	5	
Self-care: Frequency -1 (n= 155, 148, 138)	19	20	25	
Self-care: Frequency 0 (n= 155, 148, 138)	123	110	100	
Self-care: Frequency 1 (n= 155, 148, 138)	13	18	13	
Usual activities: Frequency -2 (n= 155, 148, 138)	0	1	1	
Usual activities: Frequency -1 (n= 155, 148, 138)	20	31	31	
Usual activities: Frequency 0 (n= 155, 148, 138)	126	103	98	
Usual activities: Frequency 1 (n= 155, 148, 138)	9	13	8	
Pain/discomfort: Frequency -2 (n= 155, 149, 138)	1	3	3	
Pain/discomfort: Frequency -1 (n= 155, 149, 138)	39	40	42	
Pain/discomfort: Frequency 0 (n= 155, 149, 138)	105	93	85	
Pain/discomfort: Frequency 1 (n= 155, 149, 138)	9	13	8	
Pain/discomfort: Frequency 2 (n= 155, 149, 138)	1	0	0	
Anxiety/depression:Frequency -2 (n= 155, 149, 138)	0	7	6	
Anxiety/depression:Frequency -1 (n= 155, 149, 138)	27	28	32	
Anxiety/depression:Frequency 0 (n= 155, 149, 138)	119	100	85	
Anxiety/depression:Frequency 1 (n= 155, 149, 138)	9	14	15	
Anxiety/depression:Frequency 2 (n= 155, 149, 138)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Visual Analogue Scale of EuroQoL 5-dimensions questionnaire (EQ-5D) Score From Study Baseline Visit to Control Visits of Injection Cycles

End point title	Change in Visual Analogue Scale of EuroQoL 5-dimensions questionnaire (EQ-5D) Score From Study Baseline Visit to Control Visits of Injection Cycles

End point description:

The EQ-5D is a common quality of life questionnaire to be filled out by the subject. In addition, the subject was to indicate on a visual analogue scale, ranging from 0 to 100, how good or bad their own health was on the examination day.

End point type	Secondary

End point timeframe:

From Study Baseline to Week 4, 16-20 and 28-36

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	154	148	137	
Units: units on a scale				
arithmetic mean (standard deviation)	6.7 (± 14.1)	9.6 (± 16.3)	8.6 (± 17)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change of EuroQoL 5-dimensions questionnaire (EQ-5D) Score From Study Baseline Visit to Injection Cycle Baseline Visits and End of Study Visit

End point title	Change of EuroQoL 5-dimensions questionnaire (EQ-5D) Score From Study Baseline Visit to Injection Cycle Baseline Visits and End of Study Visit

End point description:

The EQ-5D is a common quality of life questionnaire to be filled out by the subject. In addition, the subject was to indicate on a visual analogue scale, ranging from 0 to 100, how good or bad their own health was on the examination day.

End point type	Secondary

End point timeframe:

From Study Baseline to Week 12-16, 24-32 and 36-48

End point values	IncobotulinumtoxinA (Xeomin): Injection Cycle 1	IncobotulinumtoxinA (Xeomin): Injection Cycle 2	IncobotulinumtoxinA (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	152	140	137	
Units: subjects				
number (not applicable)				
Mobility: Frequency -1	10	13	16	
Mobility: Frequency 0	137	121	116	
Mobility: Frequency 1	5	5	4	
Self-care: Frequency -1	20	24	30	
Self-care: Frequency 0	120	99	97	
Self-care: Frequency 1	12	17	10	
Usual activities: Frequency -2	1	1	1	
Usual activities: Frequency -1	21	26	33	
Usual activities: Frequency 0	125	106	96	
Usual activities: Frequency 1	5	7	7	

Pain/discomfort: Frequency -2	0	0	3	
Pain/discomfort: Frequency -1	32	35	40	
Pain/discomfort: Frequency 0	100	89	81	
Pain/discomfort: Frequency 1	20	15	13	
Pain/discomfort: Frequency 2	0	1	0	
Anxiety/depression: Frequency -2	2	4	5	
Anxiety/depression: Frequency -1	29	28	30	
Anxiety/depression: Frequency 0	108	91	89	
Anxiety/depression: Frequency 1	12	17	13	
Anxiety/depression: Frequency 2	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Visual Analogue Scale of EuroQoL 5-dimensions questionnaire (EQ-5D) Score From Study Baseline Visit to Injection Cycle Baseline Visits and End of Study Visit

End point title	Change in Visual Analogue Scale of EuroQoL 5-dimensions questionnaire (EQ-5D) Score From Study Baseline Visit to Injection Cycle Baseline Visits and End of Study Visit

End point description:

The EQ-5D is a common quality of life questionnaire to be filled out by the subject. In addition, the subject was to indicate on a visual analogue scale, ranging from 0 to 100, how good or bad their own health was on the examination day.

End point type	Secondary

End point timeframe:

From Study Baseline to Week 12-16, 24-32 and 36-48

End point values	Incobotulinumtoxin A (Xeomin): Injection Cycle 1	Incobotulinumtoxin A (Xeomin): Injection Cycle 2	Incobotulinumtoxin A (Xeomin): Injection Cycle 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	151	139	136	
Units: units on a scale				
arithmetic mean (standard deviation)	7.1 (± 16.3)	6.9 (± 15.8)	10.5 (± 17.5)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time point of first injection until 16 weeks after last injection

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	IncobotulinumtoxinA (Xeomin) (up to 800 Units)

Reporting group description:

IncobotulinumtoxinA (Xeomin, also known as "NT 201" or "Botulinum toxin type A (150 kiloDalton), free from complexing proteins") (active ingredient: Clostridium Botulinum neurotoxin Type A free from complexing proteins) powder for solution for injection.

IncobotulinumtoxinA: Subjects to receive up to 3 injection cycle, with the dose titrated from 400 units to up to 800 units.
For each injection session: solution prepared by reconstitution of powder with 0.9% Sodium Chloride (NaCl), 400-800 units, volume 2.0 mL per 100 units;
Mode of administration: Intramuscular injection.

Serious adverse events	IncobotulinumtoxinA (Xeomin) (up to 800 Units)		
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 155 (10.97%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Convulsion			

subjects affected / exposed	4 / 155 (2.58%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	3 / 155 (1.94%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral infarction			
subjects affected / exposed	2 / 155 (1.29%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischemic stroke			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchopneumonia			

subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 155 (1.29%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meningitis bacterial			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinusitis			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	IncobotulinumtoxinA (Xeomin) (up to 800 Units)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 155 (21.94%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	12 / 155 (7.74%)		
occurrences (all)	17		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 155 (6.45%)		
occurrences (all)	13		
Musculoskeletal and connective tissue			

disorders Arthralgia subjects affected / exposed occurrences (all) Musculoskeletal pain subjects affected / exposed occurrences (all)	 10 / 155 (6.45%) 12 8 / 155 (5.16%) 8		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 10 / 155 (6.45%) 13		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 November 2011	Changes related to informed consent, subject card, objectives, study design, inclusion/exclusion criteria, discontinuation of subjects, Investigational product (IP) administration, efficacy variables, and safety variables.
23 February 2012	Introduction of forced expiratory volume in 1 second (FEV1) and maximal inspiratory pressure (MIP) as additional safety parameters. Introduction of study-wide stopping rules. Additional safety visits 8 weeks after injection, additional telephone contacts 2 weeks after injection.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported