Clinical trial results:
An International, Multicentre, Prospective, Single Arm Study to Assess the Effect on Voluntary Movements of AbobotulinumtoxinA 1500 U Administered in Both Upper and Lower Limbs in Conjunction with a Guided Self Rehabilitation Contract in Adult Subjects with Spastic Hemiparesis

Summary

EudraCT number	2016-001989-29
Trial protocol	CZ FR
Global end of trial date	18 July 2018

Results information

Result version number	v2 (current)
This version publication date	11 July 2020
First version publication date	01 June 2019
Version creation reason	• New data added to full data set Additional endpoint added after collection of final Modified Frenchay Scale central review data.

Trial information

Trial identification

Sponsor protocol code	F-FR-52120-228

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02969356
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ipsen
Sponsor organisation address	65 Quai Georges Gorse, Boulogne Billancourt, France, 92100
Public contact	Medical Director, Ipsen Pharma SAS, clinical.trials@ipsen.com
Scientific contact	Medical Director, Ipsen Pharma SAS, clinical.trials@ipsen.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 July 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 July 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the responder rate as defined by the improvement of composite active range of motion (AROM) in the primary targeted limb, either upper limb (UL) or lower limb (LL), depending on which one was selected as a primary treatment target (TT), following two consecutive Dysport injections combined with a Guided Self-rehabilitation Contract (GSC) in participants with spastic hemiparesis following acquired brain injury (ABI).

Protection of trial subjects:

The study was conducted under the provisions of the Declaration of Helsinki, in accordance with the International Council for Harmonisation Consolidated Guideline on Good Clinical Practice, Food and Drug Administration (FDA), 21 Code of Federal Regulations Part 11, Electronic Records, Electronic Signatures and FDA Guidance, Industry Computerized Systems Used in Clinical Trials and in compliance with Independent Ethics Committees/Institutional Review Boards and informed consent regulations. In addition, the study adhered to local regulatory requirements.

Background therapy:

Each participant received a personalised rehabilitation programme. The physiotherapist taught each participant the stretching postures and exercises to perform on a daily basis throughout the study. These were tailored to the individual participant's needs and formed the GSC therapy. The main focus was on the primary TT limb and then the other limb.

Evidence for comparator: -

Actual start date of recruitment	22 December 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Czech Republic: 58
Country: Number of subjects enrolled	Russian Federation: 50
Country: Number of subjects enrolled	United States: 30
Worldwide total number of subjects	157
EEA total number of subjects	77

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	124
From 65 to 84 years	33
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This multicentre, single-arm study was conducted in 18 centres between 22 December 2016 and 18 July 2018 in participants with spastic hemiparesis due to ABI. The study had 2 treatment cycles separated by at least 12 (maximum 20) weeks and combined with GSC for the whole study duration.

Pre-assignment

Screening details:

A total of 157 participants were treated in this study. At baseline (Cycle 1, Day 1), the primary TT limb (UL or LL) was defined by the investigator, following discussion with the participant. If the primary TT limb was the UL, the secondary TT limb was the LL (and vice versa).

Period 1

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

Arms

Arm title	Dysport

Arm description:

Dysport (AbobotulinumtoxinA) 1500 units (U) intramuscular (IM) injection, was administered as a split dose, in both the UL and LL on Day 1 of each treatment cycle. The dose given in each limb was based on which was considered the primary TT limb at baseline. At least half the total dose must have been injected in the primary TT limb and a maximum of 1000 U could be injected in an UL (even if it was the primary TT limb). There was no maximum dose that could have been injected in a LL, provided that some out of the 1500 U total was used for the UL injection.
The second Dysport injection (Cycle 2) may have been given in a different split to the first injection (Cycle 1), at the discretion of the investigator. However, the same minimal/maximal rules applied. The primary TT remained the same for both Dysport injections.
Participants were also asked to perform daily GSC therapy throughout the study.

Arm type	Experimental
Investigational medicinal product name	AbobotulinumtoxinA
Investigational medicinal product code	
Other name	Dysport, BTX-A-haemagglutinin complex
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Dysport 1500 U IM injection as a split dose on Day 1 of each cycle (2 treatment cycles, each of up to 20 weeks).

Number of subjects in period 1	Dysport
Started	157
Intent-to-Treat (ITT) Population	153
Completed	134
Not completed	23
Personal reasons	5
Consent withdrawn by subject	2
Adverse event, non-fatal	7

Did not need to be reinjected	6
Lost to follow-up	3

Baseline characteristics

Reporting groups	
Reporting group title	Dysport

Reporting group description:

Dysport (AbobotulinumtoxinA) 1500 units (U) intramuscular (IM) injection, was administered as a split dose, in both the UL and LL on Day 1 of each treatment cycle. The dose given in each limb was based on which was considered the primary TT limb at baseline. At least half the total dose must have been injected in the primary TT limb and a maximum of 1000 U could be injected in an UL (even if it was the primary TT limb). There was no maximum dose that could have been injected in a LL, provided that some out of the 1500 U total was used for the UL injection.
The second Dysport injection (Cycle 2) may have been given in a different split to the first injection (Cycle 1), at the discretion of the investigator. However, the same minimal/maximal rules applied. The primary TT remained the same for both Dysport injections.
Participants were also asked to perform daily GSC therapy throughout the study.

Reporting group values	Dysport	Total	
Number of subjects	157	157	
Age categorical Units: Subjects			
Adults (18-64 years)	124	124	
From 65-84 years	33	33	
Gender categorical Units: Subjects			
Female	53	53	
Male	104	104	

End points

End points reporting groups

Reporting group title	Dysport

Reporting group description:

Dysport (AbobotulinumtoxinA) 1500 units (U) intramuscular (IM) injection, was administered as a split dose, in both the UL and LL on Day 1 of each treatment cycle. The dose given in each limb was based on which was considered the primary TT limb at baseline. At least half the total dose must have been injected in the primary TT limb and a maximum of 1000 U could be injected in an UL (even if it was the primary TT limb). There was no maximum dose that could have been injected in a LL, provided that some out of the 1500 U total was used for the UL injection.
The second Dysport injection (Cycle 2) may have been given in a different split to the first injection (Cycle 1), at the discretion of the investigator. However, the same minimal/maximal rules applied. The primary TT remained the same for both Dysport injections.
Participants were also asked to perform daily GSC therapy throughout the study.

Primary: Percentage of Responder Participants at Week 6 After the Second Injection, According to Composite AROM in the Primary TT Limb

End point title	Percentage of Responder Participants at Week 6 After the Second Injection, According to Composite AROM in the Primary TT Limb[1]

End point description:

Percentage of responder participants according to composite AROM was measured by goniometer in the primary TT limb, using zero as the theoretical position of minimal stretch for the muscle assessed. Participants were asked to perform the active movement as far as possible against that muscle and the angle was measured. A participant was considered a responder if he/she achieved at least the predefined improvement threshold - larger or equal to 35 degrees in UL or 5 degrees in LL - in the primary TT limb (based on the composite AROM individual change from baseline to Week 6 after the second injection). The modified ITT (mITT) population included all participants who were injected at least once with the study treatment, who received at least 1 day of GSC therapy during the study, for whom a primary TT limb had been defined and who had the primary efficacy outcome assessed at Week 6, Cycle 2.

End point type	Primary

End point timeframe:

At Week 6, Cycle 2

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: Descriptive statistical analysis was performed for the outcome measure.

End point values	Dysport			
Subject group type	Reporting group			
Number of subjects analysed	136			
Units: percentage of participants				
number (confidence interval 95%)	72.1 (64.0 to 78.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Responder Participants at Week 6 After the First

Injection, According to Composite AROM in the Primary TT Limb

End point title	Percentage of Responder Participants at Week 6 After the First Injection, According to Composite AROM in the Primary TT Limb

End point description:

Percentage of responder participants according to composite AROM was measured by goniometer in the primary TT limb, using zero as the theoretical position of minimal stretch for the muscle assessed. Participants were asked to perform the active movement as far as possible against that muscle and the angle was measured. A participant was considered a responder if he/she achieved at least the predefined improvement threshold - larger or equal to 35 degrees in UL or 5 degrees in LL - in the primary TT limb (based on the composite AROM individual change from baseline to Week 6 after the first injection). The ITT population included all participants who were injected at least once with the study treatment, who received at least 1 day of GSC therapy during the study and for whom a primary TT limb had been defined.

End point type	Secondary

End point timeframe:

At Week 6, Cycle 1

End point values	Dysport			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: percentage of participants				
number (confidence interval 95%)	58.2 (50.2 to 65.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in AROM Against 10 Prespecified Muscle Groups at Week 6 and Week 12 of Each Treatment Cycle, Reinjection Cycle Visit and Last Study Visit

End point title	Mean Change From Baseline in AROM Against 10 Prespecified Muscle Groups at Week 6 and Week 12 of Each Treatment Cycle, Reinjection Cycle Visit and Last Study Visit

End point description:

AROM was measured by goniometer in primary TT limb, using zero as theoretical position of minimal stretch for muscle assessed. Participants were asked to perform active movement as far as possible against that muscle and angle was measured. Angle of joint movement was measured in 10 prespecified muscle groups (injected or noninjected); UL: shoulder extensors(SE), elbow flexors(EF), wrist flexors(WF), extrinsic finger flexors(FF) and pronator teres(PT), LL: soleus(Sol), gastrocnemius(GN), gluteus maximus(GM), hamstrings(HS) and rectus femoris(RF). Reinjection cycle visit corresponds to Week 12, 16 or 20 of injection Cycle 1. Last study visit corresponds to last post-baseline visit performed by participant. ITT population included all participants who were injected at least once with study treatment, who received at least 1 day of GSC therapy during study and for whom a primary TT limb had been defined. n= number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

Week 6 and Week 12 of each treatment cycle, reinjection cycle visit and last study visit

End point values	Dysport			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: degrees				
arithmetic mean (standard deviation)				
UL SE: Week 6, Cycle 1 (n=149)	8.9 (± 16.4)			
UL SE: Week 12, Cycle 1 (n=146)	15.8 (± 22.9)			
UL SE: Reinjection cycle visit (n=140)	13.4 (± 22.5)			
UL SE: Week 6, Cycle 2 (n=136)	19.3 (± 25.1)			
UL SE: Week 12, Cycle 2 (n=129)	21.1 (± 27.7)			
UL SE: Last study visit (n=152)	19.0 (± 24.9)			
UL EF: Week 6, Cycle 1 (n=149)	8.7 (± 25.5)			
UL EF: Week 12, Cycle 1 (n=146)	12.0 (± 27.3)			
UL EF: Reinjection cycle visit (n=140)	10.9 (± 28.3)			
UL EF: Week 6, Cycle 2 (n=137)	14.9 (± 26.2)			
UL EF: Week 12, Cycle 2 (n=130)	15.4 (± 28.1)			
UL EF: Last study visit (n=153)	13.0 (± 28.2)			
UL WF: Week 6, Cycle 1 (n=148)	11.0 (± 16.3)			
UL WF: Week 12, Cycle 1 (n=144)	10.9 (± 20.1)			
UL WF: Reinjection cycle visit (n=138)	9.6 (± 20.4)			
UL WF: Week 6, Cycle 2 (n=135)	15.6 (± 24.3)			
UL WF: Week 12, Cycle 2 (n=129)	13.6 (± 22.4)			
UL WF: Last study visit (n=151)	12.4 (± 22.3)			
UL FF: Week 6, Cycle 1 (n=148)	24.1 (± 37.1)			
UL FF: Week 12, Cycle 1 (n=144)	20.7 (± 36.0)			
UL FF: Reinjection cycle visit (n=138)	14.5 (± 36.7)			
UL FF: Week 6, Cycle 2 (n=136)	29.5 (± 43.7)			
UL FF: Week 12, Cycle 2 (n=129)	27.9 (± 49.1)			
UL FF: Last study visit (n=151)	24.5 (± 44.9)			
UL PT: Week 6, Cycle 1 (n=149)	9.0 (± 32.6)			
UL PT: Week 12, Cycle 1 (n=146)	8.0 (± 38.0)			
UL PT: Reinjection cycle visit (n=140)	7.4 (± 37.9)			
UL PT: Week 6, Cycle 2 (n=137)	11.0 (± 38.6)			
UL PT: Week 12, Cycle 2 (n=129)	9.4 (± 38.4)			
UL PT: Last study visit (n=152)	8.7 (± 41.0)			
LL Sol: Week 6, Cycle 1 (n=149)	4.7 (± 9.6)			
LL Sol: Week 12, Cycle 1 (n=145)	5.2 (± 13.8)			
LL Sol: Reinjection cycle visit (n=139)	4.5 (± 15.4)			
LL Sol: Week 6, Cycle 2 (n=137)	9.3 (± 17.9)			
LL Sol: Week 12, Cycle 2 (n=130)	9.0 (± 17.0)			
LL Sol: Last study visit (n=152)	8.2 (± 16.4)			
LL GN: Week 6, Cycle 1 (n=149)	9.0 (± 14.8)			
LL GN: Week 12, Cycle 1 (n=145)	9.9 (± 14.6)			
LL GN: Reinjection cycle visit (n=139)	7.5 (± 15.0)			
LL GN: Week 6, Cycle 2 (n=137)	12.6 (± 16.8)			
LL GN: Week 12, Cycle 2 (n=130)	11.8 (± 17.1)			
LL GN: Last study visit (n=152)	11.9 (± 17.4)			
LL GM: Week 6, Cycle 1 (n=149)	5.1 (± 15.9)			

LL GM: Week 12, Cycle 1 (n=146)	5.2 (± 15.2)			
LL GM: Reinjection cycle visit (n=140)	5.1 (± 14.7)			
LL GM: Week 6, Cycle 2 (n=137)	6.1 (± 15.9)			
LL GM: Week 12, Cycle 2 (n=130)	7.3 (± 15.2)			
LL GM: Last study visit (n=153)	6.6 (± 16.5)			
LL HS: Week 6, Cycle 1 (n=149)	0.9 (± 34.2)			
LL HS: Week 12, Cycle 1 (n=146)	4.0 (± 34.7)			
LL HS: Reinjection cycle visit (n=140)	5.6 (± 30.7)			
LL HS: Week 6, Cycle 2 (n=137)	8.2 (± 25.1)			
LL HS: Week 12, Cycle 2 (n=130)	10.3 (± 26.3)			
LL HS: Last study visit (n=153)	6.8 (± 31.1)			
LL RF: Week 6, Cycle 1 (n=148)	4.5 (± 15.0)			
LL RF: Week 12, Cycle 1 (n=146)	4.4 (± 23.1)			
LL RF: Reinjection cycle visit (n=140)	5.1 (± 25.3)			
LL RF: Week 6, Cycle 2 (n=137)	8.9 (± 24.7)			
LL RF: Week 12, Cycle 2 (n=130)	9.6 (± 23.4)			
LL RF: Last study visit (n=153)	8.6 (± 23.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Composite AROM Against Injected Muscle Groups (Any of the 10 Prespecified Muscles) at Week 6 and Week 12 of Each Treatment Cycle, Reinjection Cycle Visit and Last Study Visit

End point title	Mean Change From Baseline in Composite AROM Against Injected Muscle Groups (Any of the 10 Prespecified Muscles) at Week 6 and Week 12 of Each Treatment Cycle, Reinjection Cycle Visit and Last Study Visit

End point description:

Composite AROM (XA) was measured by goniometer in the primary TT limb (either UL or LL, depending on which one has been selected as the primary TT limb), composite AROM in the UL injected muscle groups was calculated as the sum of the AROM in the EF, WF and FF. Composite AROM in the LL injected muscle groups was calculated as the sum of the AROM in Sol and GN. The ITT population included all participants who were injected at least once with the study treatment, who received at least 1 day of GSC therapy during the study and for whom a primary TT limb had been defined. n= number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

Week 6 and Week 12 of each treatment cycle, reinjection cycle visit and last study visit

End point values	Dysport			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: degrees				
arithmetic mean (standard deviation)				
UL: Week 6, Cycle 1 (n=148)	43.1 (± 49.9)			
UL: Week 12, Cycle 1 (n=144)	42.8 (± 56.7)			
UL: Reinjection cycle visit (n=138)	34.1 (± 52.8)			

UL: Week 6, Cycle 2 (n=135)	59.5 (± 64.4)			
UL: Week 12, Cycle 2 (n=129)	56.3 (± 66.7)			
UL: Last study visit (n=151)	49.3 (± 63.4)			
LL: Week 6, Cycle 1 (n=149)	13.7 (± 18.3)			
LL: Week 12, Cycle 1 (n=145)	15.1 (± 23.4)			
LL: Reinjection cycle visit (n=139)	12.0 (± 24.5)			
LL: Week 6, Cycle 2 (n=137)	21.9 (± 28.8)			
LL: Week 12, Cycle 2 (n=130)	20.8 (± 28.8)			
LL: Last study visit (n=152)	20.1 (± 27.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Full Composite AROM Against 5 UL or 5 LL Muscle Groups, Regardless of Whether the Muscle Groups Were Injected or Not at Week 6 and Week 12 of Each Treatment Cycle, Reinjection Cycle Visit and Last Study Visit

End point title	Mean Change From Baseline in Full Composite AROM Against 5 UL or 5 LL Muscle Groups, Regardless of Whether the Muscle Groups Were Injected or Not at Week 6 and Week 12 of Each Treatment Cycle, Reinjection Cycle Visit and Last Study Visit

End point description:

Full composite AROM, regardless of whether the muscle groups was injected or not was measured by goniometer in the primary TT limb. Full Composite AROM in the UL was calculated as the sum of the AROM in the 5 UL muscle groups (SE+EF+WF+FF+PT). Full Composite AROM in the LL was calculated as the sum of the AROM in the 5 LL muscle groups (Sol+GN+GM+HS+RF). The ITT population included all participants who were injected at least once with the study treatment, who received at least 1 day of GSC therapy during the study and for whom a primary TT limb had been defined. n= number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

Week 6 and Week 12 of each treatment cycle, reinjection cycle visit and last study visit

End point values	Dysport			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: degrees				
arithmetic mean (standard deviation)				
UL: Week 6, Cycle 1 (n=148)	60.6 (± 68.4)			
UL: Week 12, Cycle 1 (n=144)	66.3 (± 75.7)			
UL: Reinjection cycle visit (n=138)	53.9 (± 69.9)			
UL: Week 6, Cycle 2 (n=134)	90.5 (± 90.1)			
UL: Week 12, Cycle 2 (n=128)	87.6 (± 94.8)			
UL: Last study visit (n=150)	77.8 (± 89.6)			
LL: Week 6, Cycle 1 (n=148)	24.4 (± 42.7)			
LL: Week 12, Cycle 1 (n=145)	28.7 (± 55.9)			
LL: Reinjection cycle visit (n=139)	28.0 (± 56.2)			
LL: Week 6, Cycle 2 (n=137)	45.1 (± 58.2)			

LL: Week 12, Cycle 2 (n=130)	48.1 (± 60.4)			
LL: Last study visit (n=152)	42.2 (± 61.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Modified Frenchay Scale (MFS) Overall Score Evaluated Locally and Centrally at Week 12 of Each Treatment Cycle and Last Study Visit

End point title	Mean Change From Baseline in Modified Frenchay Scale (MFS) Overall Score Evaluated Locally and Centrally at Week 12 of Each Treatment Cycle and Last Study Visit

End point description:

The MFS was used to measure active function in the UL. The MFS consists of 10 tasks, each of which was evaluated locally by the site investigator and centrally by a blinded central reviewer at the coordinating investigators' site, on a 10-point visual analogue scale (VAS) ranging from "No movement" to "Normal". Higher score indicates a better outcome. The MFS overall scores were obtained by averaging all individual task scores, provided that at least 8 out of 10 were not missing. The mean change from baseline was calculated for the local and central assessments and a positive change from baseline indicates an improvement in active function. The ITT population included all participants who were injected at least once with the study treatment, who received at least 1 day of GSC therapy during the study and for whom a primary TT limb had been defined. Only participants with data available at each time point are presented. n = number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

Week 12 of each treatment cycle and last study visit

End point values	Dysport			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: units on a scale				
arithmetic mean (standard deviation)				
Local assessment: Week 12, Cycle 1 (n=141)	0.44 (± 0.56)			
Local assessment: Week 12, Cycle 2 (n=125)	0.55 (± 0.65)			
Local assessment: Last study visit (n=147)	0.53 (± 0.63)			
Central assessment: Week 12, Cycle 1 (n=53)	0.08 (± 0.49)			
Central assessment: Week 12, Cycle 2 (n=47)	0.18 (± 0.61)			
Central assessment: Last study visit (n=55)	0.14 (± 0.59)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Maximal Walking Speed Barefoot at Week 12 of Each Treatment Cycle and at Last Study Visit

End point title	Mean Change From Baseline in Maximal Walking Speed Barefoot at Week 12 of Each Treatment Cycle and at Last Study Visit

End point description:

The 10-metre walking speed test (WST) was used to measure active function in the LL. The participant performed the WST barefoot without a walking aid. If it was absolutely necessary that the participant used a cane, this may have been permitted provided that the same cane was used at baseline and all other walking speed assessments for that participant. The participant was given instructions to walk at his/her maximum speed. The time taken for the participant to walk from the start to the end of the 10 metres was recorded. The ITT population included all participants who were injected at least once with the study treatment, who received at least 1 day of GSC therapy during the study and for whom a primary TT limb had been defined. n= number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

Week 12 of each treatment cycle and last study visit

End point values	Dysport			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: metres per second				
arithmetic mean (standard deviation)				
Week 12, Cycle 1 (n=140)	0.081 (± 0.161)			
Week 12, Cycle 2 (n=123)	0.116 (± 0.159)			
Last study visit (n=146)	0.097 (± 0.187)			

Statistical analyses

No statistical analyses for this end point

Secondary: Participant Satisfaction With the GSC at Week 6 and Week 12 of Each Treatment Cycle, Reinjection Cycle Visit and Last Study Visit

End point title	Participant Satisfaction With the GSC at Week 6 and Week 12 of Each Treatment Cycle, Reinjection Cycle Visit and Last Study Visit

End point description:

Each participant received a personalised rehabilitation programme. The physiotherapist taught each participant the stretching postures and exercises to perform on a daily basis throughout the study. These were tailored to the individual participant's needs and formed the GSC therapy. The main focus was on the primary TT limb and then the other limb. Participant satisfaction was determined by asking the question "How satisfied are you TODAY regarding the GSC?" Responses were recorded using a 5-level Likert scale, as follows: completely satisfied (+2), rather satisfied (+1), neither satisfied nor dissatisfied (0), rather dissatisfied (-1), and completely dissatisfied (-2). The ITT population included all participants who were injected at least once with the study treatment, who received at least 1 day of GSC therapy during the study and for whom a primary TT limb had been defined. n= number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

At baseline (for participants who had GSC previously only), Week 6 and Week 12 of each treatment cycle, reinjection cycle visit and last study visit

End point values	Dysport			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline non-naïve participants to GSC only (n=39)	1.8 (± 0.5)			
Week 6, Cycle 1 (n=149)	1.3 (± 0.9)			
Week 12, Cycle 1 (n=146)	1.4 (± 0.8)			
Reinjection cycle visit (n=140)	1.4 (± 0.7)			
Week 6, Cycle 2 (n=136)	1.4 (± 0.7)			
Week 12, Cycle 2 (n=130)	1.4 (± 0.8)			
Last study visit (n=153)	1.4 (± 0.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Participant's Beliefs That the GSC Will Help to Improve Functional Capacity at Week 6 and Week 12 of Each Treatment Cycle, Reinjection Cycle Visit and Last Study Visit

End point title	Change From Baseline in Participant's Beliefs That the GSC Will Help to Improve Functional Capacity at Week 6 and Week 12 of Each Treatment Cycle, Reinjection Cycle Visit and Last Study Visit

End point description:

Participants were asked the following question: "Do you believe that GSC will help to improve your arm and leg function?" Responses were recorded on a 5-level Likert scale, as follows: very true of what I believe (+2), somewhat true of what I believe (+1), no opinion/don't know (0), somewhat untrue of what I believe (-1), and very untrue of what I believe (-2). The ITT population included all participants who were injected at least once with the study treatment, who received at least 1 day of GSC therapy during the study and for whom a primary TT limb had been defined. n= number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

Week 6 and Week 12 of each treatment cycle, reinjection cycle visit and last study visit

End point values	Dysport			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 6, Cycle 1 (n=149)	-0.2 (± 0.9)			
Week 12, Cycle 1 (n=146)	-0.1 (± 0.8)			
Reinjection cycle visit (n=140)	-0.2 (± 0.8)			
Week 6, Cycle 2 (n=136)	-0.1 (± 0.7)			
Week 12, Cycle 2 (n=130)	-0.3 (± 0.8)			
Last study visit (n=153)	-0.2 (± 0.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Physiotherapist's Beliefs That the GSC Will Help to Improve Functional Capacity at Week 6 and Week 12 of Each Treatment Cycle, Reinjection Cycle Visit and Last Study Visit

End point title	Change From Baseline in Physiotherapist's Beliefs That the GSC Will Help to Improve Functional Capacity at Week 6 and Week 12 of Each Treatment Cycle, Reinjection Cycle Visit and Last Study Visit

End point description:

Physiotherapists were asked the following question: "Do you believe that GSC will help to improve your patient's arm and leg function?" Responses were recorded on a 5-level Likert scale, as follows: very true of what I believe (+2), somewhat true of what I believe (+1), no opinion/don't know (0), somewhat untrue of what I believe (-1), and very untrue of what I believe (-2). The ITT population included all participants who were injected at least once with the study treatment, who received at least 1 day of GSC therapy during the study and for whom a primary TT limb had been defined. n= number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

Week 6 and Week 12 of each treatment cycle, reinjection cycle visit and last study visit

End point values	Dysport			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 6, Cycle 1 (n=113)	-0.2 (± 0.6)			
Week 12, Cycle 1 (n=110)	-0.2 (± 0.6)			
Reinjection cycle visit (n=105)	-0.1 (± 0.6)			
Week 6, Cycle 2 (n=101)	-0.2 (± 0.6)			
Week 12, Cycle 2 (n=96)	-0.2 (± 0.6)			
Last study visit (n=117)	-0.2 (± 0.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Days Over Study Period When GSC Therapy Was Performed

End point title	Percentage of Days Over Study Period When GSC Therapy Was Performed

End point description:

The investigator counted the number of days when GSC therapy was not performed since the last visit. Using the total number of study days and the total number of days when GSC therapy was not performed, the number of days when GSC was performed was calculated. The ITT population included all participants who were injected at least once with the study treatment, who received at least 1 day of GSC therapy during the study and for whom a primary TT limb had been defined.

End point type	Secondary

End point timeframe:

From baseline to end of the study, up to 280 days

End point values	Dysport			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: percentage of study days				
arithmetic mean (standard deviation)	92.80 (± 9.85)			

Statistical analyses

No statistical analyses for this end point

Secondary: Global Assessment of Benefits of the Study Therapy

End point title	Global Assessment of Benefits of the Study Therapy

End point description:

A global assessment of the benefits of the study therapy was made by the investigator and the participant (or the caregiver). The participant's caregiver performed the global assessment only in those cases when the participant was not capable to do this. Participants were asked the following question: "How would you rate the overall response to study therapy since baseline?" Responses on the global assessment were recorded on a 5-level Likert scale, as follows: much better (+2), a bit better (+1), the same (0), a bit worse (-1), and much worse (-2). The ITT population included all participants who were injected at least once with the study treatment, who received at least 1 day of GSC therapy during the study and for whom a primary TT limb had been defined. n= number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

At reinjection cycle visit (Week 12, 16 or 20) and last study visit (Week 24 or 40)

End point values	Dysport			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: units on a scale				
arithmetic mean (standard deviation)				
Investigator: Reinjection cycle visit (n=138)	1.4 (± 0.6)			
Investigator: Last study visit (n=147)	1.3 (± 0.7)			
Participant: Reinjection cycle visit (n=139)	1.4 (± 0.6)			
Participant: Last study visit (n=148)	1.4 (± 0.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Satisfied With a Longer Interval Between 2 Treatment Cycles

End point title	Number of Participants Satisfied With a Longer Interval Between 2 Treatment Cycles

End point description:

Participants who were not reinjected at Week 12 of a given cycle, recorded their satisfaction with a longer interval between 2 injections collected at the corresponding reinjection visit or the last cycle visit (Week 16 or Week 20 for each cycle). To assess this, the participants were asked the following question: "Are you satisfied with a longer interval between 2 injections?". The possible answers were: Yes, No or No opinion. The ITT population included all participants who were injected at least once with the study treatment, who received at least 1 day of GSC therapy during the study and for whom a primary TT limb had been defined. Results are presented for participants who were not reinjected at Week 12 of the given cycle. n= number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

At reinjection cycle visit (Week 16 or 20) and last study visit (Week 24 or 40)

End point values	Dysport			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: participants				
Reinjection cycle visit: Yes (n=70)	52			
Reinjection cycle visit: No (n=70)	6			
Reinjection cycle visit: No opinion (n=70)	12			
Reinjection cycle visit: Missing (n=70)	0			
Last study visit: Yes (n=74)	42			
Last study visit: No (n=74)	14			
Last study visit: No opinion (n=74)	12			

Last study visit: Missing (n=74)	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Quality of Life 5 Dimensions (EQ-5D-5L) Scores at Last Study Visit

End point title	Change From Baseline in European Quality of Life 5 Dimensions (EQ-5D-5L) Scores at Last Study Visit

End point description:

Participants were asked to complete EQ-5D-5L questionnaire to assess their current health status. Questions were answered based on how participant was feeling "Today". EQ-5D-5L consists of 2 parts: EQ-5D descriptive system and EQ VAS. EQ-5D descriptive system included questions for each of following 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems and extreme problems. VAS recorded participant's self-rated health on a vertical 20-centimetre VAS where endpoints were labelled "The best health you can imagine" and "The worst health you can imagine". EQ-5D-5L questionnaire scores range from 0-100, where 0= worst self-perceived health and 100= best self-perceived health. Positive change from baseline indicates an improvement in quality of life (QoL). ITT population analysed. n= number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

At last study visit (Week 24 or 40)

End point values	Dysport			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: units on a scale				
arithmetic mean (standard deviation)				
Mobility: Last study visit (n=145)	-0.3 (± 0.8)			
Self-care: Last study visit (n=145)	-0.0 (± 0.8)			
Usual activities: Last study visit (n=145)	-0.3 (± 1.0)			
Pain/discomfort: Last study visit (n=145)	-0.3 (± 0.9)			
Anxiety/depression: Last study visit (n=145)	-0.1 (± 0.9)			
EQ VAS: Last study visit (n=145)	4.27 (± 18.71)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Short Form 12 (SF-12) Scales at Last Study

Visit

End point title	Change From Baseline in Short Form 12 (SF-12) Scales at Last Study Visit

End point description:

The SF-12 was a short form questionnaire survey consisting of 12 questions, which were a subset of the SF-36 health survey. Most of the questions were answered based on how the participant had felt over the previous 4 weeks. The SF-12 covers 8 domains, including physical functioning, role-physical, body pain, general health, vitality, social functioning, role-emotional and mental health. The SF-12 questionnaire survey scale ranges from 0-100, where 0= lowest level of health and 100= highest level of health. Positive change from baseline indicates an improvement in QoL. The ITT population included all participants who were injected at least once with the study treatment, who received at least 1 day of GSC therapy during the study and for whom a primary TT limb had been defined. n= number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

At last study visit (Week 24 or 40)

End point values	Dysport			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: units on a scale				
arithmetic mean (standard deviation)				
Physical score: Last study visit (n=145)	3.985 (± 7.358)			
Mental score: Last study visit (n=145)	-0.008 (± 9.631)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first injection of study treatment up to end of the study or early withdrawal, approximately 40 weeks.

Adverse event reporting additional description:

The safety population included all participants who were injected at least once with the study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Dysport

Reporting group description:

Dysport 1500 U IM injection, was administered as a split dose, in both the UL and LL on Day 1 of each treatment cycle. The dose given in each limb was based on which was considered the primary TT limb at baseline. At least half the total dose must have been injected in the primary TT limb and a maximum of 1000 U could be injected in an UL (even if it was the primary TT limb). There was no maximum dose that could have been injected in a LL, provided that some out of the 1500 U total was used for the UL injection.
The second Dysport injection (Cycle 2) may have been given in a different split to the first injection (Cycle 1), at the discretion of the investigator. However, the same minimal/maximal rules applied. The primary TT remained the same for both Dysport injections.
Participants were also asked to perform daily GSC therapy throughout the study.

Serious adverse events	Dysport		
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 157 (12.10%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of lung			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			

subjects affected / exposed	1 / 157 (0.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	1 / 157 (0.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Myocardial infarction				
subjects affected / exposed	2 / 157 (1.27%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ventricular extrasystoles				
subjects affected / exposed	1 / 157 (0.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Brain stem stroke				
subjects affected / exposed	1 / 157 (0.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Dysarthria				
subjects affected / exposed	1 / 157 (0.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	2 / 157 (1.27%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	1 / 157 (0.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myasthenic syndrome				

subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vith nerve paralysis			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			

subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mental status changes			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Intervertebral discitis			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 157 (1.27%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Tracheobronchitis			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Dysport		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	72 / 157 (45.86%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 157 (1.27%)		
occurrences (all)	2		
Haematoma			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Hypotension			

subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Surgical and medical procedures			
Abscess drainage			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Dental implantation			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Sinus operation			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 157 (1.91%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	5 / 157 (3.18%)		
occurrences (all)	5		
Injection site haematoma			
subjects affected / exposed	2 / 157 (1.27%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	3 / 157 (1.91%)		
occurrences (all)	3		
Pyrexia			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Gait disturbance			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Injection site rash			

subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Peripheral swelling			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Therapeutic product ineffective			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	2 / 157 (1.27%)		
occurrences (all)	2		
Cough			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Nocturnal dyspnoea			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Pulmonary embolism			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Psychiatric disorders			
Depression			
subjects affected / exposed	4 / 157 (2.55%)		
occurrences (all)	4		
Insomnia			
subjects affected / exposed	2 / 157 (1.27%)		
occurrences (all)	2		
Agitation			

subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Depressed mood			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Mental status changes			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Investigations			
Weight decreased			
subjects affected / exposed	2 / 157 (1.27%)		
occurrences (all)	2		
Angiogram abnormal			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
ECG signs of myocardial ischaemia			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Transaminases increased			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	4 / 157 (2.55%)		
occurrences (all)	9		
Fall			
subjects affected / exposed	10 / 157 (6.37%)		
occurrences (all)	12		
Joint injury			
subjects affected / exposed	2 / 157 (1.27%)		
occurrences (all)	2		
Ligament sprain			

subjects affected / exposed	2 / 157 (1.27%)		
occurrences (all)	2		
Arthropod bite			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Lip injury			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Tooth injury			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Traumatic haematoma			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	2		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Intracardiac thrombus			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Myocardial ischaemia			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 157 (2.55%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	3 / 157 (1.91%)		
occurrences (all)	3		
Clonic convulsion			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Monoparesis			

subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Seizure			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Slow speech			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Tension headache			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Transient ischaemic attack			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Vocal cord paralysis			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Vocal cord paresis			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Vertigo			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Eye disorders			
Diplopia			
subjects affected / exposed	2 / 157 (1.27%)		
occurrences (all)	2		
Photopsia			

subjects affected / exposed occurrences (all)	2 / 157 (1.27%) 2		
Vision blurred subjects affected / exposed occurrences (all)	2 / 157 (1.27%) 3		
Gastrointestinal disorders			
Dyspepsia subjects affected / exposed occurrences (all)	3 / 157 (1.91%) 3		
Diarrhoea subjects affected / exposed occurrences (all)	1 / 157 (0.64%) 1		
Dry mouth subjects affected / exposed occurrences (all)	1 / 157 (0.64%) 1		
Dysphagia subjects affected / exposed occurrences (all)	1 / 157 (0.64%) 2		
Gastritis subjects affected / exposed occurrences (all)	1 / 157 (0.64%) 1		
Nausea subjects affected / exposed occurrences (all)	1 / 157 (0.64%) 1		
Toothache subjects affected / exposed occurrences (all)	1 / 157 (0.64%) 1		
Hepatobiliary disorders			
Liver disorder subjects affected / exposed occurrences (all)	1 / 157 (0.64%) 1		
Skin and subcutaneous tissue disorders			
Erythema subjects affected / exposed occurrences (all)	1 / 157 (0.64%) 1		
Renal and urinary disorders			

Renal colic			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Urinary incontinence			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Endocrine disorders			
Thyroid disorder			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 157 (1.27%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	11 / 157 (7.01%)		
occurrences (all)	13		
Muscular weakness			
subjects affected / exposed	4 / 157 (2.55%)		
occurrences (all)	4		
Musculoskeletal pain			
subjects affected / exposed	3 / 157 (1.91%)		
occurrences (all)	3		
Neck pain			
subjects affected / exposed	2 / 157 (1.27%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	5 / 157 (3.18%)		
occurrences (all)	6		
Myalgia			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Osteoporosis			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Tenosynovitis			

subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 157 (1.91%)		
occurrences (all)	3		
Influenza			
subjects affected / exposed	2 / 157 (1.27%)		
occurrences (all)	2		
Respiratory tract infection			
subjects affected / exposed	3 / 157 (1.91%)		
occurrences (all)	3		
Urinary tract infection			
subjects affected / exposed	3 / 157 (1.91%)		
occurrences (all)	3		
Viral infection			
subjects affected / exposed	3 / 157 (1.91%)		
occurrences (all)	3		
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 157 (1.91%)		
occurrences (all)	3		
Gastroenteritis			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Respiratory tract infection viral			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	2		
Tooth infection			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		

Metabolism and nutrition disorders			
Hypochloraemia			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		
Iron deficiency			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 December 2016	• To clarify the ABI diseases authorised. • To exclude participants who had received (within 4 weeks before study entry) or might have received intrathecal baclofen. • To remove the International Normalised Ratio>3.5 in exclusion criteria as this was not an exclusion but a recommendation for dosing and clarify this was only for antivitamin K and no new oral anticoagulant in Section 6.1 of Protocol. • To clarify the recommended dose and muscles to be injected according to study drug labelling. • To add the participant satisfaction with GSC at baseline in case he/she had had GSC previously. • To add a new assessment, the physiotherapist belief in the GSC therapy at study start and during the study. • To add the participant satisfaction in case of longer interval of injection. • To authorise the use of ultrasound guiding in addition to electrical stimulation if this technique was used in routine clinical practice. • To add a visit windows of +/-7 days for all visits and +7 days only for Week 12 visit. • To add the record of any AE during the routine phone call done by the physiotherapist. • To remove the automated device for taking blood pressure. • To clarify that previous botulinum neurotoxin (BoNT) treatment was to be collected for all previous BoNT.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported