Clinical trial results:
A PHASE IIA, MULTICENTRE, DOUBLE BLIND, SINGLE DOSE, PARALLEL GROUP, PLACEBO CONTROLLED, CLINICAL PILOT STUDY TO ASSESS THE EFFICACY AND SAFETY OF SINGLE DOSE, INTRA-DETRUSOR INJECTIONS OF 750 UNITS OF DYSPORT IN SUBJECTS SUFFERING FROM NEUROGENIC DETRUSOR OVERACTIVITY FOLLOWING SPINAL CORD INJURY OR MULTIPLE SCLEROSIS

Summary

EudraCT number	2010-023210-31
Trial protocol	DE AT IT LT CZ
Global end of trial date	21 March 2013

Results information

Result version number	v1 (current)
This version publication date	11 March 2016
First version publication date	11 March 2016

Trial information

Trial identification

Sponsor protocol code	Y52-52120-155

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01357980
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ipsen Pharma
Sponsor organisation address	65 quai Georges Gorse, Boulogne-Billancourt , France, 92100
Public contact	Christine Seymour, Ipsen Innovation, +33 (0)160 92 95 38, ct-application@ipsen.com
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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	03 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 March 2013
Global end of trial reached?	Yes
Global end of trial date	21 March 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary study objective is to assess the efficacy of a single dose of Dysport (750 U) compared to placebo for the improvement in the daily incontinence episode frequency (IEF) for each administration mode (15 or 30 injection sites).

Protection of trial subjects:

The study was conducted under the provisions of the Declaration of Helsinki, IECs, informed consent regulations, International Conference on HarmonisationConsolidated Guideline on GCP [2] and also adhered to all applicable local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 May 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	4 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 4
Country: Number of subjects enrolled	France: 32
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Poland: 3
Worldwide total number of subjects	47
EEA total number of subjects	47

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	46
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were planned to be recruited at 22 centres in six countries (Austria, the Czech Republic, Germany, France, Italy and Poland), and patients were actually enrolled at 17 centres in five countries (the Czech Republic, Germany, France, Italy and Poland)

Pre-assignment

Screening details:

A screening visit was performed four to seven days prior to Baseline (Day -7 to Day -4).

At Baseline, 47 subjects were randomised in a ratio of 5:2:5:2 to one of the four treatment groups.

Period 1

Period 1 title	Randomisation
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The blind was maintained for the preparation of each subject's study treatment for injection, maintaining the blind for the subject, the investigator and the remainder of the project team.

Arms

Are arms mutually exclusive?	Yes
Arm title	Dysport 750 U (15 Injection Sites)

Arm description:

Botulinum type A toxin (Dysport®): 750 U intra detrusor injection on day 1 (single dose)

Arm type	Experimental
Investigational medicinal product name	Dysport®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

750 U with 0.5 ml per injection site

Arm title	Placebo (15 Injection Sites)

Arm description:

Placebo: Intra detrusor injection on day 1 (single dose)

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

Dosage and administration details:

0.5 ml per injection site

Arm title	Dysport 750 U (30 Injection Sites)

Arm description:

Botulinum type A toxin (Dysport®): 750 U intra detrusor injection on day 1 (single dose)

Arm type	Experimental

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

Dosage and administration details:
750 U with 0.5 ml per injection site

Arm title	Placebo (30 Injection Sites)

Arm description:
Placebo: Intra detrusor injection on day 1 (single dose)

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

Dosage and administration details:
0.5 ml per injection site

Number of subjects in period 1	Dysport 750 U (15 Injection Sites)	Placebo (15 Injection Sites)	Dysport 750 U (30 Injection Sites)
Started	16	7	17
Completed	16	6	16
Not completed	0	1	1
Consent withdrawn by subject	-	-	1
Lack of efficacy	-	1	-

Number of subjects in period 1	Placebo (30 Injection Sites)
Started	7
Completed	7
Not completed	0
Consent withdrawn by subject	-
Lack of efficacy	-

Period 2

Period 2 title	Intent To Treat (ITT) population
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes

Arm title	Dysport 750 U (15 Injection Sites)
Arm description:	
Botulinum type A toxin (Dysport®): 750 U intra detrusor injection on day 1 (single dose)	
Arm type	Experimental
Investigational medicinal product name	Dysport®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
750 U with 0.5 ml per injection site	
Arm title	Placebo (15 Injection Sites)
Arm description:	
Placebo: Intra detrusor injection on day 1 (single dose)	
Arm type	Placebo
Investigational medicinal product name	Placebo (15 Injection Sites)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5 ml per injection site	
Arm title	Dysport 750 U (30 Injection Sites)
Arm description:	
Botulinum type A toxin (Dysport®): 750 U intra detrusor injection on day 1 (single dose)	
Arm type	Experimental
Investigational medicinal product name	Dysport®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
750 U with 0.5 ml per injection site	
Arm title	Placebo (30 Injection Sites)
Arm description:	
Placebo: Intra detrusor injection on day 1 (single dose)	
Arm type	Placebo
Investigational medicinal product name	Placebo (30 Injection Sites)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5 ml per injection site	

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Baseline characteristics are assessed for ITT group.

Period 1 is for all randomized subjects [Randomization group]
Period 2 is for all Intent To Treat (ITT) population

Number of subjects in period 2[2][3]	Dysport 750 U (15 Injection Sites)	Placebo (15 Injection Sites)	Dysport 750 U (30 Injection Sites)
Started	14	6	16
Completed	14	6	16

Number of subjects in period 2[2][3]	Placebo (30 Injection Sites)
Started	6
Completed	6

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Worldwide numbers reported are per all randomized subjects (Randomization group)

However, baseline and outcomes are reported per Intent To Treat (ITT) population
[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Subjects started in Period 2 (ITT subjects) are not dependent on subjects completed in Period 1 (randomized subjects).

ITT population, which consisted of all randomized subjects who received at least one injection of study medication and completed assessment for the averaged daily IEF both at Baseline and at Day 84 (Visit 6). Of the 47 subjects randomized, 42 (89.4%) subjects were included in the ITT population. 5 subjects who did not have IEF data at Baseline and/or at Day 84 were excluded

Baseline characteristics

Reporting groups	
Reporting group title	Dysport 750 U (15 Injection Sites)
Reporting group description:	
Botulinum type A toxin (Dysport®): 750 U intra detrusor injection on day 1 (single dose)	
Reporting group title	Placebo (15 Injection Sites)
Reporting group description:	
Placebo: Intra detrusor injection on day 1 (single dose)	
Reporting group title	Dysport 750 U (30 Injection Sites)
Reporting group description:	
Botulinum type A toxin (Dysport®): 750 U intra detrusor injection on day 1 (single dose)	
Reporting group title	Placebo (30 Injection Sites)
Reporting group description:	
Placebo: Intra detrusor injection on day 1 (single dose)	

Reporting group values	Dysport 750 U (15 Injection Sites)	Placebo (15 Injection Sites)	Dysport 750 U (30 Injection Sites)
Number of subjects	14	6	16
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	41.1	46.5	50.5
standard deviation	± 12.1	± 10.7	± 11.1
Gender categorical Units: Subjects			
Female	7	2	12
Male	7	4	4
Number of subjects with Spinal Cord Injury (SCI) or Multiple Sclerosis (MS) Units: Subjects			
SCI	9	4	7
MS	5	2	9
Number of Subjects Using Anticholinergics Units: Subjects			
Yes	9	5	9
No	5	1	7

Reporting group values	Placebo (30 Injection Sites)	Total	
Number of subjects	6	42	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	40.8		
standard deviation	± 10.6	-	
Gender categorical Units: Subjects			
Female	2	23	
Male	4	19	
Number of subjects with Spinal Cord Injury (SCI) or Multiple Sclerosis (MS) Units: Subjects			
SCI	2	22	
MS	4	20	
Number of Subjects Using Anticholinergics Units: Subjects			
Yes	5	28	
No	1	14	

End points

End points reporting groups

Reporting group title	Dysport 750 U (15 Injection Sites)
Reporting group description: Botulinum type A toxin (Dysport®): 750 U intra detrusor injection on day 1 (single dose)	
Reporting group title	Placebo (15 Injection Sites)
Reporting group description: Placebo: Intra detrusor injection on day 1 (single dose)	
Reporting group title	Dysport 750 U (30 Injection Sites)
Reporting group description: Botulinum type A toxin (Dysport®): 750 U intra detrusor injection on day 1 (single dose)	
Reporting group title	Placebo (30 Injection Sites)
Reporting group description: Placebo: Intra detrusor injection on day 1 (single dose)	
Reporting group title	Dysport 750 U (15 Injection Sites)
Reporting group description: Botulinum type A toxin (Dysport®): 750 U intra detrusor injection on day 1 (single dose)	
Reporting group title	Placebo (15 Injection Sites)
Reporting group description: Placebo: Intra detrusor injection on day 1 (single dose)	
Reporting group title	Dysport 750 U (30 Injection Sites)
Reporting group description: Botulinum type A toxin (Dysport®): 750 U intra detrusor injection on day 1 (single dose)	
Reporting group title	Placebo (30 Injection Sites)
Reporting group description: Placebo: Intra detrusor injection on day 1 (single dose)	

Primary: Daily Incontinence Episode Frequency (IEF)

End point title	Daily Incontinence Episode Frequency (IEF)
End point description: Analysis based on number of subjects in the Intent to Treat (ITT) population.	
End point type	Primary
End point timeframe: Baseline and Day 84	

End point values	Dysport 750 U (15 Injection Sites)	Placebo (15 Injection Sites)	Dysport 750 U (30 Injection Sites)	Placebo (30 Injection Sites)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	6	16	6
Units: episodes per day				
arithmetic mean (standard deviation)				
Baseline	4.21 (± 2.32)	3.33 (± 2.87)	3.23 (± 1.26)	4.4 (± 1.55)
Change from baseline to Day 84	-3.51 (± 2.8)	-1.05 (± 2.95)	-2.86 (± 1.43)	-3.4 (± 1.49)

Statistical analyses

Statistical analysis title	Daily Incontinence Episode Frequency (IEF)

Statistical analysis description:

Statistical Analysis 1

Comparison of the average Daily IEF change from baseline to DAY 84 using ANCOVA with the baseline average daily IEF value as covariate.

Comparison groups	Dysport 750 U (15 Injection Sites) v Placebo (15 Injection Sites)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.11
Method	ANCOVA

Statistical analysis title	Daily Incontinence Episode Frequency (IEF)

Statistical analysis description:

Statistical Analysis 2

Comparison of the average Daily IEF change from baseline to DAY 84 using ANCOVA with the baseline average daily IEF value as covariate.

Comparison groups	Placebo (30 Injection Sites) v Dysport 750 U (30 Injection Sites)
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.07
Method	ANCOVA

Secondary: Urodynamics: Maximum Cystometric Capacity

End point title	Urodynamics: Maximum Cystometric Capacity

End point description:

Maximum Cystometric Capacity is an urodynamic parameter that indicates the volume at which a patient feels he (she) can no longer delay release of urine from the urinary bladder. Baseline urodynamics exams done at screening visit.

Analysis based on number (n) of subjects with a valid value in the Intent-to-Treat (ITT) population for the respective treatment groups.

End point type	Secondary

End point timeframe:

Baseline, Days 14, 42 and 84

End point values	Dysport 750 U (15 Injection Sites)	Placebo (15 Injection Sites)	Dysport 750 U (30 Injection Sites)	Placebo (30 Injection Sites)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	6	16	6
Units: mL				
arithmetic mean (standard deviation)				
Baseline (n=14,5,16,6)	281 (± 186)	287 (± 112)	288 (± 144)	220 (± 55)
Change from baseline to D14 (n=14,5,16,6)	186 (± 160)	-36 (± 140)	169 (± 92)	-33 (± 88)
Change from baseline to D42 (n=14,6,15,6)	163 (± 208)	45 (± 64)	185 (± 174)	3 (± 94)
Change from baseline to D84 (n=14,5,16,6)	150 (± 174)	12.5 (± 26)	196 (± 135)	50 (± 145)

Statistical analyses

Statistical analysis title	Urodynamics: Maximum Cystometric Capacity

Statistical analysis description:

Statistical Analysis 1

Comparison of the maximum Cystometric Capacity change from baseline to DAY 14 using ANCOVA with the baseline maximum Cystometric Capacity as covariate.

Comparison groups	Dysport 750 U (15 Injection Sites) v Placebo (15 Injection Sites)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.01
Method	ANCOVA

Statistical analysis title	Urodynamics: Maximum Cystometric Capacity

Statistical analysis description:

Statistical Analysis 2

Comparison of the maximum Cystometric Capacity change from baseline to DAY 14 using ANCOVA with the baseline maximum Cystometric Capacity as covariate.

Comparison groups	Dysport 750 U (30 Injection Sites) v Placebo (30 Injection Sites)
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.01
Method	ANCOVA

Statistical analysis title	Urodynamics: Maximum Cystometric Capacity

Statistical analysis description:

Statistical Analysis 3

Comparison of the maximum Cystometric Capacity change from baseline to DAY 42 using ANCOVA with the baseline maximum Cystometric Capacity as covariate.

Comparison groups	Dysport 750 U (15 Injection Sites) v Placebo (15 Injection Sites)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.09
Method	ANCOVA

Statistical analysis title	Urodynamics: Maximum Cystometric Capacity

Statistical analysis description:

Statistical Analysis 4

Comparison of the maximum Cystometric Capacity change from baseline to DAY 42 using ANCOVA with the baseline maximum Cystometric Capacity as covariate.

Comparison groups	Dysport 750 U (30 Injection Sites) v Placebo (30 Injection Sites)
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.01
Method	ANCOVA

Statistical analysis title	Urodynamics: Maximum Cystometric Capacity

Statistical analysis description:

Statistical Analysis 5

Comparison of the maximum Cystometric Capacity change from baseline to DAY 84 using ANCOVA with the baseline maximum Cystometric Capacity as covariate.

Comparison groups	Dysport 750 U (15 Injection Sites) v Placebo (15 Injection Sites)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.01
Method	ANCOVA

Statistical analysis title	Urodynamics: Maximum Cystometric Capacity

Statistical analysis description:

Statistical Analysis 6

Comparison of the maximum Cystometric Capacity change from baseline to DAY 84 using ANCOVA with the baseline maximum Cystometric Capacity as covariate.

Comparison groups	Dysport 750 U (30 Injection Sites) v Placebo (30 Injection Sites)
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.01
Method	ANCOVA

Secondary: Urodynamics:Maximum Detrusor Pressure

End point title	Urodynamics:Maximum Detrusor Pressure

End point description:

Maximum Detrusor Pressure is an urodynamic parameter that is the maximum value of the pressure within the bladder which is measured during the filling phase of the urodynamic exam. Baseline urodynamics exams done at screening visit.

Analysis based on number (n) of subjects with a valid value in the Intent-to-Treat (ITT) population for the respective treatment groups.

End point type	Secondary

End point timeframe:

Baseline, Days 14, 42 and 84

End point values	Dysport 750 U (15 Injection Sites)	Placebo (15 Injection Sites)	Dysport 750 U (30 Injection Sites)	Placebo (30 Injection Sites)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	6	16	6
Units: cm water (cm H20)				
arithmetic mean (standard deviation)				
Baseline (n=14,5,15,6)	59 (± 44)	53 (± 40)	46 (± 28)	70 (± 23)
Change from baseline to D14 (n=14,5,16,6)	-24 (± 53)	-4 (± 18)	-27 (± 22)	27 (± 48)
Change from baseline to D42 (n=14,6,15,6)	-41 (± 40)	0 (± 14)	-24 (± 24)	10 (± 42)
Change from baseline to D84 (n=13,5,16,6)	-26 (± 46)	4 (± 18)	-20 (± 23)	12 (± 29)

Statistical analyses

Statistical analysis title	Urodynamics:Maximum Detrusor Pressure

Statistical analysis description:

Statistical Analysis 1

Comparison of the maximum Detrusor Pressure change from baseline to DAY 14 using ANCOVA with the baseline Maximum Detrusor Pressure as covariate.

Comparison groups	Placebo (15 Injection Sites) v Dysport 750 U (15 Injection Sites)

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.25
Method	ANCOVA

Statistical analysis title	Urodynamics:Maximum Detrusor Pressure

Statistical analysis description:

Statistical Analysis 2

Comparison of the maximum Detrusor Pressure change from baseline to DAY 14 using ANCOVA with the baseline Maximum Detrusor Pressure as covariate.

Comparison groups	Dysport 750 U (30 Injection Sites) v Placebo (30 Injection Sites)
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.01
Method	ANCOVA

Statistical analysis title	Urodynamics:Maximum Detrusor Pressure

Statistical analysis description:

Statistical Analysis 3

Comparison of the maximum Detrusor Pressure change from baseline to DAY 42 using ANCOVA with the baseline Maximum Detrusor Pressure as covariate.

Comparison groups	Dysport 750 U (15 Injection Sites) v Placebo (15 Injection Sites)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.03
Method	ANCOVA

Statistical analysis title	Urodynamics:Maximum Detrusor Pressure

Statistical analysis description:

Statistical Analysis 4

Comparison of the maximum Detrusor Pressure change from baseline to DAY 42 using ANCOVA with the baseline Maximum Detrusor Pressure as covariate.

Comparison groups	Dysport 750 U (30 Injection Sites) v Placebo (30 Injection Sites)

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.01
Method	ANCOVA

Statistical analysis title	Urodynamics:Maximum Detrusor Pressure

Statistical analysis description:

Statistical Analysis 5

Comparison of the maximum Detrusor Pressure change from baseline to DAY 84 using ANCOVA with the baseline Maximum Detrusor Pressure as covariate.

Comparison groups	Dysport 750 U (15 Injection Sites) v Placebo (15 Injection Sites)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.01
Method	ANCOVA

Statistical analysis title	Urodynamics:Maximum Detrusor Pressure

Statistical analysis description:

Statistical Analysis 6

Comparison of the maximum Detrusor Pressure change from baseline to DAY 84 using ANCOVA with the baseline Maximum Detrusor Pressure as covariate.

Comparison groups	Dysport 750 U (30 Injection Sites) v Placebo (30 Injection Sites)
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.01
Method	ANCOVA

Secondary: Physician's Global Assessment Score of Treatment Response

End point title	Physician's Global Assessment Score of Treatment Response

End point description:

The subject’s treatment response was assessed by the physician and graded as ‘markedly worse’, ‘much worse’, ‘worse’, ‘slightly worse’, ‘no change’, ‘slightly improved’, ‘improved’, ‘much improved’, or ‘markedly improved’.

Analysis based on number of subjects in the Intent to Treat (ITT) population.

End point type	Secondary

End point timeframe:

Day 14

End point values	Dysport 750 U (15 Injection Sites)	Placebo (15 Injection Sites)	Dysport 750 U (30 Injection Sites)	Placebo (30 Injection Sites)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	6	16	6
Units: participants				
Markedly worse	0	0	0	0
Much worse	0	0	0	0
Worse	0	0	0	0
Slightly worse	1	1	0	1
No change	2	3	1	3
Slightly improved	0	0	0	0
Improved	3	1	4	2
Much improved	4	1	8	0
Markedly improved	4	0	3	0

Statistical analyses

Statistical analysis title	PGA Score of Treatment Response
Statistical analysis description: Statistical Analysis 1	
Comparison groups	Placebo (15 Injection Sites) v Dysport 750 U (15 Injection Sites)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.05
Method	Satterthwaite-Welch’s t-test

Statistical analysis title	PGA Score of Treatment Response
Statistical analysis description: Statistical Analysis 2 Comparison of the Physician's Global Assessment score at DAY 14 using a two sided Satterthwaite-Welch’s t-test for independent samples.	
Comparison groups	Dysport 750 U (30 Injection Sites) v Placebo (30 Injection Sites)
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.01
Method	Satterthwaite-Welch’s t-test

Secondary: Physician's Global Assessment Score of Treatment Response

End point title	Physician's Global Assessment Score of Treatment Response

End point description:

The subject’s treatment response was assessed by the physician and graded as ‘markedly worse’, ‘much worse’, ‘worse’, ‘slightly worse’, ‘no change’, ‘slightly improved’, ‘improved’, ‘much improved’, or ‘markedly improved’.

Analysis based on number of subjects in the Intent to Treat (ITT) population.

End point type	Secondary

End point timeframe:

Day 42

End point values	Dysport 750 U (15 Injection Sites)	Placebo (15 Injection Sites)	Dysport 750 U (30 Injection Sites)	Placebo (30 Injection Sites)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	6	16	6
Units: participants				
Markedly worse	0	0	0	0
Much worse	0	0	0	0
Worse	0	0	0	0
Slightly worse	0	1	1	0
No change	1	3	0	3
Slightly improved	0	0	0	0
Improved	3	1	4	3
Much improved	5	1	7	0
Markedly improved	5	0	4	0

Statistical analyses

Statistical analysis title	PGA Score of Treatment Response

Statistical analysis description:

Statistical Analysis 1

Comparison of the Physician's Global Assessment score at DAY 42 using a two sided Satterthwaite-Welch’s t-test for independent samples.

Comparison groups	Dysport 750 U (15 Injection Sites) v Placebo (15 Injection Sites)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.01
Method	Satterthwaite-Welch’s t-test

Statistical analysis title	PGA Score of Treatment Response

Statistical analysis description:

Statistical Analysis 2

Comparison of the Physician's Global Assessment score at DAY 42 using a two sided Satterthwaite-Welch’s t-test for independent samples.

Comparison groups	Dysport 750 U (30 Injection Sites) v Placebo (30 Injection Sites)
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.01
Method	Satterthwaite-Welch’s t-test

Secondary: Physician's Global Assessment Score of Treatment Response

End point title	Physician's Global Assessment Score of Treatment Response

End point description:

The subject’s treatment response was assessed by the physician and graded as ‘markedly worse’, ‘much worse’, ‘worse’, ‘slightly worse’, ‘no change’, ‘slightly improved’, ‘improved’, ‘much improved’, or ‘markedly improved’.

Analysis based on number of subjects in the Intent to Treat (ITT) population.

End point type	Secondary

End point timeframe:

Day 84

End point values	Dysport 750 U (15 Injection Sites)	Placebo (15 Injection Sites)	Dysport 750 U (30 Injection Sites)	Placebo (30 Injection Sites)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	6	16	6
Units: participants				
Markedly worse	0	0	0	0
Much worse	0	0	0	0
Worse	0	1	0	0
Slightly worse	0	0	0	0
No change	1	2	1	4
Slightly improved	2	1	0	0
Improved	2	1	4	2
Much improved	6	1	7	0
Markedly improved	3	0	4	0

Statistical analyses

Statistical analysis title	PGA Score of Treatment Response

Statistical analysis description:

Statistical Analysis 1

Comparison of the Physician's Global Assessment score at DAY 84 using a two sided Satterthwaite-Welch's t-test for independent samples.

Comparison groups	Dysport 750 U (15 Injection Sites) v Placebo (15 Injection Sites)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.05
Method	Satterthwaite-Welch’s t-test

Statistical analysis title	PGA Score of Treatment Response

Statistical analysis description:

Statistical Analysis 2

Comparison of the Physician's Global Assessment score at DAY 84 using a two sided Satterthwaite-Welch's t-test for independent samples.

Comparison groups	Dysport 750 U (30 Injection Sites) v Placebo (30 Injection Sites)
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.01
Method	Satterthwaite-Welch’s t-test

Secondary: Quality of Life (QoL) Total Summary Score

End point title	Quality of Life (QoL) Total Summary Score

End point description:

Mean Change from Baseline in Short Form (SF)-Qualiveen Questionnaire Calculated Total Score.

The SF-Qualiveen questionnaire is a specific health related QoL questionnaire validated for urinary disorders in subjects with neurological conditions containing 8 items looking at four scales: limitations (2 items); constraints (2 items); fears (2 items) and feelings (2 items). The 8 items each having a 5-point Likert-type scale ranging from 0=“Not at all” to 4=“Extremely” for the first 6 items, from 0=“Never” to 4=“Always” for item 7 and from 0=”Always” to 4=”Never” for item 8. The score per scale has been calculated as the mean of the two items. In case of one missing item among the 2 items for a given scale, the score has not been calculated.

Total score has been calculated as the mean of all the items completed among the 8 items.
Lower scores indicate a better QoL (i.e. no limitations, fears, constraints, or negative feelings) and higher scores indicate poorer QoL.

Analysis -ITT

End point type	Secondary

End point timeframe:

Baseline, 14, 42 and 84

End point values	Dysport 750 U (15 Injection Sites)	Placebo (15 Injection Sites)	Dysport 750 U (30 Injection Sites)	Placebo (30 Injection Sites)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	6	16	6
Units: Score on scale				
arithmetic mean (standard deviation)				
Baseline	2.4 (± 0.7)	2.7 (± 0.6)	2.4 (± 0.8)	2.3 (± 1)
Change from baseline to D14	-1.1 (± 0.9)	-0.2 (± 1)	-0.8 (± 0.8)	-0.5 (± 1.3)
Change from baseline to D42	-1 (± 0.8)	-0.6 (± 1.2)	-1.2 (± 0.8)	-0.6 (± 1.1)
Change from baseline to D84	-1.3 (± 1)	-0.2 (± 0.7)	-1.2 (± 0.9)	-0.7 (± 1.1)

Statistical analyses

Statistical analysis title	Quality of Life (QoL) Total Summary Score

Statistical analysis description:

Statistical Analysis 1

Comparison of the Quality of Life Total Summary score change from baseline to DAY 14 using ANCOVA with the baseline Quality of Life Total Summary score as covariate.

Comparison groups	Dysport 750 U (15 Injection Sites) v Placebo (15 Injection Sites)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.01
Method	ANCOVA

Statistical analysis title	Quality of Life (QoL) Total Summary Score

Statistical analysis description:

Statistical Analysis 2

Comparison of the Quality of Life Total Summary score change from baseline to DAY 14 using ANCOVA with the baseline Quality of Life Total Summary score as covariate.

Comparison groups	Dysport 750 U (30 Injection Sites) v Placebo (30 Injection Sites)
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7
Method	ANCOVA

Statistical analysis title	Quality of Life (QoL) Total Summary Score

Statistical analysis description:

Statistical Analysis 3

Comparison of the Quality of Life Total Summary score change from baseline to DAY 42 using ANCOVA with the baseline Quality of Life Total Summary score as covariate.

Comparison groups	Dysport 750 U (15 Injection Sites) v Placebo (15 Injection Sites)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3
Method	ANCOVA

Statistical analysis title	Quality of Life (QoL) Total Summary Score

Statistical analysis description:

Statistical Analysis 4

Comparison of the Quality of Life Total Summary score change from baseline to DAY 42 using ANCOVA with the baseline Quality of Life Total Summary score as covariate.

Comparison groups	Dysport 750 U (30 Injection Sites) v Placebo (30 Injection Sites)
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3
Method	ANCOVA

Statistical analysis title	Quality of Life (QoL) Total Summary Score

Statistical analysis description:

Statistical Analysis 5

Comparison of the Quality of Life Total Summary score change from baseline to DAY 84 using ANCOVA with the baseline Quality of Life Total Summary score as covariate.

Comparison groups	Dysport 750 U (15 Injection Sites) v Placebo (15 Injection Sites)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.01
Method	ANCOVA

Statistical analysis title	Quality of Life (QoL) Total Summary Score

Statistical analysis description:

Statistical Analysis 6

Comparison of the Quality of Life Total Summary score change from baseline to DAY 84 using ANCOVA with the baseline Quality of Life Total Summary score as covariate.

Comparison groups	Dysport 750 U (30 Injection Sites) v Placebo (30 Injection Sites)

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4
Method	ANCOVA

Secondary: Pain Visual Analogue Scale (VAS) Score: Before Treatment Injection

End point title	Pain Visual Analogue Scale (VAS) Score: Before Treatment Injection

End point description:

Analysis based on number of subjects in the Intent to Treat (ITT) population.

Pain assessment using the VAS. The VAS is a 100-mm (10-cm) scoring scale. Score range on VAS is from 0 to 100 where zero [0]indicates no pain and 100 indicates worst possible pain.

End point type	Secondary

End point timeframe:

Baseline

End point values	Dysport 750 U (15 Injection Sites)	Placebo (15 Injection Sites)	Dysport 750 U (30 Injection Sites)	Placebo (30 Injection Sites)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	6	16	6
Units: mm				
arithmetic mean (standard deviation)	2.7 (± 9)	12.2 (± 21.5)	1.3 (± 2.6)	6.7 (± 16.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Pain Visual Analogue Scale (VAS) Score: During Treatment Injection Procedure

End point title	Pain Visual Analogue Scale (VAS) Score: During Treatment Injection Procedure

End point description:

Analysis based on number of subjects in the Intent to Treat (ITT) population.

Pain assessment using the VAS. The VAS is a 100-mm (10-cm) scoring scale. Score range on VAS is from 0 to 100 where zero [0] indicates no pain and 100 indicates worst possible pain.

End point type	Secondary

End point timeframe:

Baseline

End point values	Dysport 750 U (15 Injection Sites)	Placebo (15 Injection Sites)	Dysport 750 U (30 Injection Sites)	Placebo (30 Injection Sites)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	6	16	6
Units: mm				
arithmetic mean (standard deviation)	13.7 (± 19.3)	11 (± 19.9)	15.8 (± 19.7)	10 (± 24.5)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 98 days	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups	
Reporting group title	Dysport 750 U (15 Injection Sites)
Reporting group description: Botulinum type A toxin (Dysport®): 750 U using different administration regimen, intra detrusor injection on day 1 (single dose)	
Reporting group title	Placebo (15 Injection Sites)
Reporting group description: Placebo: Intra detrusor injection on day 1 (single dose)	
Reporting group title	Dysport 750 U (30 Injection Sites)
Reporting group description: Botulinum type A toxin (Dysport®): 750 U using different administration regimen, intra detrusor injection on day 1 (single dose)	
Reporting group title	Placebo (30 Injection Sites)
Reporting group description: Placebo: Intra detrusor injection on day 1 (single dose)	

Serious adverse events	Dysport 750 U (15 Injection Sites)	Placebo (15 Injection Sites)	Dysport 750 U (30 Injection Sites)
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 16 (31.25%)	0 / 7 (0.00%)	1 / 17 (5.88%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Multiple sclerosis relapse			
subjects affected / exposed	1 / 16 (6.25%)	0 / 7 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 16 (0.00%)	0 / 7 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			

Muscular weakness			
subjects affected / exposed	3 / 16 (18.75%)	0 / 7 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 7 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo (30 Injection Sites)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Multiple sclerosis relapse			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 7 (0.00%)		
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	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)		
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	Dysport 750 U (15 Injection Sites)	Placebo (15 Injection Sites)	Dysport 750 U (30 Injection Sites)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 16 (43.75%)	3 / 7 (42.86%)	11 / 17 (64.71%)
Investigations			
Blood urine present			
subjects affected / exposed	0 / 16 (0.00%)	0 / 7 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 7 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Neutrophil count increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 7 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 16 (0.00%)	0 / 7 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	1 / 7 (14.29%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 7 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Influenza like illness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 7 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 7 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			

Bladder Pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 7 (14.29%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 7 (14.29%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 7 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 7 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 7 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Bacteriuria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 7 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Escherichia sepsis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 7 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Fungal infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 7 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 7 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 7 (0.00%)	3 / 17 (17.65%)
occurrences (all)	1	0	3

Non-serious adverse events	Placebo (30 Injection Sites)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 7 (57.14%)		

Investigations			
Blood urine present			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Neutrophil count increased			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Influenza like illness			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Bladder Pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Bacteriuria			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Escherichia sepsis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Fungal infection			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 January 2012	Protocol version 5.0 Changes: The protocol was amended due to questions released by the German Federal Institute for Drugs and Medical Devices (BfArM) on 09 December 2011 and the German Ethics Committee (EC) on 04 January 2012. As the new protocol was submitted in other countries, inclusion criterion #6 was updated, inclusion criterion #12 and exclusion criterion #2 were clarified and exclusion criterion #21 was added at the same time. Inclusion criterion 6 was changed: • From: Have documented SCI or MS with urodynamic measurement abnormalities within 6 months (both complete and incomplete SCIs and relevant MS with confirmed NDO as defined by ICS guidelines will be included in this study) • To: Have documented SCI or MS (both complete and incomplete SCIs and relevant MS with confirmed NDO as defined by ICS guidelines will be included in this study). Inclusion criterion 12 was changed: • From: Female subjects of childbearing potential must have a negative pregnancy test result and be willing to use reliable contraceptive measures for the duration of the study • To: Female subjects of childbearing potential must have had a negative pregnancy test result and have been willing to use reliable contraceptive measures for the duration the study (i.e. oral contraceptives and spermicide, when used in combination with condoms, etc. as a 'double barrier method') Exclusion criterion 2 was changed • From: Previous or current requirement for/diagnosis of bladder or and urethral disease or surgery, or disease/prostate cancer (PSA of >10 ng/mL). Subjects with serum PSA concentrations >4 ng/mL and <10 ng/mL must have prostate cancer excluded • To: Previous or current diagnosis of bladder and urethral disease or surgery, or prostate cancer (PSA of >10 ng/mL). Subjects with serum PSA concentrations >4 ng/mL and <10 ng/mL must have prostate cancer excluded. In light of this amendment, the CRF, local consent form, database and RAP required updating.

15 January 2013	Protocol version 6.0 The protocol was amended to increase the number of participating centres (from approximately 8 to 10 to 22 centres) and to reduce the sample size following difficulties in recruitment. The sections on Sample Size Determination were changed • From: This is a preliminary, pilot study with a limited number of subjects where the sample size of 56 subjects was based on the clinical judgement/practical constraints and not on statistical considerations. A total of 56 subjects will be randomised in this study, out of which: - 20 will receive Dysport 750 U, 0.5 mL in 15 sites - 8 will receive placebo, 0.5 mL in 15 sites - 20 will receive Dysport 750 U, 0.5 mL in 30 sites - 8 will receive placebo, 0.5 mL in 30 sites. • To: This is a preliminary, pilot study with a limited number of subjects where the sample size of at least 42 subjects was based on the clinical judgement/practical constraints and not on statistical considerations. A total of at least 42 subjects will be randomised in this study, out of which: - At least 15 will receive Dysport 750 U, 0.5 mL in 15 sites - At least 6 will receive placebo, 0.5 mL in 15 sites - At least 15 will receive Dysport 750 U, 0.5 mL in 30 sites - At least 6 will receive placebo, 0.5 mL in 30 sites. The protocol was also amended to allow the replacement of subjects who were randomised but who were not assessed on the primary efficacy variable at Baseline. In light of this amendment, the local consent form and RAP required updating.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported