Clinical trial results:
A Phase III, Multicentre, Double Blind, Prospective, Randomised, Controlled, Multiple Treatment Study Assessing Efficacy and Safety of Dysport Used in the Treatment of Upper Limb Spasticity in Children

Summary

EudraCT number	2010-021817-22
Trial protocol	CZ ES PL BE Outside EU/EEA
Global end of trial date	04 September 2018

Results information

Result version number	v2 (current)
This version publication date	13 June 2020
First version publication date	25 May 2019
Version creation reason	• Correction of full data set Paediatric regulatory detail data correction

Trial information

Trial identification

Sponsor protocol code	Y-52-52120-153

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02106351
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ipsen Innovation
Sponsor organisation address	Z.I. de Courtaboeuf, 5 Avenue du Canada, Cedex, France, 91940 Les Ulis
Public contact	Medical Director, Ipsen, clinical.trials@ipsen.com
Scientific contact	Medical Director, Ipsen, 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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 September 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main study objective was to assess the efficacy and safety of 2 doses of Dysport (8 Units per kilogram [U/kg] and 16 U/kg) administered by intramuscular (IM) injection compared to Dysport 2 U/kg (low dose control group) used in the treatment of upper limb spasticity in children.

Protection of trial subjects:

The study was conducted under the provisions of the Declaration of Helsinki in accordance with the International Conference on Harmonisation Guideline on Good Clinical Practice and in compliance with independent ethics committees/institutional review boards and informed consent regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 April 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Turkey: 44
Country: Number of subjects enrolled	United States: 63
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Czech Republic: 5
Country: Number of subjects enrolled	Israel: 23
Country: Number of subjects enrolled	Mexico: 24
Country: Number of subjects enrolled	Poland: 37
Worldwide total number of subjects	210
EEA total number of subjects	56

Notes:

Subjects enrolled per age group

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

months)	
Children (2-11 years)	143
Adolescents (12-17 years)	67
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Male and female subjects aged between 2 and 17 years with upper limb spasticity due to cerebral palsy (CP) were recruited from April 2014 and the study completed in September 2018. Subjects could receive a maximum of 4 treatment cycles (TC) over a minimum of 1 year and maximum of 1 year and 9 months, with at least 16 weeks between each TC.

Pre-assignment

Screening details:

Subjects had a body weight ≥10 kg, increased muscle tone/spasticity in at least 1 upper limb, a modified Ashworth scale (MAS) score ≥2 in the upper limb primary targeted muscle group (PTMG) of the study limb at baseline. Subjects were stratified according to age (2-9 and 10-17 years) and Botulinum Toxin (BTX) naïve or non-naïve status.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Dysport 2 U/kg

Arm description:

Subjects were randomised to receive 2 U/kg Dysport by IM injection in the study upper limb in TC 1 and Dysport 8 U/kg or 16 U/kg in subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Arm type	Control arm
Investigational medicinal product name	Dysport
Investigational medicinal product code	
Other name	Clostridium BTX-A-HAC, AbobotulinumtoxinA
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 2 U/kg Dysport by IM injection divided between the PTMG elbow and wrist flexors and other non-PTMG muscles in the study limb.

Arm title	Dysport 8 U/kg

Arm description:

Subjects were randomised to receive Dysport 8 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Arm type	Experimental
Investigational medicinal product name	Dysport
Investigational medicinal product code	
Other name	Clostridium BTX-A-HAC, AbobotulinumtoxinA
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 8 U/kg Dysport by IM injection divided between the PTMG elbow and wrist flexors and other non-PTMG muscles in the study limb, up to maximum dose of 320 U.

Arm title	Dysport 16 U/kg

Arm description:

Subjects were randomised to receive Dysport 16 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Arm type	Experimental
Investigational medicinal product name	Dysport
Investigational medicinal product code	
Other name	Clostridium BTX-A-HAC, AbobotulinumtoxinA
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 16 U/kg Dysport by IM injection divided between the PTMG elbow and wrist flexors and other non-PTMG muscles in the study limb, up to maximum dose of 640 U.

Number of subjects in period 1	Dysport 2 U/kg	Dysport 8 U/kg	Dysport 16 U/kg
Started	70	70	70
Completed	66	67	67
Not completed	4	3	3
Consent withdrawn by subject	1	-	2
Adverse event, non-fatal	2	-	-
Not specified	-	3	1
Lost to follow-up	1	-	-

Period 2

Period 2 title	Treatment Cycle 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	No
Arm title	Dysport 8 U/kg

Arm description:

Subjects were randomised to receive Dysport 8 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Arm type	Experimental

Investigational medicinal product name	Dysport
Investigational medicinal product code	
Other name	Clostridium BTX-A-HAC, AbobotulinumtoxinA
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 8 U/kg Dysport by IM injection divided between the PTMG elbow and wrist flexors and other non-PTMG muscles in the study limb, up to maximum dose of 320 U.

Arm title	Dysport 16 U/kg

Arm description:

Subjects were randomised to receive Dysport 16 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Arm type	Experimental
Investigational medicinal product name	Dysport
Investigational medicinal product code	
Other name	Clostridium BTX-A-HAC, AbobotulinumtoxinA

Arm title	Dysport 8 U/kg

Arm description:

Subjects were randomised to receive Dysport 8 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Arm type	Experimental
Investigational medicinal product name	Dysport
Investigational medicinal product code	
Other name	Clostridium BTX-A-HAC, AbobotulinumtoxinA
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 8 U/kg Dysport by IM injection divided between the PTMG elbow and wrist flexors and other non-PTMG muscles in the study limb, up to maximum dose of 320 U.

Arm title	Dysport 16 U/kg

Arm description:

Subjects were randomised to receive Dysport 16 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Arm type	Experimental
Investigational medicinal product name	Dysport
Investigational medicinal product code	
Other name	Clostridium BTX-A-HAC, AbobotulinumtoxinA
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 16 U/kg Dysport by IM injection divided between the PTMG elbow and wrist flexors and other non-PTMG muscles in the study limb, up to maximum dose of 640 U.

Number of subjects in period 3	Dysport 8 U/kg	Dysport 16 U/kg
Started	49	58
Completed	45	53
Not completed	4	5
Consent withdrawn by subject	-	2
Adverse event, non-fatal	1	-
Not specified	2	3
Lost to follow-up	1	-

Period 4

Period 4 title	Treatment Cycle 4
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Dysport 8 U/kg

Arm description:

Subjects were randomised to receive Dysport 8 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Arm type	Experimental
Investigational medicinal product name	Dysport
Investigational medicinal product code	
Other name	Clostridium BTX-A-HAC, AbobotulinumtoxinA
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 8 U/kg Dysport by IM injection divided between the PTMG elbow and wrist flexors and other non-PTMG muscles in the study limb, up to maximum dose of 320 U.

Arm title	Dysport 16 U/kg

Arm description:

Subjects were randomised to receive Dysport 16 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Arm type	Experimental
Investigational medicinal product name	Dysport
Investigational medicinal product code	
Other name	Clostridium BTX-A-HAC, AbobotulinumtoxinA
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 16 U/kg Dysport by IM injection divided between the PTMG elbow and wrist flexors and other non-PTMG muscles in the study limb, up to maximum dose of 640 U.

Number of subjects in period 4[1]	Dysport 8 U/kg	Dysport 16 U/kg
Started	22	33
Completed	21	31
Not completed	1	2
Consent withdrawn by subject	-	2
Not specified	1	-

Notes:

[1] - 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: Not all subjects who received treatment in TC 3 required retreatment in TC 4.

Baseline characteristics

Reporting groups	
Reporting group title	Dysport 2 U/kg
Reporting group description:	
Subjects were randomised to receive 2 U/kg Dysport by IM injection in the study upper limb in TC 1 and Dysport 8 U/kg or 16 U/kg in subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.	
Reporting group title	Dysport 8 U/kg
Reporting group description:	
Subjects were randomised to receive Dysport 8 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.	
Reporting group title	Dysport 16 U/kg
Reporting group description:	
Subjects were randomised to receive Dysport 16 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.	

Reporting group values	Dysport 2 U/kg	Dysport 8 U/kg	Dysport 16 U/kg
Number of subjects	70	70	70
Age categorical Units: Subjects			
2 - 9 Years	40	40	40
10 - 17 Years	30	30	30
Age continuous Units: years			
arithmetic mean	8.91	8.97	9.17
standard deviation	± 4.55	± 4.27	± 4.30
Gender categorical Units: Subjects			
Female	32	24	28
Male	38	46	42
Race, Customised Units: Subjects			
Asian	2	1	0
Black or African American	7	6	3
White	49	54	54
American Indian or Alaska Native	0	1	0
Multiple	12	8	13
Ethnicity, Customised Units: Subjects			
Hispanic or Latino	16	13	15
Not Hispanic or Latino	54	57	55
BTX Status Units: Subjects			
BTX naïve	25	23	24
BTX non-naïve	45	47	46

Baseline MAS Score in the PTMG			
The MAS has 6 grades: 0 (no increase in muscle tone), 1 (slight increase in muscle tone, manifested by a catch + release or by minimal resistance at the end of the range of motion [ROM]) when the affected part is moved in flexion/extension, 1+ (slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM), 2 (more marked increase in muscle tone), 3 (considerable increase in muscle tone) or 4 (affected part(s) rigid in flexion/extension). '1+' was given a derived score of '2'; following scores were incremented by 1.			
Units: Score on a scale			
arithmetic mean	3.1	3.1	3.1
standard deviation	± 0.3	± 0.3	± 0.5

Reporting group values	Total		
Number of subjects	210		
Age categorical Units: Subjects			
2 - 9 Years	120		
10 - 17 Years	90		
Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	84		
Male	126		
Race, Customised Units: Subjects			
Asian	3		
Black or African American	16		
White	157		
American Indian or Alaska Native	1		
Multiple	33		
Ethnicity, Customised Units: Subjects			
Hispanic or Latino	44		
Not Hispanic or Latino	166		
BTX Status Units: Subjects			
BTX naïve	72		
BTX non-naïve	138		
Baseline MAS Score in the PTMG			
The MAS has 6 grades: 0 (no increase in muscle tone), 1 (slight increase in muscle tone, manifested by a catch + release or by minimal resistance at the end of the range of motion [ROM]) when the affected part is moved in flexion/extension, 1+ (slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM), 2 (more marked increase in muscle tone), 3 (considerable increase in muscle tone) or 4 (affected part(s) rigid in flexion/extension). '1+' was given a derived score of '2'; following scores were incremented by 1.			
Units: Score on a scale arithmetic mean standard deviation	-		

End points

End points reporting groups

Reporting group title	Dysport 2 U/kg

Reporting group description:

Subjects were randomised to receive 2 U/kg Dysport by IM injection in the study upper limb in TC 1 and Dysport 8 U/kg or 16 U/kg in subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Reporting group title	Dysport 8 U/kg

Reporting group description:

Subjects were randomised to receive Dysport 8 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Reporting group title	Dysport 16 U/kg

Reporting group description:

Subjects were randomised to receive Dysport 16 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Reporting group title	Dysport 8 U/kg

Reporting group description:

Subjects were randomised to receive Dysport 8 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Reporting group title	Dysport 16 U/kg

Reporting group description:

Subjects were randomised to receive Dysport 16 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Reporting group title	Dysport 8 U/kg

Reporting group description:

Subjects were randomised to receive Dysport 8 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Reporting group title	Dysport 16 U/kg

Reporting group description:

Subjects were randomised to receive Dysport 16 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Reporting group title	Dysport 8 U/kg

Reporting group description:

Subjects were randomised to receive Dysport 8 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Reporting group title	Dysport 16 U/kg

Reporting group description:

Subjects were randomised to receive Dysport 16 U/kg by IM injection into the study upper limb in TC 1 and all subsequent TCs (2, 3 and 4). Retreatment was based on clinical need with a minimum retreatment interval of 16 weeks. From TC 2 onwards dose adaptation was permitted as well as treatment of the non-study upper limb and lower limbs.

Primary: Mean Change from Baseline to TC 1, Week 6 in MAS Score in the TC 1 PTMG	
End point title	Mean Change from Baseline to TC 1, Week 6 in MAS Score in the TC 1 PTMG

End point description:

The MAS was used to assess muscle tone in the upper limb PTMG and consists of 6 grades: 0 (no increase in muscle tone), 1 (slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the ROM) when the affected part is moved in flexion or extension, 1+ (slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM), 2 (more marked increase in muscle tone), 3 (considerable increase in muscle tone) or 4 (affected part(s) rigid in flexion or extension). The original score '+1' was given a derived numeric score of '2' and the higher numeric scores were incremented by 1 so that the MAS score range was from 0 to 5 with higher scores indicating greater muscle tone. A negative change from baseline indicates a decrease in muscle tone.

End point type	Primary

End point timeframe:

Baseline (TC 1, Day 1) and TC 1, Week 6.

End point values	Dysport 2 U/kg	Dysport 8 U/kg	Dysport 16 U/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	69	70	
Units: score on a scale				
arithmetic mean (standard deviation)	-1.5 (± 1.1)	-1.9 (± 1.0)	-2.2 (± 0.9)	

Statistical analyses

Statistical analysis title	Dysport 8 U/kg vs Dysport 2 U/kg

Statistical analysis description:

The treatment difference between Dysport 8 U/kg and Dysport 2 U/kg was analysed using an analysis of covariance (ANCOVA) on the ranked changes from baseline. The model included treatment group, the baseline value, the 2 stratification factors (age range and BTX status at baseline) and the pooled centre as fixed effects. The derived least squares (LS) means were back transformed to the original scale and the treatment difference determined.

Comparison groups	Dysport 2 U/kg v Dysport 8 U/kg
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0118 [1]
Method	ANCOVA

Notes:

[1] - ANCOVA is performed on the ranked values. The 2-tailed significance level was 0.05. LS mean difference, back transformed = -0.4

Statistical analysis title	Dysport 16 U/kg vs Dysport 2 U/kg

Statistical analysis description:

The treatment difference between Dysport 16 U/kg and Dysport 2 U/kg was analysed using an ANCOVA on the ranked changes from baseline. The model included treatment group, the baseline value, the 2 stratification factors (age range and BTX status at baseline) and the pooled centre as fixed effects. The

derived LS means were back transformed to the original scale and the treatment difference determined.

Comparison groups	Dysport 2 U/kg v Dysport 16 U/kg
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	ANCOVA

Notes:

[2] - ANCOVA is performed on the ranked values. The 2-tailed significance level was 0.05. LS mean difference, back-transformed = -0.7

Secondary: Mean Physician's Global Assessment (PGA) Score at TC 1, Week 6

End point title	Mean Physician's Global Assessment (PGA) Score at TC 1, Week 6

End point description:

The PGA of treatment response was assessed by asking the investigator the following question: 'How would you rate the response to treatment in the subject's upper limb since the start of the study?'. Answers were on a 9-point rating scale (-4: markedly worse, -3: much worse, -2: worse, -1: slightly worse, 0: no change, +1: slightly improved, +2: improved, +3: much improved and +4: markedly improved). The mean scores for each treatment group at TC 1, Week 6 are presented. Data is presented for the mITT population.

End point type	Secondary

End point timeframe:

TC 1, Week 6.

End point values	Dysport 2 U/kg	Dysport 8 U/kg	Dysport 16 U/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	68	69	70	
Units: score on a scale				
arithmetic mean (standard deviation)	1.7 (± 0.9)	2.0 (± 0.9)	2.0 (± 0.9)	

Statistical analyses

Statistical analysis title	Dysport 2 U/kg vs Dysport 8 U/kg

Statistical analysis description:

The treatment difference between Dysport 8 U/kg and Dysport 2 U/kg was analysed using an analysis of variance (ANOVA) on the rank of the PGA score at TC 1, Week 6. The model included treatment group, the 2 stratification factors (age range and BTX status at baseline) and the centre as fixed effects. The derived LS means were back transformed to the original scale and the treatment difference determined.

Comparison groups	Dysport 2 U/kg v Dysport 8 U/kg
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2043 [3]
Method	ANOVA

Notes:

[3] - ANOVA was performed on the ranked values. The 2-tailed significance level was 0.05. LS mean difference, back transformed = 0.2.

Statistical analysis title	Dysport 2 U/kg vs Dysport 16 U/kg

Statistical analysis description:

The treatment difference between Dysport 16 U/kg and Dysport 2 U/kg was analysed using an ANOVA on the rank of the PGA score at TC 1, Week 6. The model included treatment group, the 2 stratification factors (age range and BTX status at baseline) and the centre as fixed effects. The derived LS means were back transformed to the original scale and the treatment difference determined.

Comparison groups	Dysport 16 U/kg v Dysport 2 U/kg
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.188 [4]
Method	ANOVA

Notes:

[4] - ANOVA was performed on ranked values. The 2-tailed significance level was 0.05. LS mean difference, back transformed = 0.2.

Secondary: Mean Goal Attainment Scale (GAS) Total Score at TC 1, Week 6

End point title	Mean Goal Attainment Scale (GAS) Total Score at TC 1, Week 6

End point description:

The GAS is a functional 5-point scale used to measure progress towards individual therapy goals. At the start of each TC, 1 to 3 individual goals were defined for each subject by the investigator and the child's parents/guardians/caregivers prior to treatment. The outcome to reach each goal was rated on a 5-point scale (-2: much less than expected outcome, -1: somewhat less than expected outcome, 0: expected outcome, 1+: somewhat more than expected outcome, 2+: much more than expected outcome). A total GAS score was calculated taking into account the post-baseline outcome of each goal as well as the importance and difficulty of the goals and transformed into a standardised measure (T score). Therefore a score of 50 indicates that all individual goals had the expected outcome.

End point type	Secondary

End point timeframe:

TC 1, Week 6.

End point values	Dysport 2 U/kg	Dysport 8 U/kg	Dysport 16 U/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	68	66	70	
Units: score on a scale				
arithmetic mean (standard deviation)	51.3 (± 9.9)	52.6 (± 10.1)	52.0 (± 9.6)	

Statistical analyses

Statistical analysis title	Dysport 2 U/kg vs Dysport 8 U/kg

Statistical analysis description:

The treatment difference between Dysport 8 U/kg and Dysport 2 U/kg was analysed using ANOVA on the GAS Total score at TC 1, Week 6. The model included treatment group, the 2 stratification factors (age range and BTX status at baseline) and the centre as fixed effects.

Comparison groups	Dysport 2 U/kg v Dysport 8 U/kg

Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7648 [5]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	3.7

Notes:

[5] - The 2-tailed significance level was 0.05.

Statistical analysis title	Dysport 2 U/kg vs Dysport 16 U/kg

Statistical analysis description:

The treatment difference between Dysport 16 U/kg and Dysport 2 U/kg was analysed using ANOVA on the GAS Total score at TC 1, Week 6. The model included treatment group, the 2 stratification factors (age range and BTX status at baseline) and the centre as fixed effects.

Comparison groups	Dysport 2 U/kg v Dysport 16 U/kg
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7429
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	3.7

Other pre-specified: Mean Change from Baseline to TC 1 Week 16 in MAS score in the TC 1 PTMG

End point title	Mean Change from Baseline to TC 1 Week 16 in MAS score in the TC 1 PTMG

End point description:

The MAS was used to assess muscle tone in the upper limb PTMG and consists of 6 grades: 0 (no increase in muscle tone), 1 (slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the ROM) when the affected part is moved in flexion or extension, 1+ (slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM), 2 (more marked increase in muscle tone), 3 (considerable increase in muscle tone) or 4 (affected part(s) rigid in flexion or extension). The original score '+1' was given a derived numeric score of '2' and the higher numeric scores were incremented by 1 so that the MAS score range was from 0 to 5 with higher scores indicating greater muscle tone. A negative change from baseline indicates a decrease in muscle tone. Data is presented for the mITT population.

End point type	Other pre-specified

End point timeframe:

Baseline (TC 1, Day 1) and TC 1, Week 16.

End point values	Dysport 2 U/kg	Dysport 8 U/kg	Dysport 16 U/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	68	68	68	
Units: score on a scale				
arithmetic mean (standard deviation)	-1.0 (± 1.0)	-1.4 (± 1.1)	-1.6 (± 1.2)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean Change from Baseline to TC 1 Weeks 6 and 16 in MAS Score in the Elbow Flexors of the Study Limb

End point title	Mean Change from Baseline to TC 1 Weeks 6 and 16 in MAS Score in the Elbow Flexors of the Study Limb

End point description:

The MAS was used to assess muscle tone in the upper limb PTMG and consists of 6 grades: 0 (no increase in muscle tone), 1 (slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the ROM) when the affected part is moved in flexion or extension, 1+ (slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM), 2 (more marked increase in muscle tone), 3 (considerable increase in muscle tone) or 4 (affected part(s) rigid in flexion or extension). The original score '+1' was given a derived numeric score of '2' and the higher numeric scores were incremented by 1 so that the MAS score range was from 0 to 5 with higher scores indicating greater muscle tone. A negative change from baseline indicates a decrease in muscle tone. Data is presented for subjects injected in the elbow flexors. n= number of subjects analysed at each timepoint.

End point type	Other pre-specified

End point timeframe:

Baseline (TC 1, Day 1) and TC 1, Weeks 6 and 16.

End point values	Dysport 2 U/kg	Dysport 8 U/kg	Dysport 16 U/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	69	70	
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 6 n=63, 63, 62	-1.0 (± 1.1)	-1.7 (± 1.1)	-1.9 (± 1.2)	
Week 16 n= 62, 62, 60	-0.6 (± 1.0)	-1.2 (± 1.2)	-1.3 (± 1.4)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean Change from Baseline to TC 1 Weeks 6 and 16 in MAS

Score in the Wrist Flexors of the Study Limb

End point title	Mean Change from Baseline to TC 1 Weeks 6 and 16 in MAS Score in the Wrist Flexors of the Study Limb

End point description:

The MAS was used to assess muscle tone in the upper limb PTMG and consists of 6 grades: 0 (no increase in muscle tone), 1 (slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the ROM) when the affected part is moved in flexion or extension, 1+ (slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM), 2 (more marked increase in muscle tone), 3 (considerable increase in muscle tone) or 4 (affected part(s) rigid in flexion or extension). The original score '+1' was given a derived numeric score of '2' and the higher numeric scores were incremented by 1 so that the MAS score range was from 0 to 5 with higher scores indicating greater muscle tone. A negative change from baseline indicates a decrease in muscle tone. Data is presented for subjects injected in the wrist flexors. n= number of subjects analysed at each timepoint.

End point values	Dysport 2 U/kg	Dysport 8 U/kg	Dysport 16 U/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	69	70	
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 6 n=23, 23, 19	-0.8 (± 0.9)	-1.8 (± 1.1)	-1.9 (± 1.0)	
Week 16 n=22, 23, 19	-0.8 (± 1.3)	-1.3 (± 0.8)	-1.8 (± 1.0)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean PGA Score at TC 1 Week 16

End point title	Mean PGA Score at TC 1 Week 16

End point description:

The PGA of treatment response was assessed by asking the investigator the following question: 'How would you rate the response to treatment in the subject's upper limb since the start of the study?'. Answers were on a 9-point rating scale (-4: markedly worse, -3: much worse, -2: worse, -1: slightly worse, 0: no change, +1: slightly improved, +2: improved, +3: much improved and +4: markedly improved). The mean scores for each treatment group at TC 1 Week 16 are presented. n= number of subjects analysed at each timepoint.

End point type	Other pre-specified

End point timeframe:

Baseline (TC 1, Day 1) and TC 1, Week 16.

End point values	Dysport 2 U/kg	Dysport 8 U/kg	Dysport 16 U/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	69	70	
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 16 n=68, 67, 68	1.7 (± 1.0)	1.6 (± 1.1)	1.9 (± 1.2)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean GAS Total Score at TC 1 Week 16

End point title	Mean GAS Total Score at TC 1 Week 16

End point description:

The GAS is a functional scale used to measure progress towards individual therapy goals. At the start of

each TC, 1 to 3 individual goals were defined for each subject prior to treatment. The outcome to reach each goal was rated on a 5-point scale (-2: much less than expected outcome, -1: somewhat less than expected outcome, 0: expected outcome, 1: somewhat more than expected outcome, 2: much more than expected outcome). A total GAS score was calculated taking into account the post-baseline outcome of each goal as well as the importance and difficulty of the goals and transformed into a standardised measure (T score). Therefore a score of 50 indicates that all individual goals had the expected outcome. The mean GAS scores at TC 1 Week 16 are presented. n= number of subjects analysed at each timepoint.

End point type	Other pre-specified

End point timeframe:

Baseline (TC 1, Day 1) and TC 1, Week 16.

End point values	Dysport 2 U/kg	Dysport 8 U/kg	Dysport 16 U/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	69	70	
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 16 n=66, 67, 69	54.7 (± 9.8)	54.2 (± 9.7)	55.1 (± 10.1)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean Change from Baseline to TC 1, Week 16 in the Paediatric Quality of Life (PedsQL) Scores

End point title	Mean Change from Baseline to TC 1, Week 16 in the Paediatric Quality of Life (PedsQL) Scores

End point description:

Parents/guardians completed questionnaires on their child's quality of life. The PedsQL parent inventory measured heathcare concepts for children/adolescents aged 2-18 years. The Generic Core Scales include physical, emotional, social and school aspects. The CP module was also completed. Scores were transformed on a scale from 0 to 100 with higher scores indicating a better quality of life. Mean changes from baseline to TC 1, Week 16 are presented for the General Core Scale and for the CP module. A positive change from baseline indicates an improvement in quality of life. n= number of subjects analysed.

End point type	Other pre-specified

End point timeframe:

Baseline (TC 1, Day 1) and TC 1, Week 16.

End point values	Dysport 2 U/kg	Dysport 8 U/kg	Dysport 16 U/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	69	70	
Units: score on a scale				
arithmetic mean (standard deviation)				
Generic Core Scale n=67, 67, 67	3.4 (± 9.7)	3.4 (± 17.1)	2.0 (± 12.0)	
CP Module n=64, 64, 65	4.8 (± 16.8)	2.1 (± 14.9)	2.8 (± 16.2)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events (TEAEs) were collected from the first injection of study treatment up to the end of TC 4 (up to 21 months).

Adverse event reporting additional description:

TEAEs are reported for the dose received prior to onset of the AE. Due to dose adaptation due to safety lower doses were permitted for TCs 2 - 4.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	TC1: Dysport 2 U/kg

Reporting group description:

Subjects randomised to Dysport 2 U/kg in TC 1.

Reporting group title	TC 1: Dysport 8 U/kg

Reporting group description:

Subjects randomised to Dysport 8 U/kg in TC 1.

Reporting group title	TC 1: Dysport 16 U/kg

Reporting group description:

Subjects randomised to Dysport 16 U/kg in TC 1.

Reporting group title	TC 2: Dysport 8 U/kg

Reporting group description:

Subjects who received Dysport 8 U/kg in TC 2.

Reporting group title	TC 2: Dysport 16 U/kg

Reporting group description:

Subjects who received Dysport 16 U/kg in TC 2.

Reporting group title	TC 3: Dysport 8 U/kg

Reporting group description:

Subjects who received Dysport 8 U/kg in TC 3.

Reporting group title	TC 3: Dysport 16 U/kg

Reporting group description:

Subjects who received Dysport 16 U/kg in TC 3.

Reporting group title	TC 4: Dysport 8 U/kg

Reporting group description:

Subjects who received Dysport 8 U/kg in TC 4.

Reporting group title	TC 4: Dysport 16 U/kg

Reporting group description:

Subjects who received Dysport 16 U/kg in TC 4.

Serious adverse events	TC1: Dysport 2 U/kg	TC 1: Dysport 8 U/kg	TC 1: Dysport 16 U/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 70 (5.71%)	2 / 70 (2.86%)	2 / 70 (2.86%)
number of deaths (all causes)	0	0	0
number of deaths resulting from	0	0	0

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Testicular malignant teratoma			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram ST segment elevation			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	0 / 70 (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
Hand fracture			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	0 / 70 (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
Surgical and medical procedures			
Medical device removal			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle release			

subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ostectomy			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiotherapy to bone			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scoliosis surgery			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Focal dyscognitive seizures			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ventricle dilatation			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			

subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	0 / 70 (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
Vomiting			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			

subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Escherichia urinary tract infection			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	TC 2: Dysport 8 U/kg	TC 2: Dysport 16 U/kg	TC 3: Dysport 8 U/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 88 (6.82%)	1 / 90 (1.11%)	3 / 49 (6.12%)
number of deaths (all causes)	0	0	0
number of deaths resulting from	0	0	0

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Testicular malignant teratoma			
subjects affected / exposed	0 / 88 (0.00%)	1 / 90 (1.11%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 88 (1.14%)	0 / 90 (0.00%)	0 / 49 (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
Electrocardiogram ST segment elevation			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Medical device removal			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle release			

subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ostectomy			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiotherapy to bone			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scoliosis surgery			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	2 / 88 (2.27%)	0 / 90 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Focal dyscognitive seizures			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ventricle dilatation			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			

subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 90 (0.00%)	0 / 49 (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
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	1 / 88 (1.14%)	0 / 90 (0.00%)	0 / 49 (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 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Escherichia urinary tract infection			
subjects affected / exposed	1 / 88 (1.14%)	0 / 90 (0.00%)	0 / 49 (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
Gastroenteritis			
subjects affected / exposed	1 / 88 (1.14%)	0 / 90 (0.00%)	0 / 49 (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
Influenza			
subjects affected / exposed	1 / 88 (1.14%)	0 / 90 (0.00%)	0 / 49 (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
Gastroenteritis viral			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 88 (1.14%)	0 / 90 (0.00%)	0 / 49 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	TC 3: Dysport 16 U/kg	TC 4: Dysport 8 U/kg	TC 4: Dysport 16 U/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 58 (3.45%)	2 / 22 (9.09%)	1 / 33 (3.03%)
number of deaths (all causes)	0	0	0
number of deaths resulting from	0	0	0

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Testicular malignant teratoma			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram ST segment elevation			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Medical device removal			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle release			

subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ostectomy			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiotherapy to bone			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scoliosis surgery			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	2 / 58 (3.45%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Focal dyscognitive seizures			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ventricle dilatation			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			

subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 58 (1.72%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			

subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Escherichia urinary tract infection			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	TC1: Dysport 2 U/kg	TC 1: Dysport 8 U/kg	TC 1: Dysport 16 U/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 70 (21.43%)	23 / 70 (32.86%)	19 / 70 (27.14%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 70 (2.86%)	4 / 70 (5.71%)	2 / 70 (2.86%)
occurrences (all)	2	5	2
Injection site bruising			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Injection site rash			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	0 / 70 (0.00%)	5 / 70 (7.14%)	1 / 70 (1.43%)
occurrences (all)	0	6	1
Pleural effusion			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Investigations			
International normalised ratio increased			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0

Anaemia postoperative			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Postoperative ileus			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 70 (0.00%)	4 / 70 (5.71%)	2 / 70 (2.86%)
occurrences (all)	0	6	2
Epilepsy			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye pruritus			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0

Dental caries			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash erythematous			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 70 (1.43%)	3 / 70 (4.29%)	4 / 70 (5.71%)
occurrences (all)	1	3	4
Pain in extremity			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	10 / 70 (14.29%)	6 / 70 (8.57%)	6 / 70 (8.57%)
occurrences (all)	13	7	7
Upper respiratory tract infection			
subjects affected / exposed	5 / 70 (7.14%)	6 / 70 (8.57%)	8 / 70 (11.43%)
occurrences (all)	6	8	10
Pharyngitis			
subjects affected / exposed	6 / 70 (8.57%)	3 / 70 (4.29%)	4 / 70 (5.71%)
occurrences (all)	8	3	4
Sinusitis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0

Impetigo			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	TC 2: Dysport 8 U/kg	TC 2: Dysport 16 U/kg	TC 3: Dysport 8 U/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 88 (20.45%)	17 / 90 (18.89%)	14 / 49 (28.57%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	7 / 88 (7.95%)	1 / 90 (1.11%)	0 / 49 (0.00%)
occurrences (all)	8	1	0
Injection site bruising			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Injection site rash			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0

Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	1 / 88 (1.14%)	1 / 90 (1.11%)	0 / 49 (0.00%)
occurrences (all)	1	1	0
Pleural effusion			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Investigations			
International normalised ratio increased			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	1 / 88 (1.14%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Anaemia postoperative			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Postoperative ileus			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Fall			

subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Epilepsy			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye pruritus			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	3 / 49 (6.12%)
occurrences (all)	0	0	3
Nausea			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash erythematous			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	0 / 88 (0.00%)	5 / 90 (5.56%)	0 / 49 (0.00%)
occurrences (all)	0	5	0
Pain in extremity			

subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	7 / 88 (7.95%)	6 / 90 (6.67%)	6 / 49 (12.24%)
occurrences (all)	8	6	9
Upper respiratory tract infection			
subjects affected / exposed	5 / 88 (5.68%)	4 / 90 (4.44%)	0 / 49 (0.00%)
occurrences (all)	5	4	0
Pharyngitis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	4 / 49 (8.16%)
occurrences (all)	0	0	4
Sinusitis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Impetigo			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0

Insomnia			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Investigations			
International normalised ratio increased			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Anaemia postoperative			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Postoperative ileus			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Epilepsy			

subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	3	0
Eye disorders			
Eye pruritus			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	2 / 58 (3.45%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences (all)	3	0	0
Nausea			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Dental caries			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Rash erythematous			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	0 / 58 (0.00%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	5 / 58 (8.62%)	0 / 22 (0.00%)	3 / 33 (9.09%)
occurrences (all)	8	0	3
Upper respiratory tract infection			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			

subjects affected / exposed	2 / 58 (3.45%)	0 / 22 (0.00%)	0 / 33 (0.00%)
occurrences (all)	2	0	0
Sinusitis			
subjects affected / exposed	3 / 58 (5.17%)	1 / 22 (4.55%)	2 / 33 (6.06%)
occurrences (all)	3	1	2
Ear infection			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	1 / 33 (3.03%)
occurrences (all)	0	1	1
Gastroenteritis			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	1 / 33 (3.03%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	1 / 33 (3.03%)
occurrences (all)	0	1	1
Impetigo			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Laryngitis			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Viral infection			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 58 (0.00%)	1 / 22 (4.55%)	0 / 33 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 July 2017	- Change in the statistical analysis of the primary efficacy endpoint and the first secondary efficacy endpoint: MAS and PGA are ordinal scales. The sponsor proposed as primary efficacy analysis an ANCOVA analysis that instead were based on ranked MAS change from Baseline/PGA scores to better normalise the data. For sensitivity analysis, the sponsor proposed to use a proportional odds cumulative logit model that avoids scoring and retains the ordered nature of the data. -Clarification on efficacy endpoints list: those performed using the treatment cycle baseline were removed. They were replaced by endpoints for the subsets of subjects having kept the same PTMG throughout the study. -Clarification on subgroups analysis: notably those concerning physiotherapy and occupational therapy. -New subgroups added: analysis by gender for the primary and first secondary efficacy endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported