Clinical trial results:
A phase III, multicentre, double-blind, prospective, randomised, placebo controlled study, assessing the efficacy and safety of Dysport used for the treatment of lower limb spasticity in adult subjects with hemiparesis due to stroke or traumatic brain injury

Summary

EudraCT number	2009-015868-34
Trial protocol	BE CZ SK IT PT HU
Global end of trial date	13 May 2014

Results information

Result version number	v2 (current)
This version publication date	17 August 2017
First version publication date	01 August 2015
Version creation reason	• Correction of full data set Following the system outage last year; this completed record had been indicated as "Removed from public view". No applicable reason provided in options above therefore 'correction of full data set' chosen.

Trial information

Trial identification

Sponsor protocol code	Y-55-52120-140

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01249404
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 April 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 May 2014
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 Dysport compared to placebo at Week 4 on the change from baseline in the gastrocnemius-soleus complex (GSC) muscle tone (knee extended) in hemiparetic subjects with lower limb spasticity due to stroke or traumatic brain injury.

Protection of trial subjects:

This clinical study was designed and implemented and reported in accordance with the International Conference on Harmonisation (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations (including European Directive 2001/20/EC, US Code of Federal Regulations Title 21, and Japanese Ministry of Health, Labor, and Welfare), and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator:

Placebo

Actual start date of recruitment	29 March 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 86
Country: Number of subjects enrolled	Portugal: 12
Country: Number of subjects enrolled	Slovakia: 16
Country: Number of subjects enrolled	Belgium: 19
Country: Number of subjects enrolled	Czech Republic: 18
Country: Number of subjects enrolled	France: 54
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Italy: 24
Country: Number of subjects enrolled	Australia: 43
Country: Number of subjects enrolled	Russian Federation: 30
Country: Number of subjects enrolled	United States: 68
Worldwide total number of subjects	385
EEA total number of subjects	244

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)	319
From 65 to 84 years	66
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multicenter study conducted in 62 investigational sites. Subjects were screened at 53 centers and in 52 centers subjects were randomized to receive study treatment.

Pre-assignment

Screening details:

Subjects randomized were 388 and 385 subjects who received treatment were included in the safety population. Only 381 subjects were included in the intent-to-treat (ITT) population. Subjects excluded from ITT population were 7 (including 4 subjects due to no MAS score at the baseline and/or at Week 4).

Pre-assignment period milestones

Number of subjects started	456[1]
Number of subjects completed	388

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screening Failures: 68

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same. Either resolve this issue or provide a justification.

Period 1

Period 1 title	Randomised Population
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 1000 U

Arm description:

Dysport 1000 U intramuscular injection single treatment cycle on day 1

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:

Dysport 1000 U intramuscular injection single treatment cycle on day 1

Arm title	Dysport 1500 U

Arm description:

Dysport 1500 U intramuscular injection single treatment cycle on day 1

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:

Dysport 1500 U intramuscular injection single treatment cycle on day 1

Arm title	Placebo

Arm description:

Placebo intramuscular injection single treatment cycle on day 1

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Placebo intramuscular injection single treatment cycle on day 1

Number of subjects in period 1	Dysport 1000 U	Dysport 1500 U	Placebo
Started	127	129	132
Completed	125	128	128
Not completed	2	1	4
Did not meet entry criteria	-	-	2
No functional need for Dysport	-	1	-
No MAS score at baseline and/or Week 4	2	-	2

Period 2

Period 2 title	Treatment phase - ITT
Is this the baseline period?	Yes[2]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Dysport 1000 U

Arm description:

Dysport 1000 U intramuscular injection single treatment cycle on day 1

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:

Dysport 1000 U intramuscular injection single treatment cycle on day 1

Arm title	Dysport 1500 U

Arm description:

Dysport 1500 U intramuscular injection single treatment cycle on day 1

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:

Dysport 1500 U intramuscular injection single treatment cycle on day 1

Arm title	Placebo

Arm description:

Placebo intramuscular injection single treatment cycle on day 1

Arm type	Placebo
Investigational medicinal product name	Placebo Comparator
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Placebo intramuscular injection single treatment cycle on day 1

Notes:

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

Justification: Period 1 is not the baseline period. It is expected that period 1 will be the baseline period. Either resolve this issue or provide a justification

Number of subjects in period 2[3]	Dysport 1000 U	Dysport 1500 U	Placebo
Started	125	128	128
Completed	120	121	125
Not completed	5	7	3
Consent withdrawn by subject	2	2	-
Adverse event, non-fatal	2	2	2
Unspecified	1	3	1

Notes:

[3] - 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: 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. Either resolve this issue or provide a justification.

Baseline characteristics

Reporting groups	
Reporting group title	Dysport 1000 U
Reporting group description:	
Dysport 1000 U intramuscular injection single treatment cycle on day 1	
Reporting group title	Dysport 1500 U
Reporting group description:	
Dysport 1500 U intramuscular injection single treatment cycle on day 1	
Reporting group title	Placebo
Reporting group description:	
Placebo intramuscular injection single treatment cycle on day 1	

Reporting group values	Dysport 1000 U	Dysport 1500 U	Placebo
Number of subjects	125	128	128
Age categorical Units: Subjects			
Adults (18-80 years)	125	128	128
Age continuous			
ITT Population			
Units: years			
arithmetic mean	53.2	53.3	51.4
standard deviation	± 13.2	± 12	± 12.9
Gender categorical Units: Subjects			
Female	38	49	38
Male	87	79	90
Race			
ITT Population			
Units: Subjects			
Asian	3	4	3
African American	5	13	5
Caucasian/White	116	109	119
Hawaiian/Pacific	0	1	0
Multiple	1	1	1
Ethnicity			
ITT Population			
Units: Subjects			
Hispanic	14	11	11
Not Hispanic	111	117	117
Weight			
ITT Population			
Units: kg			
arithmetic mean	79.6	80.1	79.7
standard deviation	± 16.5	± 14.8	± 17.9
BMI			
ITT Population			
Units: kg/m2			
arithmetic mean	27.3	27.3	27.4

standard deviation	± 5	± 4.1	± 5.2
MAS score at Baseline			
Units: Units on a scale			
arithmetic mean	3.8	3.7	3.9
standard deviation	± 0.5	± 0.5	± 0.5
Barefoot Comfortable Walking Speed at Baseline			
Units: m/s			
arithmetic mean	0.44	0.47	0.45
standard deviation	± 0.23	± 0.22	± 0.2

Reporting group values	Total		
Number of subjects	381		
Age categorical			
Units: Subjects			
Adults (18-80 years)	381		
Age continuous			
ITT Population			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	125		
Male	256		
Race			
ITT Population			
Units: Subjects			
Asian	10		
African American	23		
Caucasian/White	344		
Hawaiian/Pacific	1		
Multiple	3		
Ethnicity			
ITT Population			
Units: Subjects			
Hispanic	36		
Not Hispanic	345		
Weight			
ITT Population			
Units: kg			
arithmetic mean			
standard deviation	-		
BMI			
ITT Population			
Units: kg/m2			
arithmetic mean			
standard deviation	-		
MAS score at Baseline			
Units: Units on a scale			
arithmetic mean			
standard deviation	-		

Barefoot Comfortable Walking Speed at Baseline Units: m/s arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	Dysport 1000 U
Reporting group description:	
Dysport 1000 U intramuscular injection single treatment cycle on day 1	
Reporting group title	Dysport 1500 U
Reporting group description:	
Dysport 1500 U intramuscular injection single treatment cycle on day 1	
Reporting group title	Placebo
Reporting group description:	
Placebo intramuscular injection single treatment cycle on day 1	
Reporting group title	Dysport 1000 U
Reporting group description:	
Dysport 1000 U intramuscular injection single treatment cycle on day 1	
Reporting group title	Dysport 1500 U
Reporting group description:	
Dysport 1500 U intramuscular injection single treatment cycle on day 1	
Reporting group title	Placebo
Reporting group description:	
Placebo intramuscular injection single treatment cycle on day 1	

Primary: Change from baseline in Modified Ashworth Scale (MAS) score in the Gastrocnemius Soleus Complex (Knee Extended)

End point title	Change from baseline in Modified Ashworth Scale (MAS) score in the Gastrocnemius Soleus Complex (Knee Extended)[1]
End point description:	
Intention to treat (ITT) population MAS is a 6-point scale which measures the amount of muscle tone by measuring the resistance of the muscle to passive lengthening or stretching. A low score indicated little or no stiffness (best). A high score indicated severe stiffness (worse). The number of participants in each score category is presented	
End point type	Primary
End point timeframe:	
At week 4	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Either resolve this issue or provide a justification.

End point values	Dysport 1000 U	Dysport 1500 U	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	128	128	
Units: Units on a scale				
least squares mean (confidence interval 95%)				
MAS score change from Baseline to Week 4	-0.6 (-0.8 to -0.5)	-0.8 (-0.9 to -0.7)	-0.5 (-0.7 to -0.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Physician’s Global Assessment of Treatment Response

End point title	Physician’s Global Assessment of Treatment Response

End point description:

ITT Population

Physician’s Global Assessment (PGA) is a 9 points scale used to assess global overall treatment response by the investigator (-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).

End point type	Secondary

End point timeframe:

At week 4

End point values	Dysport 1000 U	Dysport 1500 U	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	128	128	
Units: Units on a scale				
least squares mean (confidence interval 95%)	0.9 (0.7 to 1.1)	0.9 (0.7 to 1.1)	0.7 (0.5 to 0.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Comfortable Barefoot Walking Speed (Without Walking Aids)

End point title	Change from baseline in Comfortable Barefoot Walking Speed (Without Walking Aids)

End point description:

ITT Population
Barefoot Comfortable Walking (BCW)

End point type	Secondary

End point timeframe:

At week 4

End point values	Dysport 1000 U	Dysport 1500 U	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	124	127	126	
Units: m/s				
least squares mean (confidence interval 95%)				
BCW Speed from Baseline to Week 4	0.05 (0.03 to 0.07)	0.04 (0.03 to 0.06)	0.05 (0.03 to 0.07)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 24 ±2 weeks	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0
Reporting groups	
Reporting group title	Dysport 1000 U
Reporting group description: Safety Population	
Reporting group title	Dysport 1500 U
Reporting group description: Safety Population	
Reporting group title	Placebo
Reporting group description: Safety Population	

Serious adverse events	Dysport 1000 U	Dysport 1500 U	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 127 (3.94%)	5 / 128 (3.91%)	7 / 130 (5.38%)
number of deaths (all causes)	0	0	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pancreatic carcinoma			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 130 (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
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 130 (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
Humerus fracture			

subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 130 (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
Femoral neck fracture			
subjects affected / exposed	0 / 127 (0.00%)	0 / 128 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	0 / 127 (0.00%)	0 / 128 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 130 (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
Nervous system disorders			
Cerebrovascular accident	Additional description: Safety Population		
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 130 (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
Convulsion			
subjects affected / exposed	2 / 127 (1.57%)	0 / 128 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 127 (0.00%)	0 / 128 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 127 (0.00%)	0 / 128 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 130 (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			
Chest pain			
subjects affected / exposed	0 / 127 (0.00%)	0 / 128 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 130 (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			
Appendicitis			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 130 (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
Post procedural infection			
subjects affected / exposed	0 / 127 (0.00%)	0 / 128 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Dysport 1000 U	Dysport 1500 U	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	55 / 127 (43.31%)	52 / 128 (40.63%)	41 / 130 (31.54%)
Injury, poisoning and procedural complications			
Fall	Additional description: Safety Population		
subjects affected / exposed	12 / 127 (9.45%)	8 / 128 (6.25%)	4 / 130 (3.08%)
occurrences (all)	14	9	8
Nervous system disorders			
Headache	Additional description: Safety Population		
subjects affected / exposed	0 / 127 (0.00%)	4 / 128 (3.13%)	1 / 130 (0.77%)
occurrences (all)	0	5	1
Convulsion	Additional description: Safety Population		
subjects affected / exposed	4 / 127 (3.15%)	0 / 128 (0.00%)	1 / 130 (0.77%)
occurrences (all)	4	0	1
Paraesthesia	Additional description: Safety Population		
subjects affected / exposed	2 / 127 (1.57%)	0 / 128 (0.00%)	3 / 130 (2.31%)
occurrences (all)	2	0	3
General disorders and administration site conditions			
Fatigue	Additional description: Safety Population		
subjects affected / exposed	1 / 127 (0.79%)	5 / 128 (3.91%)	0 / 130 (0.00%)
occurrences (all)	2	5	0
Asthenia	Additional description: Safety Population		
subjects affected / exposed	3 / 127 (2.36%)	1 / 128 (0.78%)	1 / 130 (0.77%)
occurrences (all)	3	1	2
Influenza like illness	Additional description: Safety Population		
subjects affected / exposed	3 / 127 (2.36%)	0 / 128 (0.00%)	0 / 130 (0.00%)
occurrences (all)	3	0	0
Psychiatric disorders			
Depression	Additional description: Safety Population		
subjects affected / exposed	2 / 127 (1.57%)	4 / 128 (3.13%)	0 / 130 (0.00%)
occurrences (all)	2	4	0
Musculoskeletal and connective tissue disorders			
Pain in extremity	Additional description: Safety Population		
subjects affected / exposed	7 / 127 (5.51%)	8 / 128 (6.25%)	3 / 130 (2.31%)
occurrences (all)	7	9	3
Muscular weakness	Additional description: Safety Population		

subjects affected / exposed	3 / 127 (2.36%)	8 / 128 (6.25%)	4 / 130 (3.08%)
occurrences (all)	3	9	4
Arthralgia	Additional description: Safety Population		
subjects affected / exposed	5 / 127 (3.94%)	3 / 128 (2.34%)	1 / 130 (0.77%)
occurrences (all)	5	4	1
Myalgia	Additional description: Safety Population		
subjects affected / exposed	3 / 127 (2.36%)	2 / 128 (1.56%)	2 / 130 (1.54%)
occurrences (all)	3	2	2
Back pain			
subjects affected / exposed	4 / 127 (3.15%)	0 / 128 (0.00%)	2 / 130 (1.54%)
occurrences (all)	4	0	2
Infections and infestations			
Nasopharyngitis	Additional description: Safety Population		
subjects affected / exposed	0 / 127 (0.00%)	3 / 128 (2.34%)	2 / 130 (1.54%)
occurrences (all)	0	3	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 April 2011	Amendment 2: The procedure for blinding and breaking the blind was clarified. The statistical methodology for the primary and first secondary efficacy endpoints was modified to account for separate registration in US and non-US countries.
09 February 2012	Amendment 3: The definition of naïve and non naïve subjects was clarified following questions raised by the investigators. A naïve subject was one who had never received any BTX in the affected lower limb. Criterion 6, regarding exclusion due to surgery was clarified and made more specific to refer only to surgery for spasticity on the affected lower limb. Exclusion criterion 19 was added to exclude the use of intrathecal baclofen during the course of the study or during the 4 weeks before entering the study. The study duration was amended to reflect new timelines and a delay in subject recruitment.
12 July 2012	Amendment 4: Inclusion criterion 3 was altered to allow entry into the study of subjects with a nonevolutive lesion diagnosed before the stroke and in the same cerebral hemisphere. Inclusion criterion 7 was altered to include subjects with a spasticity angle greater than or equal to 5 degrees (instead of greater than 5 degrees) in the GSC of the affected leg as assessed by the TS. The wording of Section 9.5 was amended to clarify the meaning and take into account all possibilities regarding used and unused treatments and empty boxes for destruction. References to sponsor’s CDDS Department were amended to Statistics Department. The pharmacovigilance/emergency contact details for the USA were updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported