Clinical trial results:
A PHASE III PROSPECTIVE, MULTI-CENTER, RANDOMISED, EVALUATOR-BLINDED STUDY TO COMPARE NEUROMUSCULAR JUNCTION (NMJ) TARGETED TECHNIQUE FOR DYSPORT INJECTIONS IN UPPER LIMB SPASTICITY POST STROKE OR TRAUMATIC BRAIN INJURY TO THE TECHNIQUE USED IN CURRENT CLINICAL PRACTICE

Summary

EudraCT number	2011-005375-16
Trial protocol	SE FI DK
Global end of trial date	10 March 2015

Results information

Result version number	v1 (current)
This version publication date	03 April 2016
First version publication date	03 April 2016

Trial information

Trial identification

Sponsor protocol code	A-99-52120-162

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Institut Produits Synthèse (IPSEN) AB
Sponsor organisation address	Kista Science Tower, 15th floor, Färögatan 33, Kista, Sweden, SE-164 51
Public contact	Medical Department, Institut Produits Synthèse (IPSEN) AB, clinical.trials@ipsen.com
Scientific contact	Medical Department, Institut Produits Synthèse (IPSEN) AB, 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	03 March 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 March 2015
Global end of trial reached?	Yes
Global end of trial date	10 March 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to compare Dysport treatment results after current clinical practice technique and 300U/mL dilution (high-concentration dilution) to the neuromascular junction (NMJ) targeted technique and 100U/mL dilution (low-concentration dilution), in the elbow joint assessed by Modified Ashworth Scale (MAS) 4 weeks post treatment.

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, and with the ethical principles laid down in the Declaration of Helsinki).

Background therapy: -

Evidence for comparator:

Previous studies have shown benefit of an NMJ targeted injection and a low-concentration injection separately. This study was designed to show the combined effect of NMJ targeting and a low-concentration.

The possibility to reduce the number of injection points would decrease the risk of injection discomfort, pain and injection site bleeding for the patient. A simplified injection technique with one injection per muscle and in a defined location would also benefit physicians.

Actual start date of recruitment	24 September 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Norway: 7
Country: Number of subjects enrolled	Sweden: 41
Country: Number of subjects enrolled	Denmark: 41
Country: Number of subjects enrolled	Finland: 11
Worldwide total number of subjects	100
EEA total number of subjects	100

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)	62
From 65 to 84 years	38
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was performed at a total of 20 sites in four countries: Denmark (5 sites), Finland (2 sites), Norway (2 sites) and Sweden (11 sites).

Pre-assignment

Screening details:

Approximately 272 subjects were planned to be randomised (136 subjects in each group).
In total, 100 subjects were enrolled and 88 were randomised (44 subjects in each group).
All randomised subjects were included in the Intention to Treat (ITT) population and Safety population (88 subjects).
The Per Protocol (PP) population included 54 subjects

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Blinding implementation details:

This was an open study with respect to study drug. However, the treatment group assigned to a randomisation number was to be blinded while it was not allocated.

Arms

Are arms mutually exclusive?	Yes
Arm title	NMJ TARGETED

Arm description:

Procedure: NMJ targeted technique and low-concentration dilution

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:

100 U/mL

Arm title	CURRENT CLINICAL PRACTICE

Arm description:

Procedure: Current clinical practice technique and high-concentration dilution

Arm type	Active comparator
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:

300 U/mL

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: In this study, all efficacy assessments were to be performed by another qualified study personnel, blinded to the injection technique.

Number of subjects in period 1[2]	NMJ TARGETED	CURRENT CLINICAL PRACTICE
Started	44	44
Completed	40	41
Not completed	4	3
Consent withdrawn by subject	2	-
Lost to follow-up	1	2
Protocol deviation	1	1

Notes:

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

Baseline characteristics

Reporting groups

Reporting group title	Overall period

Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	88	88	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 58.7 ± 13	 -	
Gender categorical Units: Subjects			
Female	30	30	
Male	58	58	
Spasticity pattern Units: Subjects			
Type I	9	9	
Type III	50	50	
Type IV	29	29	
Height			
n=82 (missing=6)			
Units: cm arithmetic mean standard deviation	 173.2 ± 8.9	 -	
Weight			
n=86 (missing=2)			
Units: kg arithmetic mean standard deviation	 78.1 ± 15.9	 -	

End points

End points reporting groups

Reporting group title	NMJ TARGETED
Reporting group description:	
Procedure: NMJ targeted technique and low-concentration dilution	
Reporting group title	CURRENT CLINICAL PRACTICE
Reporting group description:	
Procedure: Current clinical practice technique and high-concentration dilution	
Subject analysis set title	Evaluation-Total
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Investigator Preference of Injection Technique	

Primary: Change from baseline to week 4 (Visit 2) for elbow flexors muscle as measured on the Modified Ashworth Scale (MAS) based on number of responders

End point title	Change from baseline to week 4 (Visit 2) for elbow flexors muscle as measured on the Modified Ashworth Scale (MAS) based on number of responders
End point description:	
ITT Population Responder: A change from baseline of at least one score in MAS was considered clinically relevant and the subject was classified as a responder	
End point type	Primary
End point timeframe:	
Baseline (Visit 1) and 4 weeks (Visit 4)	

End point values	NMJ TARGETED	CURRENT CLINICAL PRACTICE		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	44		
Units: Number of responders				
Number of Responders	25	32		

Statistical analyses

Statistical analysis title	Treatment
Statistical analysis description:	
ITT Population	
Comparison groups	NMJ TARGETED v CURRENT CLINICAL PRACTICE

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0986
Method	Generalised linear model

Statistical analysis title	specificity pattern
Statistical analysis description: ITT Population	
Comparison groups	NMJ TARGETED v CURRENT CLINICAL PRACTICE
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.5682
Method	Generalised linear model

Statistical analysis title	Country
Statistical analysis description: ITT Population	
Comparison groups	NMJ TARGETED v CURRENT CLINICAL PRACTICE
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.8543
Method	Generalised linear model

Statistical analysis title	MAS baseline
Statistical analysis description: ITT Population	
Comparison groups	NMJ TARGETED v CURRENT CLINICAL PRACTICE
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.9167
Method	Generalised linear model

Secondary: Change from baseline to week 12 (visit 3) for elbow flexors muscle tone as measured by the MAS based on number of responders

End point title	Change from baseline to week 12 (visit 3) for elbow flexors muscle tone as measured by the MAS based on number of responders

End point description:

ITT Population

Responder: A change from baseline of at least one score in MAS was considered clinically relevant and the subject was classified as a responder.

Change from baseline to week 12 for elbow flexors muscle tone as measured by the MAS equal to or greater than 1.

End point type	Secondary

End point timeframe:

Baseline (Visit 1) and Week 12 (Visit 3)

End point values	NMJ TARGETED	CURRENT CLINICAL PRACTICE		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	44		
Units: Number of responders				
Number of responders	13	19		

Statistical analyses

Statistical analysis title	Treatment

Statistical analysis description:

ITT Population

Comparison groups	NMJ TARGETED v CURRENT CLINICAL PRACTICE
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.242
Method	Generalised linear model

Statistical analysis title	Spasticity pattern

Statistical analysis description:

ITT Population

Comparison groups	NMJ TARGETED v CURRENT CLINICAL PRACTICE
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.38
Method	Generalised linear model

Statistical analysis title	Country

Statistical analysis description: ITT Population	
Comparison groups	NMJ TARGETED v CURRENT CLINICAL PRACTICE
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.1037
Method	Generalised linear model

Statistical analysis title	MAS baseline
Statistical analysis description: ITT Population	
Comparison groups	NMJ TARGETED v CURRENT CLINICAL PRACTICE
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.2348
Method	Generalised linear model

Secondary: Mean change from baseline of spasticity related pain measured by Visual Analogue Scale (VAS)

End point title	Mean change from baseline of spasticity related pain measured by Visual Analogue Scale (VAS)

End point description:

ITT Population

Mean change from baseline to week 4 and 12 of spasticity related pain. The VAS ruler used in this study will be a straight 10 cm (100 mm) horizontal line with anchor points of No pain (score 0) and Worst pain imaginable (score 10 [100 mm]).

End point type	Secondary
End point timeframe: Baseline (visit 1), Week 4 and 12	

End point values	NMJ TARGETED	CURRENT CLINICAL PRACTICE		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	44		
Units: mm				
arithmetic mean (standard deviation)				
Baseline	21.66 (± 28.97)	14.32 (± 22.64)		
Mean Change from Baseline to Visit 2 (week 4)	-5.8 (± 23.07)	-4.35 (± 12.29)		
Mean Change from Baseline to Visit 3 (week 12)	-0.03 (± 26.02)	0.03 (± 20.67)		

Statistical analyses

Statistical analysis title	Week 4
Statistical analysis description: ITT Population	
Comparison groups	NMJ TARGETED v CURRENT CLINICAL PRACTICE
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.9448
Method	Generalised linear model

Statistical analysis title	Week 12
Statistical analysis description: ITT Population	
Comparison groups	NMJ TARGETED v CURRENT CLINICAL PRACTICE
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.5458
Method	Generalised linear model

Secondary: Injection pain measured at baseline by Visual Analogue Scale (VAS)

End point title	Injection pain measured at baseline by Visual Analogue Scale (VAS)

End point description:

ITT Population

Subject perceived injection site pain at day 1. The VAS ruler used in this study will be a straight 10 cm (100 mm) horizontal line with anchor points of No pain (score 0) and Worst pain imaginable (score 10 [100 mm]).

End point type	Secondary

End point timeframe:

Baseline (Visit 1)

End point values	NMJ TARGETED	CURRENT CLINICAL PRACTICE		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	44		
Units: mm				
arithmetic mean (standard deviation)	25.67 (± 25.37)	30.68 (± 27.33)		

Statistical analyses

Statistical analysis title	Injection Related Pain using VAS
Statistical analysis description: ITT Population	
Comparison groups	NMJ TARGETED v CURRENT CLINICAL PRACTICE
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.4006
Method	Generalised linear model

Secondary: Achievement of the primary goal measured by Goal Attainment Scale (GAS) based on number of subjects for overall category

End point title	Achievement of the primary goal measured by Goal Attainment Scale (GAS) based on number of subjects for overall category
End point description: At baseline, the investigator will interview the subject to identify the main problem area and establish an agreed primary goal related to elbow flexion to be followed up at week 4 or 12 depending on the time point defined at the baseline visit.	
End point type	Secondary
End point timeframe: Up to Week 12	

End point values	NMJ TARGETED	CURRENT CLINICAL PRACTICE		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	44		
Units: Participants				
-2	3	1		
-1	9	15		
Zero	11	18		
+1	9	6		
+2	1	1		
Missing	11	3		

Statistical analyses

Statistical analysis title	Goal Attainment Scale (GAS)
Statistical analysis description: ITT population	
Comparison groups	CURRENT CLINICAL PRACTICE v NMJ TARGETED
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.5747
Method	Mann-Whitney U-test

Secondary: Subject global evaluation of treatment effect based on number of subjects

End point title	Subject global evaluation of treatment effect based on number of subjects
End point description: ITT Population Comparison of treatment effect between previous (pre study) and study treatment cycles assessed by the subject at the end of study (visit 3 or 4) Categorised as follows: much worse/worse/same (no change from baseline)/better/much better.	
End point type	Secondary
End point timeframe: Up to Week 24	

End point values	NMJ TARGETED	CURRENT CLINICAL PRACTICE		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	44		
Units: Participants				
Much Better	3	2		
Better	11	16		
No Change From Baseline	18	20		
Worse	7	2		
Much Worse	1	0		
Missing	4	4		

Statistical analyses

Statistical analysis title	Subject Global Evaluation of Treatment Effect
Statistical analysis description: ITT population	
Comparison groups	NMJ TARGETED v CURRENT CLINICAL PRACTICE
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.1802
Method	Mann-Whitney U-test

Secondary: Investigator Preference of Injection Technique

End point title	Investigator Preference of Injection Technique
End point description: The Investigator preference of injection technique is summarized. Only three of the 20 Investigators answered the question on preferred injection technique.	
End point type	Secondary
End point timeframe: Up to week 24	

End point values	Evaluation-Total			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Participants				
Current Clinical Practice Technique	2			
NMJ Targeted Technique	1			
Missing	17			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of subjects with summary adverse events

End point title	Number of subjects with summary adverse events
End point description:	
End point type	Other pre-specified
End point timeframe: Up to week 24	

End point values	NMJ TARGETED	CURRENT CLINICAL PRACTICE		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	44		
Units: Number of subjects				
Any Adverse Events	15	11		
Any Treatment Emergent Adverse Events (TEAEs)	15	11		
Intensity of TEAEs - Severe	3	0		
Intensity of TEAEs - Moderate	7	2		
Intensity of TEAEs - Mild	8	10		
Causality of TEAEs - Related	1	2		
Causality of TEAEs - Not related	14	10		
TEAEs Leading to Withdrawal	0	0		
TEAEs Leading to Death	0	0		
Serious Adverse Events (SAEs)	2	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Baseline (day 1) to week 24	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.0
Reporting groups	
Reporting group title	NMJ TARGETED
Reporting group description: Procedure: NMJ targeted technique and low-concentration dilution	
Reporting group title	CURRENT CLINICAL PRACTICE
Reporting group description: Procedure: Current clinical practice technique and high-concentration dilution	

Serious adverse events	NMJ TARGETED	CURRENT CLINICAL PRACTICE	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 44 (4.55%)	2 / 44 (4.55%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cystitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	NMJ TARGETED	CURRENT CLINICAL PRACTICE	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 44 (29.55%)	9 / 44 (20.45%)	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
Fall			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
Muscle strain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 44 (6.82%)	0 / 44 (0.00%)	
occurrences (all)	3	0	
Epilepsy			
subjects affected / exposed	1 / 44 (2.27%)	1 / 44 (2.27%)	
occurrences (all)	1	1	
Migraine			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Neuralgia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	
occurrences (all)	1	0	

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 44 (2.27%)	1 / 44 (2.27%)	
occurrences (all)	1	1	
Influenza like illness			
subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Injection site hypersensitivity			
subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Epididymitis			
subjects affected / exposed	1 / 44 (2.27%)	1 / 44 (2.27%)	
occurrences (all)	1	1	
Acquired hydrocele			
subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Dysphagia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Gastritis			
subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pain of skin			
subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Psychiatric disorders			

Depression			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	2 / 44 (4.55%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
Back pain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Bursitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Eye infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	0 / 44 (0.00%)	3 / 44 (6.82%)	
occurrences (all)	0	3	
Nasopharyngitis			
subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 May 2012	Amendment 1: • Subjects will not be included in the study if they meet any or the following criteria: Any elbow flexor contracture prohibiting MAS evaluation and/or elbow flexion improvement of at least 1 step on the MAS. • Efficacy assessments should be made by another qualified study personnel, blinded to the injection technique • EMG/electrical stimulation use and Dysport doses given per muscle will be recorded in the CRF.
03 March 2014	Amendment 2: • Secondary objectives - To compare Dysport treatment results between the two treatment groups with respect to: Elbow joint, assessed by MAS, 12 weeks post treatment • The following treatments for spasticity must remain unchanged during the course of the study: BoNT-A treatment of spastic muscles involved in the elbow function (same dose and concentration as pre study treatment) • Subjects in group 1 will receive the same dose of Dysport injected in the elbow flexion related muscles as during the last pre study treatment. Subjects in group 2 will receive the same dose of Dysport injected in the elbow flexion related muscles as during the last pre study treatment but with a lower concentration (higher volume) and with a different injection technique where injections are targeted at the NMJs. • Inclusion criteria: Need of the same treatment modality in m. brachialis, m. biceps brachii, m. brachioradialis, m. flex. carpi ulnaris, m. flex. carpi radialis as the previous treatment cycle. • 272 subjects suffering from upper limb spasticity post stroke or traumatic brain injury, with an elbow flexor muscle spasticity position pattern type 1, 3 or 4, will be included in the study. •Secondary Efficacy Endpoints and Evaluations: MAS of elbow flexors at 12 weeks. Change from baseline to week 12 for elbow flexors muscle tone as measured by the MAS. • The sample size calculation was made assuming alpha level 0.025, one sided test. With an estimated drop out rate of 10%, the number of subjects will be 136 in each treatment group, 272 subjects are required to be randomised in the study • Visit 1/Visit 2/Visit 3 MAS of elbow flexors • Clarification of which muscles that are evaluated for elbow flexion.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to slow recruitment rate it was clear that the study would not be completed in a reasonable time frame, therefore the study was stopped early.

Notes: