Clinical trial results:
A multicentre, randomized, double-blind, parallel and controlled with placebo pilot study to evaluate the efficacy and safety of a single dose of botulinum toxin Type A (Dysport®) associated with rehabilitation treatment, in patients with primary myofascial syndrome of cervical and dorsal localization.

Summary

EudraCT number	2004-001443-29
Trial protocol	ES
Global end of trial date	02 February 2006

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	27 April 2016

Trial information

Trial identification

Sponsor protocol code	A-92-52120-089

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Ipsen Pharma
Sponsor organisation address	S.A. Avda. Laura Miro 395, Barcelona, France, 08980
Public contact	Medical director, anestesiologia , Ipsen Pharma, clinical.trials@ipsen.com
Scientific contact	Medical director, anestesiologia , Ipsen Pharma, 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	19 February 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 February 2006
Global end of trial reached?	Yes
Global end of trial date	02 February 2006
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the efficacy and safety of a single dose of botulinum toxin associated with rehabilitation treatment, on pain control in patients with primary myofascial syndrome of cervical and dorsal localization.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 January 2005
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	22
From 65 to 84 years	2

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited at 4 investigational centres in spain.

Pre-assignment

Screening details:

A total of 24 participants were screened of which all 24 subjects were randomised to either dysport or Placebo.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

0 U, One vial containing sterile solution of sodium chloride ready for intramuscular injection.

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

Dosage and administration details:

0 U

Arm title	Dysport

Arm description:

500 U, One vial containing lyophilized powder, previous dissolution in sodium chloride (0.9%) ready for intramuscular injection.

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:

500 U

Number of subjects in period 1	Placebo	Dysport
Started	12	12
Completed	12	12

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
0 U, One vial containing sterile solution of sodium chloride ready for intramuscular injection.	
Reporting group title	Dysport
Reporting group description:	
500 U, One vial containing lyophilized powder, previous dissolution in sodium chloride (0.9%) ready for intramuscular injection.	

Reporting group values	Placebo	Dysport	Total
Number of subjects	12	12	24
Age categorical			
Units: Subjects			
Age continuous			
Total mean = 42.9 SD = ± 13.2			
Units: years			
arithmetic mean	44.8	41	
standard deviation	± 12.5	± 14.2	-
Gender categorical			
Units: Subjects			
Female	10	12	22
Male	2	0	2
Race			
Units: Subjects			
Caucasian	12	12	24
Weight			
Units: kg			
arithmetic mean	68	64.1	
standard deviation	± 12.2	± 6	-
Systolic blood pressure			
Units: mmHg			
arithmetic mean	131.8	126	
standard deviation	± 19.4	± 19	-
Diastolic blood pressure			
Units: mmHg			
arithmetic mean	73.8	73.3	
standard deviation	± 10.3	± 6.8	-
Heart rate			
Units: bpm			
arithmetic mean	73	74.2	
standard deviation	± 6	± 6.8	-
Baseline pain VAS			
Units: mm			
arithmetic mean	61.2	60.3	
standard deviation	± 11.1	± 16	-

Baseline PPT associated with the most sensitive TP			
Units: kg/cm2			
arithmetic mean	1.9	1.7	
standard deviation	± 1.1	± 0.9	-
Baseline PPT associated with all the TP			
Units: kg/cm2			
arithmetic mean	2.1	1.9	
standard deviation	± 1	± 0.9	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
0 U, One vial containing sterile solution of sodium chloride ready for intramuscular injection.	
Reporting group title	Dysport
Reporting group description:	
500 U, One vial containing lyophilized powder, previous dissolution in sodium chloride (0.9%) ready for intramuscular injection.	

Primary: Evolution of the pain visual analogue scale (VAS) score

End point title	Evolution of the pain visual analogue scale (VAS) score

End point description:

The values reported are for the change from baseline in pain visual analogue scale (VAS) score

The visual analogue scale or visual analog scale (VAS) is a psychometric response scale which can be used in questionnaires. It is a measurement instrument for subjective characteristics or attitudes that cannot be directly measured. When responding to a VAS item, respondents specify their level of agreement to a statement by indicating a position along a continuous line between two end-points.

In the VAS the best result is 0 and the worst is 100.

End point type	Primary

End point timeframe:

Baseline (Day 0), Week 2, Week 4, Week 8 and Week 12

End point values	Placebo	Dysport		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: mm				
arithmetic mean (standard deviation)				
Week 2	-17.75 (± 20.53)	-9.83 (± 23.22)		
Week 4	-22.08 (± 21)	-22 (± 18.2)		
Week 8	-19.92 (± 26.03)	-23.42 (± 17.86)		
Week 12	-15.92 (± 21.38)	-26.92 (± 19.45)		

Statistical analyses

Statistical analysis title	Main analysis(repeated measures)- Treatment effect
Comparison groups	Placebo v Dysport

Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.832
Method	ANCOVA

Statistical analysis title	Main analysis(repeated measures)- visit effect
Comparison groups	Placebo v Dysport
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.048
Method	ANCOVA

Statistical analysis title	Main analysis(repeated measures)- Baseline VAS
Comparison groups	Placebo v Dysport
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.778
Method	ANCOVA

Primary: Evolution of pressure pain threshold (PPT) associated with the most sensitive trigger point (TP)

End point title	Evolution of pressure pain threshold (PPT) associated with the most sensitive trigger point (TP)

End point description:

The values reported are for the change from baseline in pressure pain threshold (PPT)

End point type	Primary

End point timeframe:

Baseline (Day 0), Week 2, Week 4, Week 8 and Week 12

End point values	Placebo	Dysport		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: kg/cm2				
arithmetic mean (standard deviation)				
Week 2	0.75 (± 1.2)	0.33 (± 0.62)		
Week 4	0.78 (± 1.35)	0.68 (± 0.77)		
Week 8	1 (± 1.33)	0.76 (± 0.99)		

Week 12	0.68 (± 1.36)	0.99 (± 1.07)		

Statistical analyses

Statistical analysis title	Main analysis(repeated measures)- Treatment effect
Comparison groups	Placebo v Dysport
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.748
Method	ANCOVA

Statistical analysis title	Main analysis(repeated measures)- Visit effect
Comparison groups	Dysport v Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.115
Method	ANCOVA

Statistical analysis title	Main analysis(repeated measures)- Baseline VAS
Comparison groups	Placebo v Dysport
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.187
Method	ANCOVA

Primary: Evolution of pressure pain threshold (PPT) associated with all trigger points (TP)

End point title	Evolution of pressure pain threshold (PPT) associated with all trigger points (TP)

End point description:

The values reported are for the change from baseline in pressure pain threshold (PPT)

End point type	Primary

End point timeframe:

Baseline (Day 0), Week 2, Week 4, Week 8 and Week 12

End point values	Placebo	Dysport		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: kg/cm2				
arithmetic mean (standard deviation)				
Week 2	0.74 (± 1.23)	0.29 (± 0.73)		
Week 4	0.82 (± 1.37)	0.72 (± 0.75)		
Week 8	1.01 (± 1.42)	0.68 (± 0.99)		
Week 12	0.66 (± 1.35)	0.92 (± 1.03)		

Statistical analyses

Statistical analysis title	Main analysis(repeated measures)- Treatment effect
Comparison groups	Placebo v Dysport
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.679
Method	ANCOVA

Statistical analysis title	Main analysis(repeated measures)- Visit effect
Comparison groups	Placebo v Dysport
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.053
Method	ANCOVA

Statistical analysis title	Main analysis(repeated measures)- Baseline VAS
Comparison groups	Placebo v Dysport
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.147
Method	ANCOVA

Secondary: Evolution of global assessment of improvement by the investigator

End point title	Evolution of global assessment of improvement by the investigator

End point description:

End point type	Secondary

End point timeframe:

Baseline (Day 0), Week 2, Week 4, Week 8 and Week 12

End point values	Placebo	Dysport		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Participants				
Week 2 Worsening	2	2		
Week 2 No change	3	4		
Week 2 Improvement	7	6		
Week 4 Worsening	1	2		
Week 4 No change	3	1		
Week 4 Improvement	8	9		
Week 8 Worsening	0	2		
Week 8 No change	5	0		
Week 8 Improvement	7	10		
Week 12 Worsening	0	1		
Week 12 No change	5	0		
Week 12 Improvement	7	11		

Statistical analyses

Statistical analysis title	Treatment effect
Comparison groups	Dysport v Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.985
Method	Regression, Logistic

Statistical analysis title	Visit effect
Comparison groups	Dysport v Placebo

Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.049
Method	Regression, Logistic

Secondary: Evolution of global assessment of improvement by the patient

End point title	Evolution of global assessment of improvement by the patient

End point description:

End point type	Secondary

End point timeframe:

Baseline (Day 0), Week 2, Week 4, Week 8 and Week 12

End point values	Placebo	Dysport		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Participants				
Week 2 Worsening	2	2		
Week 2 No change	2	5		
Week 2 Improvement	8	5		
Week 4 Worsening	1	3		
Week 4 No change	3	1		
Week 4 Improvement	8	8		
Week 8 Worsening	2	2		
Week 8 No change	1	2		
Week 8 Improvement	9	8		
Week 12 Worsening	1	1		
Week 12 No change	4	1		
Week 12 Improvement	7	10		

Statistical analyses

Statistical analysis title	Treatment effect
Comparison groups	Placebo v Dysport
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.574
Method	Regression, Logistic

Notes:

[1] - Method: Logistic regression for longitudinal data.

Statistical analysis title	Visit effect
Comparison groups	Placebo v Dysport
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.103 [2]
Method	Regression, Logistic

Notes:

[2] - Method: Logistic regression for longitudinal data.

Secondary: Modification in usual analgesic intake

End point title	Modification in usual analgesic intake

End point description:

End point type	Secondary

End point timeframe:

Week 2 to 12

End point values	Placebo	Dysport		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Participants				
Patients with at least one new drug along study	4	5		
Patients with at least one drug stopped	5	9		
Patients with atleast 1 dose increase during study	1	5		
Patients with at least 1 dose decrease during the	1	5		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to Week 12	
Adverse event reporting additional description:	
Non-Serious Treatment Emergent Adverse Events are reported under non-serious adverse events	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
0 U, One vial containing sterile solution of sodium chloride ready for intramuscular injection.	
Reporting group title	Dysport
Reporting group description:	
500 U, One vial containing lyophilized powder, previous dissolution in sodium chloride (0.9%) ready for intramuscular injection.	

Serious adverse events	Placebo	Dysport	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Placebo	Dysport	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 12 (41.67%)	5 / 12 (41.67%)	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
General disorders and administration			

site conditions			
Adverse event			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	0 / 12 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Hepatomegaly			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Muscle contracture			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Muscle weakness			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Pharyngotonsillitis			

subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 12 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported