



Clinical trial results:

A phase III, multicentre, prospective, double blind, randomised, placebo controlled study, assessing the efficacy and safety of Dysport intramuscular injections used for the treatment of upper limb spasticity in adult subjects with spastic hemiparesis due to stroke or traumatic brain injury.

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2010-019069-28 |
| Trial protocol | BE CZ SK PL IT HU |
| Global end of trial date | 04 September 2013 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 25 March 2016 |
| First version publication date | 25 March 2016 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | Y-52-52120-145 |
|-----------------------|----------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Ipsen Innovation |
| Sponsor organisation address | 5 Avenue du Canada, Les Ulis, France, 91940 |
| Public contact | Medical Director, Neurology, Ipsen Innovation, clinical.trials@ipsen.com |
| Scientific contact | Medical Director, Neurology., Ipsen Innovation, 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 | 17 April 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 04 September 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 04 September 2013 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary study objective is to assess the efficacy of Dysport compared to placebo in reducing upper limb muscle tone in hemiparetic subjects with upper limb spasticity due to stroke or traumatic brain injury. The primary study objective will be assessed by comparing between treatment groups at Week 4 the change from baseline in muscle tone (using the Modified Ashworth Scale (MAS)) in the primary targeted muscle group

Protection of trial subjects:

This clinical study was designed and implemented and reported in accordance with the International Conference on Harmonization (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: -

| | |
|---|----------------|
| Actual start date of recruitment | 04 August 2011 |
| 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 | Russian Federation: 22 |
| Country: Number of subjects enrolled | United States: 95 |
| Country: Number of subjects enrolled | Poland: 29 |
| Country: Number of subjects enrolled | Slovakia: 11 |
| Country: Number of subjects enrolled | Belgium: 15 |
| Country: Number of subjects enrolled | Czech Republic: 22 |
| Country: Number of subjects enrolled | France: 34 |
| Country: Number of subjects enrolled | Hungary: 8 |
| Country: Number of subjects enrolled | Italy: 7 |
| Worldwide total number of subjects | 243 |
| EEA total number of subjects | 126 |

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) | 193 |
| From 65 to 84 years | 50 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This multi-center study was conducted in 34 investigation sites. Subjects screened were 281 and randomized and treated were 243.

Pre-assignment

Screening details:

A total of 281 subjects were screened and 243 were randomised and treated into study.

Period 1

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

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| 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

| | |
|------------------|---------------|
| Arm title | Dysport 500 U |
|------------------|---------------|

Arm description:

Botulinum type A toxin (Dysport) 500 U intramuscular injection single treatment cycle on day 1

| | |
|--|------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Dysport 500 U |
| Investigational medicinal product code | |
| Other name | Botulinum type A toxin |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Botulinum type A toxin (Dysport) 500 U intramuscular injection single treatment cycle on day 1

| | |
|------------------|----------------|
| Arm title | Dysport 1000 U |
|------------------|----------------|

Arm description:

Botulinum type A toxin (Dysport) 1000 U intramuscular injection single treatment cycle on day 1

| | |
|--|------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Dysport 1000 U |
| Investigational medicinal product code | |
| Other name | Botulinum type A toxin |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Botulinum type A toxin (Dysport) 1000 U intramuscular injection single treatment cycle on day 1

| Number of subjects in period 1 | Placebo | Dysport 500 U | Dysport 1000 U |
|---------------------------------------|---------|---------------|----------------|
| Started | 81 | 81 | 81 |
| Completed | 74 | 78 | 77 |
| Not completed | 7 | 3 | 4 |
| lack of subject compliance | - | - | 1 |
| Protocol violation | 2 | - | - |
| Family reason and moved out of state | - | 2 | - |
| Adverse event | 3 | 1 | 1 |
| Withdrawal by Subject | 1 | - | 2 |
| Lost to follow-up | 1 | - | - |

Baseline characteristics

Reporting groups

| | |
|---|----------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Placebo intramuscular injection single treatment cycle on day 1 | |
| Reporting group title | Dysport 500 U |
| Reporting group description: | |
| Botulinum type A toxin (Dysport) 500 U intramuscular injection single treatment cycle on day 1 | |
| Reporting group title | Dysport 1000 U |
| Reporting group description: | |
| Botulinum type A toxin (Dysport) 1000 U intramuscular injection single treatment cycle on day 1 | |

| Reporting group values | Placebo | Dysport 500 U | Dysport 1000 U |
|--|---------|---------------|----------------|
| Number of subjects | 81 | 81 | 81 |
| Age categorical | | | |
| Units: Subjects | | | |
| <65 years | 66 | 66 | 61 |
| >=65 years | 15 | 15 | 20 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 52.9 | 52.8 | 53.2 |
| standard deviation | ± 13.8 | ± 12.8 | ± 13.8 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 31 | 28 | 28 |
| Male | 50 | 53 | 53 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| Asian | 1 | 3 | 2 |
| Black/African American | 9 | 7 | 11 |
| Caucasian/White | 71 | 70 | 67 |
| Multiple | 0 | 1 | 1 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic/Latino | 5 | 3 | 10 |
| Not Hispanic/Latino | 76 | 78 | 71 |
| BMI | | | |
| Aggregate analysis for BMI is 27.33(5.17) for participants Placebo: N=78, Dysport 500 U: N=80, and Dysport 1000 U: N=80. | | | |
| Units: kg/m ² | | | |
| arithmetic mean | 26.78 | 27.63 | 27.58 |
| standard deviation | ± 5.38 | ± 4.61 | ± 5.51 |
| Modified Ashworth Scale Score | | | |
| Aggregate analysis for MAS at baseline is 3.9(0.4) for participants Placebo:N=79, Dysport500U:N=80 & Dysport1000U:N=79. | | | |
| MAS scale is used to assess MT using a 6-point scale where:0=No increase in MT, 1=Slight increase in MT,1±=Slight increase in MT manifested by a catch followed by minimal resistance throughout remainder of ROM,2=Marked increase in MT through most of ROM but affected part easily moved,3=Considerable increase in MT passive movement difficult or 4=Affected part(s) rigid in flexion | | | |

| | | | |
|---|-------|-------|-------|
| extension. The MAS has been derived for analyses as follows:0=0 ; 1=1; 1+=2; 2=3; 3=4; 4=5. | | | |
| Units: units on a scale | | | |
| arithmetic mean | 3.9 | 3.9 | 3.9 |
| standard deviation | ± 0.4 | ± 0.5 | ± 0.4 |
| Disability Assessment Scale Score | | | |
| Aggregate analysis for DAS at baseline is 2.6(0.5) for participants Placebo:N=79 Dysport500U:N=80 Dysport1000U:N=78 | | | |
| DAS is a 4-point scale used to determine the extent of functional impairment in 4 functional domains(dressing, hygiene, limb position and pain). DAS scale rating: 0=No disability,1=Mild disability (noticeable but does not interfere significantly with normal activities),2=Moderate disability (normal activities require increased effort and/or assistance),3=Severe disability (normal activities limited). If the subject chose Hygiene as PTT the score collected will be between 0 & 3 | | | |
| Units: units on a scale | | | |
| arithmetic mean | 2.6 | 2.6 | 2.5 |
| standard deviation | ± 0.5 | ± 0.5 | ± 0.5 |

| | | | |
|---|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 243 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| <65 years | 193 | | |
| >=65 years | 50 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | - | | |
| standard deviation | | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 87 | | |
| Male | 156 | | |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| Asian | 6 | | |
| Black/African American | 27 | | |
| Caucasian/White | 208 | | |
| Multiple | 2 | | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic/Latino | 18 | | |
| Not Hispanic/Latino | 225 | | |
| BMI | | | |
| Aggregate analysis for BMI is 27.33(5.17) for participants Placebo: N=78, Dysport 500 U: N=80, and Dysport 1000 U: N=80. | | | |
| Units: kg/m2 | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Modified Ashworth Scale Score | | | |
| Aggregate analysis for MAS at baseline is 3.9(0.4) for participants Placebo:N=79, Dysport500U:N=80 & Dysport1000U:N=79. | | | |
| MAS scale is used to assess MT using a 6-point scale where:0=No increase in MT, 1=Slight increase in MT,1±=Slight increase in MT manifested by a catch followed by minimal resistance throughout remainder of ROM,2=Marked increase in MT through most of ROM but affected part easily moved,3=Considerable increase in MT passive movement difficult or 4=Affected part(s) rigid in flexion or | | | |

| | | | |
|---|---|--|--|
| extension. The MAS has been derived for analyses as follows:0=0 ; 1=1; 1+=2; 2=3; 3=4; 4=5. | | | |
| Units: units on a scale arithmetic mean standard deviation | - | | |
| Disability Assessment Scale Score | | | |
| <p>Aggregate analysis for DAS at baseline is 2.6(0.5) for participants Placebo:N=79 Dysport500U:N=80 Dysport1000U:N=78</p> <p>DAS is a 4-point scale used to determine the extent of functional impairment in 4 functional domains(dressing, hygiene, limb position and pain). DAS scale rating: 0=No disability,1=Mild disability (noticeable but does not interfere significantly with normal activities),2=Moderate disability (normal activities require increased effort and/or assistance),3=Severe disability (normal activities limited). If the subject chose Hygiene as PTT the score collected will be between 0 & 3</p> | | | |
| Units: units on a scale arithmetic mean standard deviation | - | | |

End points

End points reporting groups

| | |
|---|----------------|
| Reporting group title | Placebo |
| Reporting group description: Placebo intramuscular injection single treatment cycle on day 1 | |
| Reporting group title | Dysport 500 U |
| Reporting group description: Botulinum type A toxin (Dysport) 500 U intramuscular injection single treatment cycle on day 1 | |
| Reporting group title | Dysport 1000 U |
| Reporting group description: Botulinum type A toxin (Dysport) 1000 U intramuscular injection single treatment cycle on day 1 | |

Primary: Change From Baseline in MAS Score in the Primary Targeted Muscle Group (PTMG)

| | |
|--|--|
| End point title | Change From Baseline in MAS Score in the Primary Targeted Muscle Group (PTMG) ^[1] |
| End point description: MAS scale is used to assess muscle tone (MT) using a 6-point scale where: 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 range of motion (ROM) when the part is flexed or extended, 1±Slight increase in muscle tone manifested by a catch followed by minimal resistance throughout the remainder of the ROM, 2=Marked increase in muscle tone through most of the ROM but affected part easily moved, 3=Considerable increase in muscle tone passive movement difficult or 4=Affected part(s) rigid in flexion or extension. The MAS has been derived for analyses as follows: 0=0 ; 1=1; 1+=2; 2=3; 3=4 and 4=5. Intention to treat (ITT) population included all randomized subjects who received at least one injection of study drug and had a MAS score at baseline (pretreatment) and at week 4. Total 5 subjects were excluded from ITT population as they did not have MAS score at baseline or/and at week 4. | |
| End point type | Primary |
| End point timeframe: From Baseline (Day 1) to 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 for this endpoint.

| End point values | Placebo | Dysport 500 U | Dysport 1000 U | |
|---|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 79 | 80 | 79 | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change From Baseline in MAS Score in the PTMG | -0.3 (± 0.6) | -1.2 (± 1) | -1.4 (± 1.1) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Physician's Global Assessment (PGA) of Treatment Response

| | |
|-----------------|---|
| End point title | Physician's Global Assessment (PGA) of Treatment Response |
|-----------------|---|

End point description:

PGA is a 9-point 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).

ITT population. Two subjects each from Placebo and Dysport 1000 U had missed PGA assessment at week 4

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At week 4

| End point values | Placebo | Dysport 500 U | Dysport 1000 U | |
|--------------------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 78 | 80 | 78 | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| PGA of Treatment Response | 0.6 (± 1) | 1.4 (± 1.1) | 1.8 (± 1.1) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in DAS Score for the Principal Target of Treatment (PTT)

| | |
|-----------------|---|
| End point title | Change From Baseline in DAS Score for the Principal Target of Treatment (PTT) |
|-----------------|---|

End point description:

DAS is a 4-point scale used to determine the extent of functional impairment in 4 functional domains (dressing, hygiene, limb position and pain). DAS scale rating: 0=No disability, 1=Mild disability (noticeable but does not interfere significantly with normal activities), 2=Moderate disability (normal activities require increased effort and/or assistance) and 3=Severe disability (normal activities limited).

If subject chose 'Hygiene' as PTT the score collected will be between 0 and 3.

ITT population. Two subjects from Placebo and one subject from Dysport 1000 U had missed DAS assessment at baseline and week 4.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline (Day 1) to Week 4

| End point values | Placebo | Dysport 500 U | Dysport 1000 U | |
|--------------------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 79 | 80 | 78 | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | -0.5 (± 0.7) | -0.7 (± 0.8) | -0.7 (± 0.7) | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 24±2 weeks

Adverse event reporting additional description:

Non-serious adverse event affecting >2% of total subjects are reported.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 16.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Placebo intramuscular injection single treatment cycle on day 1

| | |
|-----------------------|---------------|
| Reporting group title | Dysport 500 U |
|-----------------------|---------------|

Reporting group description:

Botulinum type A toxin (Dysport) 500 U intramuscular injection single treatment cycle on day 1

| | |
|-----------------------|----------------|
| Reporting group title | Dysport 1000 U |
|-----------------------|----------------|

Reporting group description:

Botulinum type A toxin (Dysport) 1000 U intramuscular injection single treatment cycle on day 1

| Serious adverse events | Placebo | Dysport 500 U | Dysport 1000 U |
|---|----------------|----------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 81 (3.70%) | 3 / 81 (3.70%) | 3 / 81 (3.70%) |
| number of deaths (all causes) | 1 | 1 | 0 |
| number of deaths resulting from adverse events | 1 | 1 | 0 |
| Injury, poisoning and procedural complications | | | |
| Craniocerebral injury | | | |
| subjects affected / exposed | 1 / 81 (1.23%) | 0 / 81 (0.00%) | 0 / 81 (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 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 81 (0.00%) | 0 / 81 (0.00%) | 1 / 81 (1.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Behcet's syndrome | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 81 (0.00%) | 1 / 81 (1.23%) | 0 / 81 (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 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 81 (1.23%) | 0 / 81 (0.00%) | 0 / 81 (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 |
| Cardiac disorders | | | |
| Cardiovascular disorder | | | |
| subjects affected / exposed | 0 / 81 (0.00%) | 1 / 81 (1.23%) | 0 / 81 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 81 (0.00%) | 0 / 81 (0.00%) | 1 / 81 (1.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Partial seizures | | | |
| subjects affected / exposed | 0 / 81 (0.00%) | 0 / 81 (0.00%) | 1 / 81 (1.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 81 (0.00%) | 0 / 81 (0.00%) | 1 / 81 (1.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Death | | | |
| subjects affected / exposed | 1 / 81 (1.23%) | 0 / 81 (0.00%) | 0 / 81 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary oedema | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 81 (1.23%) | 0 / 81 (0.00%) | 0 / 81 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 81 (0.00%) | 1 / 81 (1.23%) | 0 / 81 (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 |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 81 (1.23%) | 0 / 81 (0.00%) | 0 / 81 (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 |
| Infections and infestations | | | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 81 (0.00%) | 1 / 81 (1.23%) | 0 / 81 (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: 2 %

| Non-serious adverse events | Placebo | Dysport 500 U | Dysport 1000 U |
|---|------------------|------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 10 / 81 (12.35%) | 25 / 81 (30.86%) | 18 / 81 (22.22%) |
| Investigations | | | |
| Blood glucose increased | | | |
| subjects affected / exposed | 0 / 81 (0.00%) | 2 / 81 (2.47%) | 0 / 81 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Blood pressure increased | | | |
| subjects affected / exposed | 0 / 81 (0.00%) | 1 / 81 (1.23%) | 2 / 81 (2.47%) |
| occurrences (all) | 0 | 1 | 2 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 81 (0.00%) | 3 / 81 (3.70%) | 1 / 81 (1.23%) |
| occurrences (all) | 0 | 3 | 1 |
| Gamma glutamyl transferase increased | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 81 (0.00%) 0 | 2 / 81 (2.47%) 2 | 2 / 81 (2.47%) 2 |
| Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all) | 0 / 81 (0.00%) 0 | 1 / 81 (1.23%) 1 | 2 / 81 (2.47%) 2 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 81 (0.00%) 0 | 1 / 81 (1.23%) 1 | 2 / 81 (2.47%) 2 |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) | 1 / 81 (1.23%) 1 | 2 / 81 (2.47%) 2 | 0 / 81 (0.00%) 0 |
| Injection site bruising subjects affected / exposed occurrences (all) | 2 / 81 (2.47%) 2 | 1 / 81 (1.23%) 1 | 1 / 81 (1.23%) 1 |
| Injection site erythema subjects affected / exposed occurrences (all) | 0 / 81 (0.00%) 0 | 0 / 81 (0.00%) 0 | 2 / 81 (2.47%) 2 |
| Injection site pain subjects affected / exposed occurrences (all) | 3 / 81 (3.70%) 3 | 1 / 81 (1.23%) 1 | 0 / 81 (0.00%) 0 |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 0 / 81 (0.00%) 0 | 2 / 81 (2.47%) 2 | 1 / 81 (1.23%) 1 |
| Nausea subjects affected / exposed occurrences (all) | 0 / 81 (0.00%) 0 | 3 / 81 (3.70%) 3 | 0 / 81 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 0 / 81 (0.00%) 0 | 2 / 81 (2.47%) 3 | 1 / 81 (1.23%) 1 |
| Epistaxis | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 81 (0.00%) 0 | 2 / 81 (2.47%) 3 | 0 / 81 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 81 (1.23%) | 2 / 81 (2.47%) | 1 / 81 (1.23%) |
| occurrences (all) | 1 | 4 | 1 |
| Back pain | | | |
| subjects affected / exposed | 1 / 81 (1.23%) | 0 / 81 (0.00%) | 2 / 81 (2.47%) |
| occurrences (all) | 1 | 0 | 2 |
| Muscular Weakness | | | |
| subjects affected / exposed | 1 / 81 (1.23%) | 2 / 81 (2.47%) | 4 / 81 (4.94%) |
| occurrences (all) | 1 | 2 | 4 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 81 (1.23%) | 2 / 81 (2.47%) | 1 / 81 (1.23%) |
| occurrences (all) | 1 | 2 | 1 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 81 (1.23%) | 7 / 81 (8.64%) | 1 / 81 (1.23%) |
| occurrences (all) | 1 | 7 | 1 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 81 (0.00%) | 2 / 81 (2.47%) | 1 / 81 (1.23%) |
| occurrences (all) | 0 | 2 | 1 |
| Urinary tract infections | | | |
| subjects affected / exposed | 0 / 81 (0.00%) | 2 / 81 (2.47%) | 1 / 81 (1.23%) |
| occurrences (all) | 0 | 2 | 1 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 14 April 2011 | Protocol amendment 1: Made the following changes: <ul style="list-style-type: none">• The primary efficacy analysis was changed from a Hochberg procedure to a hierarchical testing procedure following feedback from the Food and Drug Administration.• The procedure for breaking the blind was clarified.• The definition of treatment naïve was harmonised to that used in similar protocols.• Minor formatting and typographical issues were corrected. |
| 17 February 2012 | Protocol amendment 2: Made the following changes: <ul style="list-style-type: none">• In inclusion criterion 2, it was clarified that subjects had to have a diagnosis of hemiparesis.• In inclusion criterion 5, the definition of naïve/non-naïve subjects was clarified. Naïve subjects were defined as those who had never previously received BTX in the injected upper limb.• In exclusion criterion 6, the text for exclusion due to surgery was clarified and made more specific.• Exclusion criterion 20 was added to exclude the use of intrathecal baclofen during or for the 4 weeks prior to the study.• For the PTMG for elbow flexors, a clarification was added regarding the choice of 'brachialis' or 'brachialis and brachioradialis'.• For the assessments of upper limb muscle groups, assessments for elbow pronators were removed owing to the number of evaluations to be performed.• Minor formatting and typographical issues were corrected.• The time for which subjects were required to be supine before ECG was recorded was corrected.• Text was added to item 9 in the Modified Frenchay Scale to clarify that the affected hand holds the fork during the assessment. In light of the amendment, the CRF, database and RAP required updating. |
| 12 July 2012 | Protocol amendment 3, dated 12 July 2012, made the following changes: <ul style="list-style-type: none">• The pharmacovigilance/emergency contact details for the USA were updated.• Inclusion criterion 3 was altered to allow entry into the study of subjects with a non-evolutive lesion diagnosed before the stroke and in the same cerebral hemisphere.• Inclusion criterion 7 was altered to include subjects with a spasticity angle of 10°.• 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.• Instructions for disposal of used vials were clarified. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported