# Clinical trial results:
# A Phase III Multicenter, Randomized, Double-Blind, Placebo-Controlled Study of the Efficacy and Safety of Dysport® for the Treatment of Cervical Dystonia

## Summary

| | |
|---|---|
| EudraCT number | 2005-000709-70 |
| Trial protocol | DE |
| Global end of trial date | 07 September 2006 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 06 February 2016 |
| First version publication date | 06 February 2016 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | Y-47-52120-051 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Ipsen Group |
| Sponsor organisation address | 27 Maple Street, Milford, MA, United States, 01757 |
| Public contact | Medical Director, Neurology, Ipsen, clinical.trials@ipsen.com |
| Scientific contact | Medical Director, Neurology, Ipsen, clinical.trials@ipsen.com |

Notes:

**Paediatric regulatory details**

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 19 October 2007 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 07 September 2006 |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 September 2006 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of intramuscular administration of Dysport (500 units) compared to placebo for the treatment of cervical dystonia

Protection of trial subjects:

The study was conducted in accordance with the applicable Food and Drug Administration (FDA) regulations and/or guidelines, the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (GCP), and the Declaration of Helsinki. Dysport® for Injection (hereinafter referred to as Dysport) is an injectable form of Botulinum Toxin Type A (BTX-A). Dysport is licensed in many European countries for use in the treatment of a number of focal dystonias, including blepharospasm, spasmodic torticollis (cervical dystonia), and relief of hemifacial spasm.
Clinical studies conducted to date have identified 500 units of Dysport as the optimal dose for the treatment of the signs and symptoms of cervical dystonia.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 10 October 2005 |
| 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: 28 |
| Country: Number of subjects enrolled | United States: 88 |
| Worldwide total number of subjects | 116 |
| EEA total number of subjects | 0 |

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) | 96 |
| From 65 to 84 years | 20 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Date of first enrollment: 10 October 2005 and Date of last completed: 07 September 2006. The study was conducted at sixteen centers in the USA and four centers in Russia.

### Pre-assignment

Screening details:

A total of 127 subjects were screened across 20 centers. 116 subjects were randomized with 55 and 61 in the Dysport and placebo treatment groups.

### Period 1

| | |
|---|---|
| Period 1 title | Overall Trial (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** | Dysport |

Arm description:

A single dose of Dysport was administered by intramuscular injection to a maximum of four clinically indicated muscles. The total dose was 500 Dysport units in a single dosing session.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Dysport |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

A single dose of 500 units of Dysport

| | |
|---|---|
| **Arm title** | Placebo |

Arm description:

A single dose of 500 units of placebo by intramuscular injection

Principal Investigator (PI)

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

Dosage and administration details:

A single dose of 500 units of placebo by intramuscular injection

| **Number of subjects in period 1** | Dysport | Placebo |
|---|---|---|
| Started | 55 | 61 |
| Completed | 45 | 38 |
| Not completed | 10 | 23 |
| Consent withdrawn by subject | 2 | - |
| PI & Subject Schedule Conflicts | 1 | - |
| Lost to follow-up | 1 | - |
| No Longer Wanted to do Blood Draws | 1 | - |
| Lack of efficacy | 5 | 23 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Dysport |
| Reporting group description: | |
| A single dose of Dysport was administered by intramuscular injection to a maximum of four clinically indicated muscles. The total dose was 500 Dysport units in a single dosing session. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| A single dose of 500 units of placebo by intramuscular injection | |
| Principal Investigator (PI) | |

| Reporting group values | Dysport | Placebo | Total |
|---|---|---|---|
| Number of subjects | 55 | 61 | 116 |
| Age categorical | | | |
| Units: Subjects | | | |
| Between 18 and 65 years | 46 | 50 | 96 |
| >=65 years | 9 | 11 | 20 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 51.9 | 53.9 | |
| standard deviation | ± 13.4 | ± 12.5 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 37 | 38 | 75 |
| Male | 18 | 23 | 41 |
| Race | | | |
| Units: Subjects | | | |
| Caucasian/White | 55 | 61 | 116 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic/Latino | 3 | 4 | 7 |
| Not Hispanic/Latino | 52 | 57 | 109 |
| Height | | | |
| Dysport: N= 53<br>Placebo: N= 60 | | | |
| Units: cm | | | |
| arithmetic mean | 167 | 170 | |
| standard deviation | ± 10.3 | ± 8.5 | - |
| Weight | | | |
| Dysport: N= 55<br>Placebo: N= 60 | | | |
| Units: kg | | | |
| arithmetic mean | 73.4 | 77.4 | |
| standard deviation | ± 13.8 | ± 15 | - |
| TWSTRS Total Score | | | |
| Units: Points on a scale | | | |
| arithmetic mean | 43.83 | 45.81 | |
| standard deviation | ± 7.97 | ± 8.78 | - |

| | | | |
|---|---|---|---|
| Subject’s VAS for Symptom Assessment | | | |
| Dysport: N= 55<br>Placebo: N= 57 | | | |
| Units: Points on a scale | | | |
| arithmetic mean | 67.7 | 63.6 | |
| standard deviation | ± 19.7 | ± 18.9 | - |
| Investigator’s VAS for Symptom Assessment | | | |
| Dysport: N= 54<br>Placebo: N= 59 | | | |
| Units: Points on a scale | | | |
| arithmetic mean | 62.3 | 65.3 | |
| standard deviation | ± 15.8 | ± 18 | - |
| SF-36 Scores - Mental Health Summary | | | |
| Dysport: N= 54<br>Placebo: N= 59<br><br>Short Form 36 Quality of Life questionnaire (SF-36) | | | |
| Units: Points on a scale | | | |
| arithmetic mean | 44.52 | 43.31 | |
| standard deviation | ± 10.41 | ± 11.14 | - |
| SF-36 Scores - Physical Health Summary | | | |
| Dysport: N= 54<br>Placebo: N= 59 | | | |
| Units: Points on a scale | | | |
| arithmetic mean | 39.42 | 43.18 | |
| standard deviation | ± 8.84 | ± 7.89 | - |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Dysport |
| Reporting group description: | |
| A single dose of Dysport was administered by intramuscular injection to a maximum of four clinically indicated muscles. The total dose was 500 Dysport units in a single dosing session. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| A single dose of 500 units of placebo by intramuscular injection<br><br>Principal Investigator (PI) | |

### Primary: Change from Baseline in TWSTRS Total Score at week 4

| | |
|---|---|
| End point title | Change from Baseline in TWSTRS Total Score at week 4 |
| End point description: | |
| Intention-to Treat (ITT) Population<br><br>Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS)<br><br>TWSTRS is comprised of three different components which are severity, disability & pain. There is an ordinal scale for each component and the score range for each is the following: for severity from 0 (absence of severity) to 35 (max severity), for disability from 0 (no disability) to 30 (max disability) and for pain from 0 (no pain) to 20 (max pain). TWSTRS total score is the sum of the 3 component scores, with a range from 0 to a maximum of 85. The change in TWSTRS total score is the score at week 4 minus the score at baseline.<br><br>The analysis was performed on the intention to treat population which consisted of 55 subjects receiving Dysport and 61 Placebo. There were 4 subjects for Dysport and 3 for placebo who were not assessed on TWSTRS score at Week 4. As there was no imputation of missing TWSTRS score values, these 7 subjects were not taken into account. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline (week 0) and week 4 | |

| **End point values** | Dysport | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 55 | 61 | | |
| Units: points on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 (N=51,58) | -13.99 (± 12.33) | -5.23 (± 9.33) | | |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Treatment Difference (Dysport & Placebo) - Week 4 |
| Statistical analysis description: | |
| Baseline TWSTRS total scores are analysed for all subjects of ITT population, while the analysis at Week | |

4 excludes the scores for the 7 subjects who were not assessed.
Mean difference = difference in adjusted least squares mean (Dysport - Placebo).

| | |
|---|---|
| Comparison groups | Dysport v Placebo |
| Number of subjects included in analysis | 116 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |

## Secondary: Change from Baseline in TWSTRS Total Score week 8 and 12

| | |
|---|---|
| End point title | Change from Baseline in TWSTRS Total Score week 8 and 12 |

End point description:

Week 8: The analysis was performed on the intention to treat population which consisted of 55 subjects receiving Dysport and 61 Placebo. There were 9 subjects for Dysport and 15 for placebo who were not assessed on TWSTRS score at Week 8. As there was no imputation of missing TWSTRS score values, these 24 subjects were not taken into account.

Week 12: The analysis was performed on the intention to treat population which consisted of 55 subjects receiving Dysport and 61 Placebo. There were 10 subjects for Dysport and 17 for placebo who were not assessed on TWSTRS score at Week 12. As there was no imputation of missing TWSTRS score values, these 27 subjects were not taken into account.

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

End point timeframe:

Baseline (week 0), week 8 and week 12

| **End point values** | Dysport | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 55 | 61 | | |
| Units: points on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8 (N=46,46) | -13.82 (± 11.53) | -5.59 (± 11.37) | | |
| Week 12 (N=45,44) | -6.98 (± 11.12) | -4.53 (± 7.75) | | |

## Statistical analyses

| **Statistical analysis title** | Treatment Difference (Dysport & Placebo) - Week 8 |
|---|---|

Statistical analysis description:

Baseline TWSTRS total scores are analysed for all subjects of ITT population, while the Week 8 analysis excludes the scores for the 24 subjects who were not assessed.

Mean difference = difference in adjusted least squares mean (Dysport - Placebo).

| | |
|---|---|
| Comparison groups | Dysport v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 116 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |

| **Statistical analysis title** | Treatment Difference (Dysport & Placebo) - Week 12 |
|---|---|

Statistical analysis description:

Baseline TWSTRS total scores are analysed for all subjects of ITT population, while the Week 12 analysis excludes the scores for the 27 subjects who were not assessed.

Mean difference = difference in adjusted least squares mean (Dysport - Placebo).

| | |
|---|---|
| Comparison groups | Dysport v Placebo |
| Number of subjects included in analysis | 116 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.019 |
| Method | ANCOVA |

## Secondary: Change from Baseline in Subject’s VAS for Symptom Assessment

| End point title | Change from Baseline in Subject’s VAS for Symptom Assessment |
|---|---|

End point description:

Visual Analog Scale (VAS): The assessment was a continuous 100 mm horizonal line with a scale of 0 mm (no symptoms)to 100 mm (worst possible symptoms).
Week 4:Analysis was performed on ITT population which consisted of 55 subjects on Dysport and 61 Placebo.There were 5 subjects on Dysport and 8 on placebo who were not assessed on the change in subject VAS score for CD symptoms at Week 4.There was no imputation of missing VAS scores, so these 13 subjects were not taken into account.
Week 8:Analysis was performed on ITT population which consisted of 55 subjects receiving Dysport and 61 Placebo.There were 3 subjects for Dysport and 5 for placebo who were not assessed on the change in investigator VAS score at Week 4. As there was no imputation of missing VAS scores, these 8 subjects were not taken into account.
Week 12:Analysis was performed on ITT population which consisted of 55 subjects on Dysport and 61 on Placebo.Missing assessments at Week 8 were imputed using LOCF Methodolgy.

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

End point timeframe:

Baseline (week 0), weeks 4, 8 and 12

| **End point values** | Dysport | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 55 | 61 | | |
| Units: points on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 (N=50,53) | -24.2 (± 29.5) | -6.7 (± 20.8) | | |
| Week 8 (N=55,57) | -24.6 (± 30) | -5.4 (± 25.4) | | |
| Week 12 (N=55,57) | -14.4 (± 25.2) | -4.6 (± 23.3) | | |

## Statistical analyses

| **Statistical analysis title** | Treatment Difference (Dysport & Placebo) - Week 4 |
|---|---|

Statistical analysis description:

Analysis at baseline (and on change at Week 4) excludes 4 subjects (and 13 subjects respectively) of ITT population who were not assessed. Mean difference=difference in adjusted least squares mean (Dysport-placebo)

| | |
|---|---|
| Comparison groups | Dysport v Placebo |
| Number of subjects included in analysis | 116 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| **Statistical analysis title** | Treatment Difference (Dysport & Placebo) - Week 8 |
|---|---|

Statistical analysis description:

Analysis at baseline (and on change at Week 8) excludes 4 subjects (and 4 subjects respectively) of ITT population who were not assessed. Mean difference=difference in adjusted least squares mean (Dysport-placebo)

| | |
|---|---|
| Comparison groups | Dysport v Placebo |
| Number of subjects included in analysis | 116 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| **Statistical analysis title** | Treatment Difference (Dysport & Placebo) - Week 12 |
|---|---|

Statistical analysis description:

Analysis at baseline (and on change at Week 12) excludes 4 subjects (and 4 subjects respectively) of ITT population who were not assessed. Mean difference=difference in adjusted least squares mean (Dysport-placebo)

| | |
|---|---|
| Comparison groups | Dysport v Placebo |
| Number of subjects included in analysis | 116 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.007 |
| Method | ANCOVA |

## Secondary: Change from Baseline in Investigator’s VAS for Symptom Assessment

| End point title | Change from Baseline in Investigator's VAS for Symptom Assessment |
|---|---|

End point description:

Week 4: Analysis was performed on intention to treat population which consisted of 55 subjects receiving Dysport and 61 Placebo. There were 3 subjects for Dysport and 5 for placebo who were not assessed on the change in investigator VAS score at Week 4. As there was no imputation of missing VAS scores, these 8 subjects were not taken into account.
Week 8: Analysis was performed on intention to treat population which consisted of 55 subjects on Dysport and 61 on Placebo. Missing assessments at Week 8 were imputed using Last Observation Carried Forward (LOCF) methodology. There was no imputation for 3 patients with missing baseline and Week 4 values.
Week 12: Analysis was performed on intention to treat population which consisted of 55 subjects on Dysport and 61 on Placebo. Missing assessments at Week 12 were imputed using Last Observation Carried Forward (LOCF) methodology. There was no imputation for 3 patients with missing baseline, Week 4 and Week 8 values.

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

End point timeframe:

Baseline (week 0), weeks 4, 8 and 12,

| **End point values** | Dysport | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 55 | 61 | | |
| Units: points on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 (N=52,56) | -23.1 (± 22.1) | -9.1 (± 20.2) | | |
| Week 8 (N=54,59) | -20.5 (± 22.7) | -5 (± 21.3) | | |
| Week 12 (N=54,59) | -8.5 (± 18.9) | -5.8 (± 15.8) | | |

## Statistical analyses

| **Statistical analysis title** | Treatment Difference (Dysport & Placebo) - Week 4 |
|---|---|

Statistical analysis description:

Analysis at baseline (and on change at Week 4) excludes 3 subjects (and 8 subjects respectively) of ITT population who were not assessed. Mean difference=difference in adjusted least squares mean (Dysport-placebo)

| Comparison groups | Dysport v Placebo |
|---|---|
| Number of subjects included in analysis | 116 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| **Statistical analysis title** | Treatment Difference (Dysport & Placebo) - Week 8 |
|---|---|

Statistical analysis description:

Analysis at baseline (and on change at Week 8) excludes 3 subjects (and 3 subjects respectively) of ITT population who were not assessed. Mean difference=difference in adjusted least squares mean (Dysport-placebo)

| Comparison groups | Dysport v Placebo |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 116 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| **Statistical analysis title** | Treatment Difference (Dysport & Placebo) - Week 12 |
|---|---|

Statistical analysis description:

Analysis at baseline (and on change at Week 12) excludes 3 subjects (and 3 subjects respectively) of ITT population who were not assessed. Mean difference=difference in adjusted least squares mean (Dysport-placebo)

| | |
|---|---|
| Comparison groups | Dysport v Placebo |
| Number of subjects included in analysis | 116 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.028 |
| Method | ANCOVA |

## Secondary: Change from Baseline in SF-36 Scores

| | |
|---|---|
| End point title | Change from Baseline in SF-36 Scores |

End point description:

Mental and Physical Health Summaries (ITT Population)
SF-36 is a Quality of Life scale comprising eight individual domains. The QoL score for each domain is on a scale from 0 (worst health possible) to 100 (best health possible). SF-36 Mental Health Summary Score is derived from four individual domains (vitality, social functioning, role limitations due to emotional problems and mental health).
SF-36 Physical Health Summary Score is derived from four individual domains (physical functioning, role physical, bodily pain and general health).
MHS and PHS: Analysis was performed on intention to treat population which consisted of 55 subjects on Dysport and 61 on Placebo. There were 13 subjects on Dysport and 24 on placebo who were not assessed on the change in mental and physical health summary at Week 8. There was no imputation of missing scores, so these 37 subjects were not taken into account.

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

End point timeframe:

Baseline (week 0) and at week 8

| **End point values** | Dysport | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 55 | 61 | | |
| Units: points on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8: Mental Health Summary (N=42,37) | 4.11 (± 9.18) | 2.48 (± 8.12) | | |
| Week 8: Physical Health Summary (N=42,37) | 4.37 (± 5.46) | -0.64 (± 6.41) | | |

## Statistical analyses

| **Statistical analysis title** | Treatment Difference (Dysport & Placebo) - Week 8 |
|---|---|

Statistical analysis description:

Mental Health Summary (MHS)
Analysis at baseline (and on change at Week 8) excludes 3 subjects (and 37 subjects respectively) of ITT population who were not assessed. Mean difference=difference in adjusted least squares mean (Dysport-placebo)

| | |
|---|---|
| Comparison groups | Dysport v Placebo |
| Number of subjects included in analysis | 116 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.061 |
| Method | ANCOVA |

| **Statistical analysis title** | Treatment Difference (Dysport & Placebo) - Week 8 |
|---|---|

Statistical analysis description:

Physical Health Summary (PHS)
Analysis at baseline (and on change at Week 8) excludes 3 subjects (and 37 subjects respectively) of ITT population who were not assessed. Mean difference=difference in adjusted least squares mean (Dysport-placebo)

| | |
|---|---|
| Comparison groups | Dysport v Placebo |
| Number of subjects included in analysis | 116 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | ANCOVA |

## Secondary: Number of Subjects Considered by the Investigator to be Overall Treatment Successes

| End point title | Number of Subjects Considered by the Investigator to be Overall Treatment Successes |
|---|---|

End point description:

Overall treatment success was defined by a global efficacy assessment of “better” or “much better” and a global safety assessment of no worse than “moderate”.

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

End point timeframe:

At week 12

| End point values | Dysport | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 55 | 61 | | |
| Units: participants | 32 | 10 | | |

### Statistical analyses

| Statistical analysis title | Dysport - Placebo |
|---|---|
| Comparison groups | Dysport v Placebo |
| Number of subjects included in analysis | 116 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [1] |
| Method | Odds Ratio |

Notes:

[1] - The odds ratio represents the odds of success on Dysport versus Placebo stratified for strata and country

### Other pre-specified: Number of Subjects with Adverse Event

| End point title | Number of Subjects with Adverse Event |
|---|---|

End point description:

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Up to 12 Months

| End point values | Dysport | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 55 | 61 | | |
| Units: Number of subjects | | | | |
| number (not applicable) | | | | |
| Any adverse event | 26 | 27 | | |
| Any treatment related adverse event | 12 | 9 | | |
| Any severe adverse event | 4 | 4 | | |
| Any severe treatment related adverse event | 4 | 2 | | |
| Any serious adverse event | 0 | 1 | | |
| Any adverse events leading to withdrawal | 0 | 0 | | |
| Adverse event leading to death | 0 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Up to 12 Months | |
| Assessment type | Non-systematic |
| **Dictionary used** | |
| Dictionary name | MedDRA |
| Dictionary version | 9.0 |
| **Reporting groups** | |
| Reporting group title | Dysport |
| Reporting group description: | |
| A single dose of Dysport was administered by intramuscular injection to a maximum of four clinically indicated muscles. The total dose was 500 Dysport units in a single dosing session | |
| Reporting group title | Placebo |
| Reporting group description: | |
| A single dose of 500 units of placebo by intramuscular injection | |

| Serious adverse events | Dysport | Placebo | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 61 (1.64%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Psychiatric disorders | | | |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 61 (1.64%) | |
| 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: 5 %

| Non-serious adverse events | Dysport | Placebo | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 11 / 55 (20.00%) | 5 / 61 (8.20%) | |
| General disorders and administration site conditions | | | |
| Injection site pain | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | 2 / 61 (3.28%) | |
| occurrences (all) | 3 | 2 | |
| Gastrointestinal disorders | | | |

| | | | |
|---|---|---|---|
| Dysphagia | | | |
| subjects affected / exposed | 5 / 55 (9.09%) | 0 / 61 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Neck pain | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | 3 / 61 (4.92%) | |
| occurrences (all) | 4 | 4 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 31 May 2006 | Changes were mostly administrative, but also included an update to the Subject Informed Consent form, providing further information on the potential for Adverse Event (AEs) due to study treatment. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported