Clinical trial results:
A Phase II, Double Blind, Randomised, Placebo and Active Comparator Controlled Study to Assess the Safety and Efficacy of Three Doses of Dysport RU (20 U, 50 U, and 75 U) Administered as a Single Treatment Cycle to Improve the Appearance of Moderate to Severe Glabellar Lines

Summary

EudraCT number	2010-019085-82
Trial protocol	DE
Global end of trial date	27 September 2011

Results information

Result version number	v2 (current)
This version publication date	11 March 2016
First version publication date	12 August 2015
Version creation reason	• Correction of full data set Review and correction.

Trial information

Trial identification

Sponsor protocol code	Y-52-52120-146

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 Les Ulis Cedex, Canada, France, 91940
Public contact	Medical Director, Ipsen Innovation, clinical.trials@ipsen.com
Scientific contact	Medical Director, 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	13 December 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 September 2011
Global end of trial reached?	Yes
Global end of trial date	27 September 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the dose response versus placebo of a single treatment of Dysport RU (Dysport RU, Ready to Use, for injection), for the improvement in appearance of moderate to severe glabellar lines at maximum frown.

Protection of trial subjects:

The study and the archiving of essential documents were performed in compliance with Good Clinical Practice (GCP) and in accordance with the Declaration of Helsinki. The present study was designed to assess the efficacy and safety of different doses of the new formulation, Dysport NG (20 Units (U), 50 U and 75 U), when used for the same indication. Additionally, the study aimed to assess the relative efficacy and safety of the different doses of this new formulation compared with the optimal dose of Dysport (50 U) when used to improve the appearance of moderate to severe glabellar lines.

Background therapy: -

Evidence for comparator:

The study aimed to assess the relative efficacy and safety of the different doses of new formulation [Dysport NG (20 Units (U), 50 U and 75 U)] compared with the optimal dose of Dysport (50 U) when used to improve the appearance of moderate to severe glabellar lines.

Actual start date of recruitment	30 March 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	4 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 85
Country: Number of subjects enrolled	France: 91
Worldwide total number of subjects	176
EEA total number of subjects	176

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)	176
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was performed as a multicentre study at eight investigational sites in France and Germany. Date of first enrolment: 30-Mar-2011 and Date of last completed: 27-Sep-2011.

Pre-assignment

Screening details:

A total of 178 patients were screened. 2 patient did not meet the entry criteria. 176 patients were randomized.Patients were radomized into 5 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	Placebo

Arm description:

Intramuscular injections on Day 1 (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)

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

Dosage and administration details:

On Day 1 (Intramuscular injections on Day 1 (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)

The placebo was supplied for administration as a liquid in a PFS containing only the excipients of Dysport NG, i.e. without the toxin. The placebo was to be prepared in the same way as Dysport NG

Arm title	Dysport NG 20 U

Arm description:

Botulinum type A toxin (Dysport RU), Intramuscular injections on Day 1 in the muscle (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)

Ready to Use (RU)
Next Generation (NG)

Arm type	Experimental
Investigational medicinal product name	DYSPORT NG
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Botulinum type A toxin (Dysport RU), Intramuscular injections on Day 1 in the muscle (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was

injected into five pre-defined sites across the glabellar region) (single treatment cycle)

Arm title	Dysport NG 50 U

Arm description:

Botulinum type A toxin (Dysport RU), Intramuscular injections on Day 1 in the muscle (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)

Arm type	Experimental
Investigational medicinal product name	DYSPORT NG
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Botulinum type A toxin (Dysport RU), Intramuscular injections on Day 1 in the muscle (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)

Arm title	Dysport NG 75 U

Arm description:

Botulinum type A toxin (Dysport RU), Intramuscular injections on Day 1 in the muscle (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)

Arm type	Experimental
Investigational medicinal product name	DYSPORT NG
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Botulinum type A toxin (Dysport RU), Intramuscular injections on Day 1 in the muscle (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)

Arm title	Dysport 50 U

Arm description:

Botulinum type A toxin (Azzalure®), Intramuscular injections on Day 1 (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)

Arm type	Active comparator
Investigational medicinal product name	Azzalure®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Botulinum type A toxin (Azzalure®), Intramuscular injections on Day 1 (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)

Number of subjects in period 1	Placebo	Dysport NG 20 U	Dysport NG 50 U
Started	35	36	35
Completed	34	36	35
Not completed	1	0	0
Lost to follow-up	1	-	-

Number of subjects in period 1	Dysport NG 75 U	Dysport 50 U
Started	35	35
Completed	34	35
Not completed	1	0
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Intramuscular injections on Day 1 (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)	
Reporting group title	Dysport NG 20 U
Reporting group description:	
Botulinum type A toxin (Dysport RU), Intramuscular injections on Day 1 in the muscle (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle) Ready to Use (RU) Next Generation (NG)	
Reporting group title	Dysport NG 50 U
Reporting group description:	
Botulinum type A toxin (Dysport RU), Intramuscular injections on Day 1 in the muscle (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)	
Reporting group title	Dysport NG 75 U
Reporting group description:	
Botulinum type A toxin (Dysport RU), Intramuscular injections on Day 1 in the muscle (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)	
Reporting group title	Dysport 50 U
Reporting group description:	
Botulinum type A toxin (Azzalure®), Intramuscular injections on Day 1 (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)	

Reporting group values	Placebo	Dysport NG 20 U	Dysport NG 50 U
Number of subjects	35	36	35
Age categorical Units: Subjects			
Age 30 - 60 years	35	36	35
Age continuous Units: years			
arithmetic mean	46.8	46.7	48.1
standard deviation	± 6.4	± 8.4	± 6.9
Gender categorical Units: Subjects			
Female	35	36	35
Male	0	0	0
Race Units: Subjects			
Caucasian/White	35	36	35
Ethnicity Units: Subjects			
Hispanic/Latino	0	2	0
Not Hispanic/Latino	35	34	35

Reporting group values	Dysport NG 75 U	Dysport 50 U	Total
Number of subjects	35	35	176
Age categorical Units: Subjects			
Age 30 - 60 years	35	35	176
Age continuous Units: years			
arithmetic mean	47.9	47	
standard deviation	± 6	± 6.6	-
Gender categorical Units: Subjects			
Female	35	35	176
Male	0	0	0
Race Units: Subjects			
Caucasian/White	35	35	176
Ethnicity Units: Subjects			
Hispanic/Latino	2	1	5
Not Hispanic/Latino	33	34	171

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Intramuscular injections on Day 1 (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)

Reporting group title	Dysport NG 20 U

Reporting group description:

Botulinum type A toxin (Dysport RU), Intramuscular injections on Day 1 in the muscle (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)

Ready to Use (RU)
Next Generation (NG)

Reporting group title	Dysport NG 50 U

Reporting group description:

Botulinum type A toxin (Dysport RU), Intramuscular injections on Day 1 in the muscle (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)

Reporting group title	Dysport NG 75 U

Reporting group description:

Botulinum type A toxin (Dysport RU), Intramuscular injections on Day 1 in the muscle (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)

Reporting group title	Dysport 50 U

Reporting group description:

Botulinum type A toxin (Azzalure®), Intramuscular injections on Day 1 (total injection volume of 0.25 ml divided into five intramuscular injections of 0.05 mL per injection each of which was injected into five pre-defined sites across the glabellar region) (single treatment cycle)

Primary: Percentage of Subjects as Responders in the ILA (Using Validated 4 point Photographic Scale) and the SSA of Glabellar Lines at Maximum Frown

End point title	Percentage of Subjects as Responders in the ILA (Using Validated 4 point Photographic Scale) and the SSA of Glabellar Lines at Maximum Frown[1]

End point description:

Investigator’s live assessment (ILA), subject’s self assessment (SSA), Next Generation (NG)
4-point photographic scale: Investigator's live assessment: None - 0; Mild - 1; Moderate - 2; Severe - 3;
4-point photographic scale: Subject's Self assessment: No wrinkles - 0; Mild wrinkles - 1; Moderate wrinkles - 2; Severe wrinkles - 3;
A responder at maximum frown was defined as a subject having a severity grade of none or mild at maximum frown on Day 29 and a severity grade of moderate or severe at maximum frown at Visit 2

Intent-to-Treat Population: The intent-to-treat (ITT) population included all randomised subjects who received study treatment, regardless of the actual amount injected. N’=number of subjects with assessment

End point type	Primary

End point timeframe:

Day 29

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The primary objectives was to assess the relative safety and efficacy of Dysport NG

compared to Placebo

End point values	Placebo	Dysport NG 20 U	Dysport NG 50 U	Dysport NG 75 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	36	35	33
Units: percentage of subjects				
number (not applicable)				
ILA (N'=34,36,35,33)	0	88.9	91.4	87.9
SSA (N'=34,36,35,33)	2.9	91.7	85.7	81.8

Statistical analyses

Statistical analysis title	ILA - Dysport NG 20 U Vs Placebo
Comparison groups	Placebo v Dysport NG 20 U
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Chi-squared

Statistical analysis title	SSA - Dysport NG 20 U Vs Placebo
Comparison groups	Placebo v Dysport NG 20 U
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Chi-squared

Statistical analysis title	ILA - Dysport NG 50 U Vs Placebo
Comparison groups	Placebo v Dysport NG 50 U
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Chi-squared

Statistical analysis title	ILA - Dysport NG 75 U Vs Placebo
Comparison groups	Dysport NG 75 U v Placebo

Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Chi-squared

Statistical analysis title	SSA - Dysport NG 50 U Vs Placebo
Comparison groups	Placebo v Dysport NG 50 U
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Chi-squared

Statistical analysis title	SSA - Dysport NG 75 U Vs Placebo
Comparison groups	Placebo v Dysport NG 75 U
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Chi-squared

Secondary: Percentage of subjects as assessed as responders, by both Investigator's live assessment and the subject's self-assessment at maximum frown

End point title	Percentage of subjects as assessed as responders, by both Investigator's live assessment and the subject's self-assessment at maximum frown

End point description:

A responder at maximum frown was defined as a subject having a severity grade of none or mild at maximum frown on the visit day and a severity grade of moderate or severe at maximum frown at Visit 2.

ITT Population; Day 29 (N'=34,36,35,33,35); N’= number of subjects with an Investigator's live assessment and a subject's self assessment of glabellar lines at maximum frown for the given post-Baseline visit

End point type	Secondary

End point timeframe:

Day 29

End point values	Placebo	Dysport NG 20 U	Dysport NG 50 U	Dysport NG 75 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	36	35	33
Units: percentage of subjects				
number (not applicable)	0	86.1	85.7	81.8

End point values	Dysport 50 U			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: percentage of subjects				
number (not applicable)	77.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects as Responders at Maximum Frown as Measured by the Investigator's Live Assessment

End point title	Percentage of Subjects as Responders at Maximum Frown as Measured by the Investigator's Live Assessment[2]

End point description:

ITT Population; N'=number of subjects with an Investigator's live assessment of glabellar lines at maximum frown for the given post-Baseline visit

End point type	Secondary

End point timeframe:

Days 8, 15, 57, 85 and Day 113

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The secondary objectives were to assess the relative safety and efficacy of Dysport NG compared to Placebo

End point values	Placebo	Dysport NG 20 U	Dysport NG 50 U	Dysport NG 75 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	36	35	35
Units: percentage of subjects				
number (not applicable)				
ILA: Day 8 (N'=34,36,35,35)	0	77.8	80	82.9
ILA: Day 15 (N'=33,36,35,35)	3	80.6	94.3	91.4
ILA: Day 57 (N'=33,35,34,34)	0	77.1	79.4	82.4
ILA: Day 85 (N'=34,33,34,32)	0	48.5	58.8	75
ILA: Day 113 (N'=34,36,35,34)	0	22.2	42.9	55.9

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects as responders at maximum frown as measured by the subject's self-assessment

End point title	Percentage of subjects as responders at maximum frown as measured by the subject's self-assessment[3]

End point description:

ITT Population; N'= number of subjects with a subject's self assessment of glabellar lines at maximum frown for the given post-Baseline visit

End point type	Secondary

End point timeframe:

Days 8, 15, 57, 85 and 113

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The secondary objectives were to assess the relative safety and efficacy of Dysport NG compared to Placebo

End point values	Placebo	Dysport NG 20 U	Dysport NG 50 U	Dysport NG 75 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	36	35	35
Units: percentage of subjects				
number (not applicable)				
SSA: Day 8 (N'=34,36,35,35)	2.9	66.7	65.7	74.3
SSA: Day 15 (N'=33,36,35,35)	3	80.6	82.9	80
SSA: Day 57 (N'=34,35,34,34)	0	80	67.6	82.4
SSA: Day 85 (N'=34,35,34,32)	0	57.1	47.1	62.5
SSA: Day 113 (N'=34,36,35,34)	0	36.1	34.3	52.9

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects assessed as responders, by both the Investigator's live assessment and the subject's self-assessment at maximum frown

End point title	Percentage of subjects assessed as responders, by both the Investigator's live assessment and the subject's self-assessment at maximum frown

End point description:

ITT Population; N'= number of subjects with an Investigator's live assessment and a subject's self assessment of glabellar lines at maximum frown for the given post-Baseline visit

End point type	Secondary

End point timeframe:

Days 8, 15, 57, 85 and 113

End point values	Placebo	Dysport NG 20 U	Dysport NG 50 U	Dysport NG 75 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	36	35	35
Units: percentage of subjects				
number (not applicable)				
Day 8 (N'=34,36,35,35,35)	0	61.1	62.9	74.3
Day 15 (N'=34,36,35,35,34)	0	75	82.9	80
Day 57 (N'=34,35,34,34,34)	0	74.3	67.6	79.4
Day 85 (N'=34,33,34,32,34)	0	42.4	44.1	62.5
Day 113 (N'=34,36,35,34,35)	0	19.4	34.3	41.2

End point values	Dysport 50 U			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: percentage of subjects				
number (not applicable)				
Day 8 (N'=34,36,35,35,35)	51.4			
Day 15 (N'=34,36,35,35,34)	67.6			
Day 57 (N'=34,35,34,34,34)	64.7			
Day 85 (N'=34,33,34,32,34)	38.2			
Day 113 (N'=34,36,35,34,35)	25.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects as responders at rest as measured by the Investigator's live assessment

End point title	Percentage of subjects as responders at rest as measured by the Investigator's live assessment[4]

End point description:

A responder at rest was defined as a subject having a severity grade of none or mild at rest on the visit day and a severity grade of moderate or severe at rest at Visit 2.

ITT Population; N'= number of subjects with an Investigator's live assessment of glabellar lines at rest of moderate or severe at Baseline and with an assessment at the given post-Baseline visit;

End point type	Secondary

End point timeframe:

Days 8, 15, 29, 57, 85 and 113

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The secondary objectives were to assess the relative safety and efficacy of Dysport NG compared to Placebo

End point values	Placebo	Dysport NG 20 U	Dysport NG 50 U	Dysport NG 75 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	17	13	14
Units: percentage of subjects				
number (not applicable)				
ILA: Day 8 (N'=18,17,13,14)	11.1	70.6	76.9	71.4
ILA: Day 15 (N'=18,17,13,14)	11.1	70.6	92.3	78.6
ILA: Day 29 (N'=18,17,13,14)	5.6	82.4	76.9	85.7
ILA: Day 57 (N'=17,16,13,14)	11.8	81.3	76.9	78.6
ILA: Day 85 (N'=18,17,12,14)	5.6	82.4	75	64.3
ILA: Day 113 (N'=18,17,13,14)	11.1	52.9	53.8	57.1

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects as responders at maximum frown on Day 29 who remain responders

End point title	Percentage of subjects as responders at maximum frown on Day 29 who remain responders

End point description:

A responder at maximum frown was defined as a subject having a severity grade of none or mild at maximum frown on the visit day and a severity grade of moderate or severe at maximum frown at Visit 2.

ITT Population; N'=number of responders at Day 29

End point type	Secondary

End point timeframe:

Day 113

End point values	Placebo	Dysport NG 20 U	Dysport NG 50 U	Dysport NG 75 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	33	32	29
Units: percentage of subjects				
number (not applicable)				
ILA: Day 29 (N'=0,32,32,29,27)	0	25	46.9	65.5
SSA: Day 29 (N'=1,33,30,27,29)	0	36.4	40	63

End point values	Dysport 50 U			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: percentage of subjects				
number (not applicable)				
ILA: Day 29 (N'=0,32,32,29,27)	40.7			

SSA: Day 29 (N'=1,33,30,27,29)	34.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with a reduction of two or more grades in the severity of glabellar lines at maximum frown as measured by the Investigator's live assessment

End point title	Percentage of subjects with a reduction of two or more grades in the severity of glabellar lines at maximum frown as measured by the Investigator's live assessment

End point description:

A reduction of two or more grades in the severity of glabellar lines at maximum frown was a change from Visit 2 severity of glabellar lines from severe to mild/none or from Visit 2 severity of moderate to none after treatment as measured by the Investigator's live assessment

ITT Population; N'= number of subjects with an Investigator's live assessment of glabellar lines at maximum frown for the given post-Baseline visit

End point type	Secondary

End point timeframe:

Days 8, 15, 29, 57, 85 and 113

End point values	Placebo	Dysport NG 20 U	Dysport NG 50 U	Dysport NG 75 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	36	35	35
Units: percentage of subjects				
number (not applicable)				
ILA: Day 8 (N'=34,36,35,35,35)	0	30.6	45.7	45.7
ILA: Day 15 (N'=33,36,35,35,34)	0	50	62.9	57.1
ILA: Day 29 (N'=34,36,35,33,35)	0	55.6	68.6	63.6
ILA: Day 57 (N'=33,35,34,34,34)	0	34.3	47.1	44.1
ILA: Day 85 (N'=34,33,34,32,34)	0	24.2	29.4	31.3
ILA: Day 113 (N'=34,36,35,34,35)	0	13.9	14.3	20.6

End point values	Dysport 50 U			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: percentage of subjects				
number (not applicable)				
ILA: Day 8 (N'=34,36,35,35,35)	31.4			
ILA: Day 15 (N'=33,36,35,35,34)	50			
ILA: Day 29 (N'=34,36,35,33,35)	57.1			

ILA: Day 57 (N'=33,35,34,34,34)	41.2			
ILA: Day 85 (N'=34,33,34,32,34)	26.5			
ILA: Day 113 (N'=34,36,35,34,35)	8.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with a reduction of two or more grades in the severity of glabellar lines at rest as measured by the Investigator's live assessment

End point title	Percentage of subjects with a reduction of two or more grades in the severity of glabellar lines at rest as measured by the Investigator's live assessment

End point description:

A reduction of two or more grades in the severity of glabellar lines at rest was a change from Visit 2 severity of glabellar lines from severe to mild or from Visit 2 severity of moderate to none after treatment as measured by the Investigator's live assessment.

ITT Population; N'= number of subjects with an Investigator's live assessment of glabellar lines at rest of moderate or severe at Baseline and with an assessment at the given post-Baseline visit

End point type	Secondary

End point timeframe:

Days 8, 15, 29, 57, 85 and 113

End point values	Placebo	Dysport NG 20 U	Dysport NG 50 U	Dysport NG 75 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	17	13	14
Units: percentage of subjects				
number (not applicable)				
ILA: Day 8 (N'=18,17,13,14,19)	5.6	5.9	23.1	21.4
ILA: Day 15 (N'=18,17,13,14,18)	5.6	17.6	23.1	21.4
ILA: Day 29 (N'=18,17,13,14,19)	0	11.8	23.1	28.6
ILA: Day 57 (N'=17,16,13,14,19)	5.9	18.8	15.4	21.4
ILA: Day 85 (N'=18,17,12,14,19)	0	17.6	16.7	7.1
ILA: Day 113 (N'=18,17,13,14,19)	0	5.9	23.1	14.3

End point values	Dysport 50 U			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: percentage of subjects				
number (not applicable)				
ILA: Day 8 (N'=18,17,13,14,19)	10.5			
ILA: Day 15 (N'=18,17,13,14,18)	16.7			
ILA: Day 29 (N'=18,17,13,14,19)	21.1			
ILA: Day 57 (N'=17,16,13,14,19)	15.8			

ILA: Day 85 (N'=18,17,12,14,19)	15.8			
ILA: Day 113 (N'=18,17,13,14,19)	5.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with a reduction of two or more grades in the severity of glabellar lines at maximum frown as measured by the subject's self-assessment

End point title	Percentage of subjects with a reduction of two or more grades in the severity of glabellar lines at maximum frown as measured by the subject's self-assessment

End point description:

A reduction of two or more grades in the severity of glabellar lines at maximum frown was a change from Visit 2 severity of glabellar lines from severe to mild/no wrinkles or from Visit 2 severity of moderate to no wrinkles after treatment as measured by the subjects self assessment.

ITT Population; N'= number of subjects with a subject's self assessment of glabellar lines at maximum frown for the given post-Baseline visit

End point type	Secondary

End point timeframe:

Days 8, 15, 29, 57, 85 and 113

End point values	Placebo	Dysport NG 20 U	Dysport NG 50 U	Dysport NG 75 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	36	35	35
Units: percentage of subjects				
number (not applicable)				
SSA: Day 8 (N'=34,36,35,35,35)	0	25	42.9	40
SSA: Day 15 (N'=33,36,35,35,34)	0	52.8	57.1	54.3
SSA: Day 29 (N'=34,36,35,33,35)	0	52.8	60	57.6
SSA: Day 57 (N'=34,35,34,34,34)	0	40	52.9	44.1
SSA: Day 85 (N'=34,35,34,32,34)	0	28.6	29.4	31.3
SSA: Day 113 (N'=34,36,35,34,35)	0	8.3	22.9	11.8

End point values	Dysport 50 U			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: percentage of subjects				
number (not applicable)				
SSA: Day 8 (N'=34,36,35,35,35)	34.3			
SSA: Day 15 (N'=33,36,35,35,34)	47.1			
SSA: Day 29 (N'=34,36,35,33,35)	57.1			

SSA: Day 57 (N'=34,35,34,34,34)	47.1			
SSA: Day 85 (N'=34,35,34,32,34)	29.4			
SSA: Day 113 (N'=34,36,35,34,35)	17.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects as Responders, as Measured by the Investigator's Live Assessment at Maximum Frown (Comparison with Dysport 50 U)

End point title	Percentage of subjects as Responders, as Measured by the Investigator's Live Assessment at Maximum Frown (Comparison with Dysport 50 U)[5]

End point description:

ITT Population; N'=number of subjects with assessment

End point type	Secondary

End point timeframe:

Days 8, 15, 29, 57, 85 and 113

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The secondary objectives were to assess the relative safety and efficacy of Dysport NG compared to Dysport U

End point values	Dysport NG 20 U	Dysport NG 50 U	Dysport NG 75 U	Dysport 50 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	35	35
Units: percentage of subjects				
number (not applicable)				
ILA: Day 8 (N'=36,35,35,35)	77.8	80	82.9	57.1
ILA: Day 15 (N'=36,35,35,34)	80.6	94.3	91.4	73.5
ILA: Day 29 (N'=36,35,33,35)	88.9	91.4	87.9	77.1
ILA: Day 57 (N'=35,34,34,34)	77.1	79.4	82.4	70.6
ILA: Day 85 (N'=33,34,32,34)	48.5	58.8	75	52.9
ILA: Day 113 (N'=36,35,34,35)	22.2	42.9	55.9	31.4

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects as Responders, as Measured by the Subject's Self assessment at Maximum Frown (Comparison with Dysport 50 U)

End point title	Percentage of subjects as Responders, as Measured by the Subject's Self assessment at Maximum Frown (Comparison with Dysport 50 U)[6]

End point description:

ITT Population; N'=number of subjects with assessment

End point type	Secondary

End point timeframe:

Days 8, 15, 29, 57, 85 and 113

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The secondary objectives were to assess the relative safety and efficacy of Dysport NG compared to Dysport U

End point values	Dysport NG 20 U	Dysport NG 50 U	Dysport NG 75 U	Dysport 50 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	35	35
Units: percentage of subjects				
number (not applicable)				
SSA: Day 8 (N'=36,35,35,35)	66.7	65.7	74.3	57.1
SSA: Day 15 (N'=36,35,35,34)	80.6	82.9	80	73.5
SSA: Day 29 (N'=36,35,33,35)	91.7	85.7	81.8	82.9
SSA: Day 57 (N'=35,34,34,34)	80	67.6	82.4	73.5
SSA: Day 85 (N'=35,34,32,34)	57.1	47.1	62.5	41.2
SSA: Day 113 (N'=36,35,34,35)	36.1	34.3	52.9	28.6

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects as Responders, as Measured by the Investigator's Live Assessment at Rest (Comparison with Dysport 50 U)

End point title	Percentage of subjects as Responders, as Measured by the Investigator's Live Assessment at Rest (Comparison with Dysport 50 U)[7]

End point description:

ITT Population; N'=number of subjects with an Investigator's live assessment of glabellar lines at rest of moderate or severe at Baseline and with an assessment at the given post-Baseline visit

End point type	Secondary

End point timeframe:

Days 8, 15, 29, 57, 85 and 113

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The secondary objectives were to assess the relative safety and efficacy of Dysport NG compared to Dysport U

End point values	Dysport NG 20 U	Dysport NG 50 U	Dysport NG 75 U	Dysport 50 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	13	14	19
Units: percentage of subjects				
number (not applicable)				
ILA: Day 8 (N'=17,13,14,19)	70.6	76.9	71.4	63.2
ILA: Day 15 (N'=17,13,14,18)	70.6	92.3	78.6	72.2
ILA: Day 29 (N'=17,13,14,19)	82.4	76.9	85.7	84.2
ILA: Day 57 (N'=16,13,14,19)	81.3	76.9	78.6	84.2
ILA: Day 85 (N'=17,12,14,19)	82.4	75	64.3	68.4

ILA: Day 113 (N'=17,13,14,19)	52.9	53.8	57.1	52.6

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects as Responders at Day 29 by the Investigator's Live Assessment and by Subject's Self assessment of Glabellar Lines at Maximum Frown (Assay Sensitivity)

End point title	Percentage of subjects as Responders at Day 29 by the Investigator's Live Assessment and by Subject's Self assessment of Glabellar Lines at Maximum Frown (Assay Sensitivity)[8]

End point description:

ITT Population; N'=number of subjects with an assessment at Day 29

End point type	Secondary

End point timeframe:

Day 29

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The secondary objectives were to assess the relative safety and efficacy of Dysport 50 U compared to Placebo

End point values	Placebo	Dysport 50 U		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	35		
Units: percentage of subjects				
number (not applicable)				
ILA: (N'=34,35)	0	77.1		
SSA: (N'=34,35)	2.9	82.9		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects Reporting at least one Treatment Emergent Adverse Event during the study

End point title	Number of Subjects Reporting at least one Treatment Emergent Adverse Event during the study

End point description:

Treatment Emergent Adverse Event (TEAE)

Safety Population: The safety population included all randomised subjects who received study treatment, regardless of the actual amount injected

End point type	Other pre-specified

End point timeframe:

Up to Day 113 (±3 days)

End point values	Placebo	Dysport NG 20 U	Dysport NG 50 U	Dysport NG 75 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	36	35	35
Units: participants				
number (not applicable)				
TEAE	12	15	10	11
Severe TEAE	0	1	0	0
Related TEAE	5	6	4	4
Related and severe TEAE	0	0	0	0
TEAE leading to withdrawal	0	0	0	0
TEAE leading to death	0	0	0	0
Serious Adverse Event (SAE)	0	1	0	0

End point values	Dysport 50 U			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: participants				
number (not applicable)				
TEAE	10			
Severe TEAE	0			
Related TEAE	2			
Related and severe TEAE	0			
TEAE leading to withdrawal	0			
TEAE leading to death	0			
Serious Adverse Event (SAE)	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to Day 113 (±3 days)	
Adverse event reporting additional description:	
Serious Adverse Event (SAE) Treatment Emergent Adverse Event (TEAE)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Intramuscular injections on Day 1 (0.05 mL per injection) (single treatment cycle)	
Reporting group title	Dysport NG 20 U
Reporting group description:	
Botulinum type A toxin (Dysport RU), Intramuscular injections on Day 1 in the muscle (0.05 mL per injection) (single treatment cycle)	
Reporting group title	Dysport NG 50 U
Reporting group description:	
Botulinum type A toxin (Dysport RU), Intramuscular injections on Day 1 in the muscle (0.05 mL per injection) (single treatment cycle)	
Reporting group title	Dysport NG 75 U
Reporting group description:	
Botulinum type A toxin (Dysport RU), Intramuscular injections on Day 1 in the muscle (0.05 mL per injection) (single treatment cycle)	
Reporting group title	Dysport 50 U
Reporting group description:	
Botulinum type A toxin ((Azzalure®), Intramuscular injections on Day 1 (0.05 mL per injection) (single treatment cycle)	

Serious adverse events	Placebo	Dysport NG 20 U	Dysport NG 50 U
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 35 (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
Ear and labyrinth disorders			
Vertigo			

subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 35 (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

Serious adverse events	Dysport NG 75 U	Dysport 50 U	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Dysport NG 20 U	Dysport NG 50 U
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 35 (34.29%)	14 / 36 (38.89%)	10 / 35 (28.57%)
Vascular disorders			
Venous thrombosis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	1 / 35 (2.86%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	1	2	1
Injection site discomfort			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0

Asthenia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Injection site haemorrhage			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Injection site reaction			
subjects affected / exposed	1 / 35 (2.86%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Injection site swelling			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Injection site anaesthesia			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0

Rhinorrhoea			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Investigations			
Laparoscopy			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	2 / 35 (5.71%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Animal bite			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Heat stroke			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Periorbital haematoma			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Arthropod bite			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Face injury			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

Headache			
subjects affected / exposed	4 / 35 (11.43%)	2 / 36 (5.56%)	3 / 35 (8.57%)
occurrences (all)	4	2	3
Migraine			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Syncope			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Eye disorders			
Eyelid oedema			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Eyelid ptosis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Keratitis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Periorbital oedema			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Visual acuity reduced			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Nausea			

subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Abdominal discomfort			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Periarthritis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	4 / 35 (11.43%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	4	0	1
Influenza			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	1 / 35 (2.86%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Oral herpes			
subjects affected / exposed	1 / 35 (2.86%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Pharyngitis			
subjects affected / exposed	1 / 35 (2.86%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Eczema infected			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Dysport NG 75 U	Dysport 50 U	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 35 (31.43%)	10 / 35 (28.57%)	
Vascular disorders			
Venous thrombosis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	2 / 35 (5.71%)	1 / 35 (2.86%)	
occurrences (all)	2	1	
Injection site discomfort			

subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Asthenia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Injection site haemorrhage			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Injection site reaction			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Injection site swelling			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Injection site anaesthesia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Nasal congestion			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Rhinitis allergic			

subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Rhinorrhoea			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Investigations			
Laparoscopy			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Road traffic accident			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Animal bite			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Heat stroke			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Laceration			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Periorbital haematoma			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Arthropod bite			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Face injury			

subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 35 (5.71%)	3 / 35 (8.57%)	
occurrences (all)	3	3	
Migraine			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Eyelid oedema			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Dry eye			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Eyelid ptosis			
subjects affected / exposed	2 / 35 (5.71%)	0 / 35 (0.00%)	
occurrences (all)	2	0	
Keratitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Periorbital oedema			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Visual acuity reduced			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Diarrhoea			

subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Haemorrhoids			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Abdominal discomfort			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Ecchymosis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 35 (0.00%)	2 / 35 (5.71%)	
occurrences (all)	0	2	
Periarthritis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Neck pain			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			

subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 35 (2.86%)	2 / 35 (5.71%)	
occurrences (all)	1	3	
Influenza			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Tooth abscess			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Oral herpes			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Pharyngitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	
Eczema infected			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 October 2010	Addition of contact information for the Coordinating Investigator on the cover page. Reference to Azzalure Summary of Product Characteristics (SmPC) rather than the Dysport NG Investigator's Brochure (IB) for the assessment of expectedness. Additional photographs to be used for each grade in the photographic scale. Minor consistency changes.
01 February 2011	The changes to the protocol were the result of feedback from Investigator training meetings. The following changes were agreed to by the Investigators and study team members: Maximum age for inclusion in the study was increased to 60 years. Exclusion criteria were modified to reflect specific time points wherein subjects having received dermatological procedures would be excluded from the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported