Clinical trial results:
A double-blind, randomised, placebo controlled, proof-of-concept study in subjects with abdominal or thoracic chronic scar pain to assess the analgesic properties of intradermal doses of Dysport®

Summary

EudraCT number	2018-001703-37
Trial protocol	GB
Global end of trial date	08 November 2019

Results information

Result version number	v1 (current)
This version publication date	27 November 2020
First version publication date	27 November 2020

Trial information

Trial identification

Sponsor protocol code	D-FR-52120-244

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03663101
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ipsen Innovation SAS
Sponsor organisation address	ZI de Courtaboeuf, 5 avenue du Canada, Les Ulis Cedex, France, 91966
Public contact	Medical Director, Ipsen Innovation SAS, clinical.trials@ipsen.com
Scientific contact	Medical Director, Ipsen Innovation SAS, 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	08 November 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 November 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to describe the pharmacodynamic analgesic profile (time of onset of meaningful analgesic effect, peak effect, time to peak effect, duration of effect) of intradermal doses of Dysport in participants with abdominal or thoracic chronic scar pain.

Protection of trial subjects:

The study was conducted under the provisions of the Declaration of Helsinki in accordance with the International Council on Harmonisation Consolidated Guideline on Good Clinical Practice. The study also complied with Independent Ethics Committees and informed consent regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 October 2018
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	United Kingdom: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	14
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase II proof-of-concept study was conducted at single investigational site in the United Kingdom. The study consisted of two sequential parts: Part A (Pre-randomisation run-in period) and Part B (Randomised double-blind period). Part A was considered as an extended screening period.

Pre-assignment

Screening details:

Part A was conducted to identify participants who would potentially benefit from Dysport injection, 'responders'. Part B was a double-blind study of Dysport or placebo injection in responders from Part A. Of the 46 participants who were included in Part A, 17 were responders. Of which, 16 participants were randomised into Part B of the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received a single dose of placebo (matching with Dysport) intradermal injection per injection point (maximum of 10 injection points) on Day 1.

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

Dosage and administration details:

Placebo (matching with Dysport) per injection point (maximum of 10 injection points). Injections were performed under a constant volume of 0.2 milliliter (mL).

Arm title	Dysport 2.5 U/Injection Site

Arm description:

Participants received a single dose of Dysport 2.5 Units (U) intradermal injection per injection point (maximum of 10 injection points) on Day 1. The maximal total dose was 25 U.

Arm type	Experimental
Investigational medicinal product name	Dysport
Investigational medicinal product code	
Other name	AboBoNT-A, Abobotulinumtoxin-A, Botulinum neurotoxin serotype A
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

Dysport per injection point (maximum of 10 injection points). Injections were performed under a constant volume of 0.2 mL.

Arm title	Dysport 10 U/Injection Site

Arm description:

Participants received a single dose of Dysport 10 U intradermal injection per injection point (maximum

of 10 injection points) on Day 1. The maximal total dose was 100 U.

Arm type	Experimental
Investigational medicinal product name	Dysport
Investigational medicinal product code	
Other name	AboBoNT-A, Abobotulinumtoxin-A, Botulinum neurotoxin serotype A
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

Dysport per injection point (maximum of 10 injection points). Injections were performed under a constant volume of 0.2 mL.

Arm title	Dysport 20 U/Injection Site

Arm description:

Participants received a single dose of Dysport 20 U intradermal injection per injection point (maximum of 10 injection points) on Day 1. The maximal total dose was 200 U.

Arm type	Experimental
Investigational medicinal product name	Dysport
Investigational medicinal product code	
Other name	AboBoNT-A, Abobotulinumtoxin-A, Botulinum neurotoxin serotype A
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

Dysport per injection point (maximum of 10 injection points). Injections were performed under a constant volume of 0.2 mL.

Number of subjects in period 1	Placebo	Dysport 2.5 U/Injection Site	Dysport 10 U/Injection Site
Started	4	3	5
Completed	4	3	5

Number of subjects in period 1	Dysport 20 U/Injection Site
Started	4
Completed	4

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received a single dose of placebo (matching with Dysport) intradermal injection per injection point (maximum of 10 injection points) on Day 1.	
Reporting group title	Dysport 2.5 U/Injection Site
Reporting group description:	
Participants received a single dose of Dysport 2.5 Units (U) intradermal injection per injection point (maximum of 10 injection points) on Day 1. The maximal total dose was 25 U.	
Reporting group title	Dysport 10 U/Injection Site
Reporting group description:	
Participants received a single dose of Dysport 10 U intradermal injection per injection point (maximum of 10 injection points) on Day 1. The maximal total dose was 100 U.	
Reporting group title	Dysport 20 U/Injection Site
Reporting group description:	
Participants received a single dose of Dysport 20 U intradermal injection per injection point (maximum of 10 injection points) on Day 1. The maximal total dose was 200 U.	

Reporting group values	Placebo	Dysport 2.5 U/Injection Site	Dysport 10 U/Injection Site
Number of subjects	4	3	5
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	3	5
From 65-84 years	1	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	56.5	49.7	46.0
standard deviation	± 10.7	± 6.0	± 11.3
Gender categorical Units: Subjects			
Female	3	3	3
Male	1	0	2
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	3
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	4	3	2

More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Dysport 20 U/Injection Site	Total	
Number of subjects	4	16	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	3	14	
From 65-84 years	1	2	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	48.8		
standard deviation	± 16.7	-	
Gender categorical Units: Subjects			
Female	2	11	
Male	2	5	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	4	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	3	12	
More than one race	0	0	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received a single dose of placebo (matching with Dysport) intradermal injection per injection point (maximum of 10 injection points) on Day 1.	
Reporting group title	Dysport 2.5 U/Injection Site
Reporting group description:	
Participants received a single dose of Dysport 2.5 Units (U) intradermal injection per injection point (maximum of 10 injection points) on Day 1. The maximal total dose was 25 U.	
Reporting group title	Dysport 10 U/Injection Site
Reporting group description:	
Participants received a single dose of Dysport 10 U intradermal injection per injection point (maximum of 10 injection points) on Day 1. The maximal total dose was 100 U.	
Reporting group title	Dysport 20 U/Injection Site
Reporting group description:	
Participants received a single dose of Dysport 20 U intradermal injection per injection point (maximum of 10 injection points) on Day 1. The maximal total dose was 200 U.	

Primary: Time to Onset of Effect in the Spontaneous Numerical Rating Scale (NRS) Score

End point title	Time to Onset of Effect in the Spontaneous Numerical Rating Scale (NRS) Score[1]

End point description:

The time to onset of effect was defined as time to a decrease from baseline of two points or greater in the spontaneous NRS score. Pain intensity was scored using an 11-point NRS score ranging from 0 to 10, where 0= no pain and 10= worst possible pain. Participants were provided with an Actiwatch® during an Actiwatch® training visit to record their spontaneous NRS scores at home. The Actiwatch® alerted the participants twice a day to record their average and maximal NRS scores over the preceding 12 hours. The questions were asked of the participants by the Actiwatch®: "Please rate your pain by selecting the one number that best describes your pain on average during the last 12 hours." and "Please rate your pain by selecting the one number that best describes your pain at its worst during the last 12 hours." Randomised population included all participants randomised in the double-blind period (Part B). Here, n= number of participants who reached the time to onset.

End point type	Primary

End point timeframe:

Part B: From baseline (defined as mean of all predose data from Day -7 and including predose on Day 1) up to end of study (Week 16) or early discontinuation.

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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Placebo	Dysport 2.5 U/Injection Site	Dysport 10 U/Injection Site	Dysport 20 U/Injection Site
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	4
Units: days				
arithmetic mean (standard deviation)				
Worst NRS score (n=2,3,5,2)	4.41 (± 4.92)	15.11 (± 25.17)	29.45 (± 39.82)	0.65 (± 0.32)

Average NRS score (n=3,3,4,2)	6.75 (± 2.74)	31.63 (± 53.78)	4.60 (± 6.55)	0.90 (± 0.03)

Statistical analyses

No statistical analyses for this end point

Primary: Peak Effect in the Spontaneous NRS Score

End point title	Peak Effect in the Spontaneous NRS Score[2]

End point description:

The peak effect was defined as the maximal decrease from baseline in the spontaneous NRS score over a 12-hour period. Pain intensity was scored using an 11-point NRS score ranging from 0 to 10, where 0= no pain and 10= worst possible pain. Participants were provided with an Actiwatch® during an Actiwatch® training visit to record their spontaneous NRS scores at home. The Actiwatch® alerted the participants twice a day to record their average and maximal NRS scores over the preceding 12 hours. The questions were asked of the participants by the Actiwatch®: "Please rate your pain by selecting the one number that best describes your pain on average during the last 12 hours." and "Please rate your pain by selecting the one number that best describes your pain at its worst during the last 12 hours." Greater reductions in change from baseline correspond to greater pain relief. Randomised population included all participants randomised in the double-blind period (Part B).

End point type	Primary

End point timeframe:

Part B: From baseline (defined as mean of all predose data from Day -7 and including predose on Day 1) up to end of study (Week 16) or early discontinuation.

Notes:

[2] - 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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Placebo	Dysport 2.5 U/Injection Site	Dysport 10 U/Injection Site	Dysport 20 U/Injection Site
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	4
Units: score on a scale				
arithmetic mean (standard deviation)				
Worst NRS score	-2.36 (± 1.58)	-4.73 (± 0.55)	-3.54 (± 2.15)	-2.82 (± 2.91)
Average NRS score	-2.52 (± 0.91)	-3.53 (± 0.45)	-3.72 (± 1.57)	-2.12 (± 2.37)

Statistical analyses

No statistical analyses for this end point

Primary: Time to Peak Effect in the Spontaneous NRS Score

End point title	Time to Peak Effect in the Spontaneous NRS Score[3]

End point description:

The time to peak effect was defined as the time to reach the peak effect over a 12-hour period. Pain intensity was scored using an 11-point NRS score ranging from 0 to 10, where 0= no pain and 10= worst possible pain. Participants were provided with an Actiwatch® during an Actiwatch® training visit to record their spontaneous NRS scores at home. The Actiwatch® alerted the participants twice a day to

record their average and maximal NRS scores over the preceding 12 hours. The questions were asked of the participants by the Actiwatch®: "Please rate your pain by selecting the one number that best describes your pain on average during the last 12 hours." and "Please rate your pain by selecting the one number that best describes your pain at its worst during the last 12 hours." Randomised population included all participants randomised in the double-blind period (Part B).

End point type	Primary

End point timeframe:

Part B: From baseline (defined as mean of all predose data from Day -7 and including predose on Day 1) up to end of study (Week 16) or early discontinuation.

Notes:

[3] - 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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Placebo	Dysport 2.5 U/Injection Site	Dysport 10 U/Injection Site	Dysport 20 U/Injection Site
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	4
Units: days				
arithmetic mean (standard deviation)				
Worst NRS score	10.63 (± 10.18)	33.46 (± 51.41)	41.94 (± 35.72)	3.11 (± 1.56)
Average NRS score	12.51 (± 7.26)	33.13 (± 52.51)	11.04 (± 11.58)	26.49 (± 49.89)

Statistical analyses

No statistical analyses for this end point

Primary: Duration of Effect in the Spontaneous NRS Score

End point title	Duration of Effect in the Spontaneous NRS Score[4]

End point description:

The duration of effect was defined as the duration between time to onset and last timepoint for which decrease from baseline in the spontaneous NRS score was two points or greater. Pain intensity was scored using an 11-point NRS score ranging from 0 to 10, where 0= no pain and 10= worst possible pain. Participants were provided with an Actiwatch® during an Actiwatch® training visit to record their spontaneous NRS scores at home. The Actiwatch® alerted the participants twice a day to record their average and maximal NRS scores over the preceding 12 hours. The questions were asked of the participants by the Actiwatch®: "Please rate your pain by selecting the one number that best describes your pain on average during the last 12 hours." and "Please rate your pain by selecting the one number that best describes your pain at its worst during the last 12 hours." Here, n= number of participants who reached the time to onset.

End point type	Primary

End point timeframe:

Part B: From baseline (defined as mean of all predose data from Day -7 and including predose on Day 1) up to end of study (Week 16) or early discontinuation.

Notes:

[4] - 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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Placebo	Dysport 2.5 U/Injection Site	Dysport 10 U/Injection Site	Dysport 20 U/Injection Site
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[5]	3[6]	5[7]	4[8]
Units: days				
arithmetic mean (standard deviation)				
Worst NRS score (n=2,3,5,2)	86.04 (± 25.52)	86.68 (± 23.89)	66.80 (± 44.28)	110.52 (± 0.74)
Average NRS score (n=3,3,4,2)	53.53 (± 51.44)	65.17 (± 58.21)	102.75 (± 18.36)	110.02 (± 1.45)

Notes:

[5] - Randomised population.

[6] - Randomised population.

[7] - Randomised population.

[8] - Randomised population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Spontaneous NRS Score Throughout the Study

End point title	Change From Baseline in the Spontaneous NRS Score Throughout the Study

End point description:

Pain intensity was scored using an 11-point NRS score ranging from 0 to 10, where 0= no pain and 10= worst possible pain. Participants were provided with an Actiwatch® during an Actiwatch® training visit to record their spontaneous NRS scores at home. The Actiwatch® alerted the participants twice a day to record their average and maximal NRS scores over the preceding 12 hours. The questions were asked of the participants by the Actiwatch®: "Please rate your pain by selecting the one number that best describes your pain on average during the last 12 hours." and "Please rate your pain by selecting the one number that best describes your pain at its worst during the last 12 hours." Greater reductions in change from baseline correspond to greater pain relief. Randomised population included all participants randomised in the double-blind period (Part B). Here, n= number of participants analysed at specific time point.

End point type	Secondary

End point timeframe:

Part B: From baseline (defined as mean of all predose data from Day -7 and including predose on Day 1) up to end of study (Week 16) or early discontinuation.

End point values	Placebo	Dysport 2.5 U/Injection Site	Dysport 10 U/Injection Site	Dysport 20 U/Injection Site
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	4
Units: score on a scale				
arithmetic mean (standard deviation)				
Daily worst NRS score: Baseline (n=4,3,5,4)	5.1 (± 1.0)	5.1 (± 1.0)	5.3 (± 1.6)	5.8 (± 0.9)
Daily worst NRS score: Week 2 (n=4,3,4,4)	-0.6 (± 0.9)	-2.1 (± 2.1)	-1.4 (± 3.5)	-1.1 (± 2.7)
Daily worst NRS score: Week 4 (n=4,3,4,4)	-1.6 (± 1.8)	-2.1 (± 1.8)	-1.4 (± 4.2)	-1.6 (± 2.7)

Daily worst NRS score: Week 6 (n=4,3,4,4)	-1.1 (± 0.7)	-0.1 (± 1.0)	-1.7 (± 2.9)	-1.6 (± 2.6)
Daily worst NRS score: Week 12 (n=3,3,5,4)	-0.5 (± 1.4)	-1.4 (± 0.6)	-0.7 (± 1.1)	-0.8 (± 3.3)
Daily worst NRS score: Week 16 (n=3,3,5,4)	-0.0 (± 2.0)	-1.4 (± 1.1)	-1.3 (± 3.1)	-0.3 (± 1.7)
Daily average NRS score: Baseline (n=4,3,5,4)	4.5 (± 1.1)	3.9 (± 1.0)	4.7 (± 1.2)	4.9 (± 1.2)
Daily average NRS score: Week 2 (n=4,3,4,4)	-0.9 (± 1.0)	-2.0 (± 1.8)	-2.1 (± 2.8)	-1.7 (± 2.5)
Daily average NRS score: Week 4 (n=4,3,4,4)	-1.6 (± 1.9)	-1.9 (± 1.3)	-2.1 (± 3.2)	-1.4 (± 2.0)
Daily average NRS score: Week 6 (n=4,3,4,4)	-1.0 (± 0.9)	-0.4 (± 2.0)	-2.0 (± 2.6)	-1.4 (± 2.0)
Daily average NRS score: Week 12 (n=3,3,5,4)	-0.5 (± 1.6)	-1.5 (± 0.6)	-1.2 (± 1.9)	-0.6 (± 2.5)
Daily average NRS score: Week 16 (n=3,3,5,4)	-0.6 (± 1.5)	-0.9 (± 0.8)	-1.6 (± 2.3)	-0.4 (± 1.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Stimulus-Evoked NRS Score on the Painful Area at Weeks 6 and 12

End point title	Change From Baseline in the Stimulus-Evoked NRS Score on the Painful Area at Weeks 6 and 12

End point description:

For stimulus-evoked NRS score during Quantitative Sensory Testing (QST), participants were submitted to stimuli of various nature (light touch, pressure and temperature) applied to the painful area. Pain intensity was scored using an 11-point NRS score ranging from 0 to 10, where 0= no pain and 10= worst possible pain. Randomised population included all participants randomised in the double-blind period (Part B).

End point type	Secondary

End point timeframe:

Part B: Baseline (defined as mean of all predose data from Day -7 and including predose on Day 1) and Weeks 6 and 12

End point values	Placebo	Dysport 2.5 U/Injection Site	Dysport 10 U/Injection Site	Dysport 20 U/Injection Site
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	4
Units: score on a scale				
arithmetic mean (standard deviation)				
Static mechanical allodynia: Baseline	1.3 (± 1.5)	3.0 (± 3.6)	4.2 (± 1.1)	4.5 (± 3.1)
Static mechanical allodynia: Week 6	1.0 (± 1.2)	-1.7 (± 4.0)	-2.6 (± 1.8)	-1.0 (± 5.5)
Static mechanical allodynia: Week 12	0.8 (± 1.0)	-0.3 (± 5.7)	-2.0 (± 1.4)	-0.8 (± 5.1)
Dynamic mechanical allodynia: Baseline	1.3 (± 1.0)	2.3 (± 3.2)	2.4 (± 1.7)	5.3 (± 1.0)
Dynamic mechanical allodynia: Week 6	-0.5 (± 1.0)	-1.7 (± 2.1)	-2.0 (± 1.9)	-2.5 (± 2.6)
Dynamic mechanical allodynia: Week 12	-0.3 (± 2.1)	-1.3 (± 1.5)	-0.2 (± 1.5)	-2.0 (± 2.7)
Temporal summation: Baseline	1.5 (± 1.3)	0.3 (± 1.5)	3.6 (± 3.0)	1.8 (± 2.1)

Temporal summation: Week 6	1.8 (± 2.1)	0.3 (± 0.6)	1.8 (± 1.1)	2.8 (± 1.7)
Temporal summation: Week 12	2.0 (± 0.8)	0.3 (± 3.1)	1.4 (± 1.1)	2.8 (± 1.7)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events were collected from the start of study drug administration (Day 1) in Part B up to end of study visit or early discontinuation, approximately 16 weeks.

Adverse event reporting additional description:

Safety population included all participants who received at least one dose of the study drug during the randomised double-blind period (Part B).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received a single dose of placebo (matching with Dysport) intradermal injection per injection point (maximum of 10 injection points) on Day 1.

Reporting group title	Dysport 2.5 U/Injection Site

Reporting group description:

Participants received a single dose of Dysport 2.5 U intradermal injection per injection point (maximum of 10 injection points) on Day 1. The maximal total dose was 25 U.

Reporting group title	Dysport 10 U/Injection Site

Reporting group description:

Participants received a single dose of Dysport 10 U intradermal injection per injection point (maximum of 10 injection points) on Day 1. The maximal total dose was 100 U.

Reporting group title	Dysport 20 U/Injection Site

Reporting group description:

Participants received a single dose of Dysport 20 U intradermal injection per injection point (maximum of 10 injection points) on Day 1. The maximal total dose was 200 U.

Serious adverse events	Placebo	Dysport 2.5 U/Injection Site	Dysport 10 U/Injection Site
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Metabolism and nutrition disorders			
Pancreatogenous diabetes			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (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 20 U/Injection Site		
Total subjects affected by serious adverse events			

subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Metabolism and nutrition disorders			
Pancreatogenous diabetes			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	Dysport 2.5 U/Injection Site	Dysport 10 U/Injection Site
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	3 / 3 (100.00%)	4 / 5 (80.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Injection site bruising			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Injection site rash			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Rhinorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1

Cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Product issues			
Device physical property issue			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood triglycerides increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Congenital, familial and genetic disorders			
Hereditary non-polyposis colorectal cancer syndrome			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Hyporeflexia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			

subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Sensory loss			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Gastric mucosa erythema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hiatus hernia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pancreatic failure			

subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pancreatitis acute			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	2 / 5 (40.00%)
occurrences (all)	3	0	2
Rash pustular			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	Dysport 20 U/Injection Site		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Melanocytic naevus subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
General disorders and administration site conditions Injection site bruising subjects affected / exposed occurrences (all) Injection site rash subjects affected / exposed occurrences (all)	 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0		
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	 0 / 4 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	 0 / 4 (0.00%) 0 1 / 4 (25.00%) 1 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0		
Psychiatric disorders Depressed mood subjects affected / exposed occurrences (all)	 0 / 4 (0.00%) 0		
Product issues			

Device physical property issue subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Investigations Blood triglycerides increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Congenital, familial and genetic disorders Hereditary non-polyposis colorectal cancer syndrome subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Hyporeflexia subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all) Sensory loss subjects affected / exposed occurrences (all)	3 / 4 (75.00%) 3 1 / 4 (25.00%) 1 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0		
Blood and lymphatic system disorders Lymphadenitis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Gastrointestinal disorders			

Diarrhoea subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Vomiting subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Abdominal pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Gastric mucosa erythema subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Hiatus hernia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Pancreatic failure subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Pancreatitis acute subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Renal and urinary disorders Urinary retention subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Musculoskeletal and connective tissue disorders			

Arthralgia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Rash pustular subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 1 / 4 (25.00%) 1		
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all)	 0 / 4 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 August 2018	Updated Section "Early Discontinuation or End of Study Visit" and "Study Schedule of Assessments" to ensure participant beneficence and to clarify how participants were monitored through each stage of the study. Updated inclusion and exclusion criteria. Updated the list of medications that should not start during the study.
04 December 2018	Maximum age of the participant for inclusion to the study was increased to 75 years old. The time from surgery which caused the painful scar for inclusion to the study was extended to 10 years. Updated Section "Pre-randomisation Run-in Period (Part A)" to permit the scar area to return to baseline after examination, test dosing or QST procedures. Two parts of the QST test, punctate hyperalgesia and vibration disappearance were not performed. Section "Stimulus-evoked NRS Score during Quantitative Sensory Testing" was modified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Recruitment was closed prematurely by 30 June 2019 due to slow enrolment, which meant Sponsor did not believe it was feasible to continue study in an acceptable timeframe. The decision was not related to any safety/tolerability concern with Dysport.

Notes: