Clinical trial results:
A Phase II, Single Centre, Randomized, Double-Blind, Parallel And Placebo Controlled, Pilot Study to Evaluate the Efficacy and Safety of Somatuline Autogel 60 mg in Patients with Active Thyroid-Associated Ophthalmopathy of Moderate Intensity

Summary

EudraCT number	2004-003937-14
Trial protocol	ES
Global end of trial date	27 October 2006

Results information

Result version number	v1 (current)
This version publication date	05 January 2017
First version publication date	05 January 2017

Trial information

Trial identification

Sponsor protocol code	A-92-52030-164

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00288522
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ipsen Pharma, S.A.
Sponsor organisation address	Avda. Laura Miro 395, 08980 Sant Feliu de Llobregat, Barcelona, Spain,
Public contact	Medical Director, Ipsen Pharma, S.A., clinical.trials@ipsen.com
Scientific contact	Medical Director, Ipsen Pharma, S.A., 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	27 October 2006
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 October 2006
Global end of trial reached?	Yes
Global end of trial date	27 October 2006
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of 3 doses of Somatuline Autogel (60 milligram [mg]) in the control of the infiltration and oedema of the muscle and retrobulbar connective tissue and in the retraction and contraction of the extraocular musculature in patients with active thyroid-associated opthalmopathy of moderate intensity.

Protection of trial subjects:

The clinical study was conducted in accordance with the International Conference on Harmonisation Consolidated Guideline on Good Clinical Practice, under the ethical principles laid down in the Declaration of Helsinki. In addition, this clinical study adhered to all local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 January 2006
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	Spain: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was designed as a randomized, double-blind, parallel and placebo controlled study at a single investigational site in Spain. First patient enrolled: 20 January 2006; last patient completed: 27 October 2006.

Pre-assignment

Screening details:

The inclusion of 20 patients in the study was planned, but only 5 patients were enrolled over a period of 12 months and before the study was prematurely terminated.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Somatuline Autogel

Arm description:

Somatuline Autogel 60 mg was administered by subcutaneous (s.c.) injection once every 28 days. Duration of treatment was 12 weeks (3 doses received). Study treatment was administered in the upper external quadrant of the buttock, alternating right and left sides at every administration.

Arm type	Experimental
Investigational medicinal product name	Somatuline Autogel
Investigational medicinal product code	
Other name	lanreotide
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Treatment consisted of a single s.c. injection of Somatuline Autogel (60 mg, 0.25 millilitre [mL]), once every 28 days, on 3 separate visits (Day 0, Week 4 and Week 8).

Arm title	Placebo

Arm description:

Placebo (saline solution) was administered by s.c. injection once every 28 days. Duration of treatment was 12 weeks (3 doses received). Study treatment was administered in the upper external quadrant of the buttock, alternating right and left sides at every administration.

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

Dosage and administration details:

Treatment consisted of a single s.c. injection of saline solution (0.25 mL), once every 28 days, on 3 separate visits (Day 0, Week 4 and Week 8).

Number of subjects in period 1	Somatuline Autogel	Placebo
Started	3	2
Completed	3	2

Baseline characteristics

Reporting groups	
Reporting group title	Somatuline Autogel
Reporting group description:	
Somatuline Autogel 60 mg was administered by subcutaneous (s.c.) injection once every 28 days. Duration of treatment was 12 weeks (3 doses received). Study treatment was administered in the upper external quadrant of the buttock, alternating right and left sides at every administration.	
Reporting group title	Placebo
Reporting group description:	
Placebo (saline solution) was administered by s.c. injection once every 28 days. Duration of treatment was 12 weeks (3 doses received). Study treatment was administered in the upper external quadrant of the buttock, alternating right and left sides at every administration.	

Reporting group values	Somatuline Autogel	Placebo	Total
Number of subjects	3	2	5
Age categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	50.3	38	
standard deviation	± 3.2	± 12.7	-
Gender Categorical			
Units: Subjects			
Female	3	2	5
Male	0	0	0

End points

End points reporting groups

Reporting group title	Somatuline Autogel

Reporting group description:

Somatuline Autogel 60 mg was administered by subcutaneous (s.c.) injection once every 28 days. Duration of treatment was 12 weeks (3 doses received). Study treatment was administered in the upper external quadrant of the buttock, alternating right and left sides at every administration.

Reporting group title	Placebo

Reporting group description:

Placebo (saline solution) was administered by s.c. injection once every 28 days. Duration of treatment was 12 weeks (3 doses received). Study treatment was administered in the upper external quadrant of the buttock, alternating right and left sides at every administration.

Primary: Eye inspection (at Day 0 and Weeks 4, 8 and 12): assessment of conjunctival injection presence, chemosis, cheratitis and eyelid oedema; extrinsic muscle function evaluation and eyelid retraction

End point title	Eye inspection (at Day 0 and Weeks 4, 8 and 12): assessment of conjunctival injection presence, chemosis, cheratitis and eyelid oedema; extrinsic muscle function evaluation and eyelid retraction[1]

End point description:

Assessment of the retraction and contraction of the extraocular musculature measuring the palpebral retraction by evaluation of the visual exam of the upper sclereocorneal limbo and visible adjacent sclerotic; and assessment of the function of the extraocular musculature by evaluation of the Hess Weiss's diagram (for motility) and with the Maddox cross (for diplopia).

End point type	Primary

End point timeframe:

12 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was performed for this end point

End point values	Somatuline Autogel	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Not applicable				

Notes:

[2] - Due to the small sample of patients, end point data was listed only. No summarised results reported.
[3] - Due to the small sample of patients, end point data was listed only. No summarised results reported.

Statistical analyses

No statistical analyses for this end point

Primary: Extraocular muscle infiltration and oedema exam by evaluating (at Day 0 and Weeks 4, 8 and 12): extraocular muscle size, proptosis and intraocular pressure (tonometry)

End point title	Extraocular muscle infiltration and oedema exam by evaluating (at Day 0 and Weeks 4, 8 and 12): extraocular muscle size,

	proptosis and intraocular pressure (tonometry)[4]

End point description:

Assessment of the oedema and the infiltration of the extraocular muscles and connective tissue measuring the extraocular muscle size by using orbital computerised tomography, assessment of the proptosis by using a Hertel's exophthalmometer and measurement of the intraocular pressure with a Perkin's tonometer.

End point type	Primary

End point timeframe:

12 weeks

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: No statistical analysis was performed for this end point

End point values	Somatuline Autogel	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[5]	0[6]		
Units: Not applicable				

Notes:

[5] - Due to the small sample of patients, end point data was listed only. No summarised results reported.
[6] - Due to the small sample of patients, end point data was listed only. No summarised results reported.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 12

Adverse event reporting additional description:

Adverse event (AE) data is reported as treatment-emergent AEs

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	Somatuline Autogel

Reporting group description:

Somatuline Autogel 60 milligram (mg) were administered by subcutaneous (s.c.) injection once every 28 days. Duration of treatment was 12 weeks (3 doses received). Study treatment was administered in the upper external quadrant of the buttock, alternating right and left sides at every administration.

Reporting group title	Placebo

Reporting group description:

Placebo (saline solution) was administered by s.c. injection once every 28 days. Duration of treatment was 12 weeks (3 doses received). Study treatment was administered in the upper external quadrant of the buttock, alternating right and left sides at every administration.

Serious adverse events	Somatuline Autogel	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
In hostital to practice hepatic biopsy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
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: 0 %

Non-serious adverse events	Somatuline Autogel	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	2 / 2 (100.00%)	
Nervous system disorders			

Unspecified event term for nervous system disorders			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Unspecified event term for gastrointestinal disorders			
subjects affected / exposed	1 / 3 (33.33%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Unspecified event term for reproductive system and breast disorders			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Sludge			
subjects affected / exposed	1 / 3 (33.33%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Unspecified event term for hepatobiliary disorders			
subjects affected / exposed	1 / 3 (33.33%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Pruriginous erythema on the right thigh			
subjects affected / exposed	1 / 3 (33.33%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Contracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	

Infections and infestations			
Syndrome			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Unspecified event term for infections and infestations			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study was prematurely terminated due to poor recruitment; 20 patients were planned but only 5 were included over a 12-month period. The limited efficacy data was listed only; no descriptive or inferential statistical analysis was performed.

Notes: