Clinical trial results:
PHASE IIIb, MULTICENTRE, OPEN-LABEL, SINGLE-ARM, STUDY TO ASSESS THE EFFICACY AND SAFETY OF LANREOTIDE AUTOGEL 120 mg ADMINISTERED EVERY 28 DAYS AS PRIMARY MEDICAL TREATMENT IN ACROMEGALIC PATIENTS WITH MACROADENOMA.

Summary

EudraCT number	2007-000155-34
Trial protocol	NL FR ES SE GB BE CZ FI DE IT
Global end of trial date	13 February 2012

Results information

Result version number	v1 (current)
This version publication date	16 March 2016
First version publication date	16 March 2016
Summary attachment (see zip file)	Publication of results in J Clin Endo Metab (Caron et al 2013 JCEM_PRIMARYs.pdf)

Trial information

Trial identification

Sponsor protocol code	2 79 52030 207

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00690898
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ipsen
Sponsor organisation address	65, quai Georges Gorse, Boulogne Billancourt Cedex, France, 92650
Public contact	Medical Director, Endocrinology, Medical Director, Endocrinology Ipsen, clinical.trials@ipsen.com
Scientific contact	Medical Director, Endocrinology, Medical Director, Endocrinology Ipsen, clinical.trials@ipsen.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 July 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 February 2012
Global end of trial reached?	Yes
Global end of trial date	13 February 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of Lanreotide Autogel 120 mg when used as primary medical treatment in untreated de novo acromegalic patients with macroadenoma, as assessed by evaluating the change in pituitary tumor volume at Week 48 (after 12 injection – V5) compared to baseline volume (V1).
A 20% reduction from baseline (as measured by MRI at V1) will be considered to be clinically significant.

Protection of trial subjects:

The study was conducted under the provisions of the Declaration of Helsinki, and in accordance with the International Conference of Harmonisation (ICH) Consolidated Guideline on Good Clinical Practice (GCP) and all local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 May 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Finland: 3
Country: Number of subjects enrolled	France: 42
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	United Kingdom: 17
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	Turkey: 2
Worldwide total number of subjects	90
EEA total number of subjects	88

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)	80
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

108 participants screened.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	108[1]
Number of subjects completed	90

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 2
Reason: Number of subjects	Adverse event, non-fatal: 1
Reason: Number of subjects	Entry criteria: 15

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Pre-assignment subject number includes screen failure subjects; whereas worldwide subjects number includes only enrolled subjects.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Lanreotide Autogel 120 mg

Arm description:

Lanreotide Autogel 120 mg injection was administered subcutaneously (SC) every 28 days for 12 courses as primary medical treatment in newly diagnosed acromegaly patients with pituitary tumour.

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

Dosage and administration details:

Patients received Lanreotide Autogel 120 mg administered every 28 days (±one day) via deep subcutaneous route in the upper external quadrant of the buttock, alternating the side at each administration. In order to ensure the performance of all protocol assessments, it was recommended to do the administration in the morning, approximately at 9:00 am after all the study assessments. The dose of Lanreotide Autogel was the same throughout the study. A total of 12 injections were administered during the study.

Number of subjects in period 1	Lanreotide Autogel 120 mg
Started	90
Completed	64
Not completed	26
Consent withdrawn by subject	4
Adverse event, non-fatal	3
Other reason	1
Lack of efficacy	18

Baseline characteristics

Reporting groups	
Reporting group title	Lanreotide Autogel 120 mg
Reporting group description:	
Lanreotide Autogel 120 mg injection was administered subcutaneously (SC) every 28 days for 12 courses as primary medical treatment in newly diagnosed acromegaly patients with pituitary tumour.	

Reporting group values	Lanreotide Autogel 120 mg	Total	
Number of subjects	90	90	
Age categorical Units: Subjects			
Adults (18-84 years)	90	90	
Age continuous Units: years arithmetic mean standard deviation	 49.5 ± 12.4	 -	
Gender categorical Units: Subjects			
Female Male	47 43	47 43	
Height Units: Cm arithmetic mean standard deviation	 172.7 ± 10.4	 -	
Weight Units: Kg arithmetic mean standard deviation	 83.4 ± 18.8	 -	
BMI Units: kg/m² arithmetic mean standard deviation	 27.7 ± 4.6	 -	
Maximum pituitary adenoma diameter (Visit 1) Units: mm arithmetic mean standard deviation	 19 ± 7.1	 -	
Acromegaly Symptom - Headache			
Acromegaly symptoms assessed on a scale of 0 to 8 (0- no symptoms to 8-severe/incapacitating).			
Units: score on a scale arithmetic mean standard deviation	 2.8 ± 2.6	 -	
Acromegaly Symptom - Excessive perspiration Units: score on a scale arithmetic mean standard deviation	 4.1 ± 2.4	 -	
Acromegaly Symptom - Fatigue			

Units: score on a scale			
arithmetic mean	4.2		
standard deviation	± 2.5	-	
Acromegaly Symptom - Soft tissue swelling			
Units: score on a scale			
arithmetic mean	4.1		
standard deviation	± 2.4	-	
Acromegaly Symptom - Arthralgia			
Units: score on a scale			
arithmetic mean	3.5		
standard deviation	± 2.6	-	
Time since acromegaly diagnosis			
Units: Days			
arithmetic mean	121.2		
standard deviation	± 149.9	-	
Pituitary gland MRI volume (Visit 1)			
Units: mm3			
arithmetic mean	2739.3		
standard deviation	± 3262.7	-	
Growth Hormone (GH) level			
Units: mcg/L			
arithmetic mean	15		
standard deviation	± 18.8	-	
Insulin-like Growth Factor 1 (IGF-1) level			
Units: mcg/L			
arithmetic mean	810		
standard deviation	± 300	-	
Prolactin level			
Units: mcg/L			
arithmetic mean	19		
standard deviation	± 20.2	-	
Global AcroQoL score			
Acromegaly Quality of Life Assessment (AcroQoL) questionnaire response scores range from 0 to 100. Higher scores indicate best possible Quality of Life. AcroQoL not assessed in patients from Turkey and Finland.			
Units: Score on a scale			
arithmetic mean	56.4		
standard deviation	± 16.1	-	

End points

End points reporting groups

Reporting group title	Lanreotide Autogel 120 mg

Reporting group description:

Lanreotide Autogel 120 mg injection was administered subcutaneously (SC) every 28 days for 12 courses as primary medical treatment in newly diagnosed acromegaly patients with pituitary tumour.

Primary: Percentage of patients With Significant Reduction in Pituitary Tumour Volume (as Measured by MRI) From Baseline Volume (Visit 1) to Week 48 (After 12 Injections at Visit 5)

End point title	Percentage of patients With Significant Reduction in Pituitary Tumour Volume (as Measured by MRI) From Baseline Volume (Visit 1) to Week 48 (After 12 Injections at Visit 5)[1]

End point description:

A blinded, centrally assessed evaluation of all MRIs was performed. A 20% reduction from the volume at Visit 1 was considered to be clinically relevant.

Analysis based on intent-to-treat (ITT) population comprised of 89 patients.

End point type	Primary

End point timeframe:

Week 1 (Baseline) and 48

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 available.

End point values	Lanreotide Autogel 120 mg			
Subject group type	Reporting group			
Number of subjects analysed	89			
Units: percentage of subjects				
number (confidence interval 95%)				
Greater than or equal to 20%	62.9 (52 to 72.9)			
Less than 20%	37.1 (27.1 to 48)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients With at Least a 20% Reduction in Tumour Volume From Baseline Volume (Visit 1) to Week 12 (Visit 3) and Week 24 (Visit 4)

End point title	Number of Patients With at Least a 20% Reduction in Tumour Volume From Baseline Volume (Visit 1) to Week 12 (Visit 3) and Week 24 (Visit 4)

End point description:

Analysis based on number (n) of subjects in the Intent to Treat population (ITT) with a valid value.

End point type	Secondary
End point timeframe:	
Week 1 (Baseline), 12 and 24	

End point values	Lanreotide Autogel 120 mg			
Subject group type	Reporting group			
Number of subjects analysed	89			
Units: Participants				
Greater than or equal to 20% at week 12 (n=85)	46			
Less than 20% at week 12 (n=85)	39			
Greater than or equal to 20% at week 24 (n=80)	45			
Less than 20% at week 24 (n=80)	35			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Variation From Baseline to Visit 3, 4 and 5 (Week 12, 24, and 48) of IGF-1 Levels

End point title	Percent Variation From Baseline to Visit 3, 4 and 5 (Week 12, 24, and 48) of IGF-1 Levels
End point description:	
Analysis based on number (n) of patients with a valid value in the intent-to-treat (ITT) population.	
End point type	Secondary
End point timeframe:	
Week 1 (Baseline), 12, 24 and 48	

End point values	Lanreotide Autogel 120 mg			
Subject group type	Reporting group			
Number of subjects analysed	89			
Units: percentage change				
arithmetic mean (confidence interval 95%)				
Baseline to week 12 (n=85)	-43.8 (-50.1 to -37.5)			
Baseline to week 24 (n=78)	-47.4 (-53.6 to -41.2)			
Baseline to week 48 (n=62)	-56.7 (-62.1 to -51.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Variation From Baseline to Visit 3, 4 and 5 (Week 12, 24, and 48) of Serum GH Levels.

End point title	Percent Variation From Baseline to Visit 3, 4 and 5 (Week 12, 24, and 48) of Serum GH Levels.

End point description:

Analysis based on number (n) of subjects in the Intent to Treat population (ITT) with a valid value.

End point type	Secondary

End point timeframe:

Week 1 (Baseline), 12, 24 and 48

End point values	Lanreotide Autogel 120 mg			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: percentage change				
arithmetic mean (confidence interval 95%)				
Baseline to week 12 (n=85)	-62.1 (-70.5 to -53.6)			
Baseline to week 24 (n=78)	-64.6 (-72.3 to -57)			
Baseline to week 48 (n=63)	-70.9 (-79.2 to -62.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Visit 3, 4 and 5 (Week 12, 24, and 48) of Prolactin Levels

End point title	Change From Baseline to Visit 3, 4 and 5 (Week 12, 24, and 48) of Prolactin Levels

End point description:

Analysis based on the number (n) of subjects with baseline level between 20 ng/ml and 100 ng/ml in the ITT population with a valid value.

End point type	Secondary

End point timeframe:

Weeks 12, 24 and 48

End point values	Lanreotide Autogel 120 mg			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: mcg/L				
arithmetic mean (standard deviation)				
Change from Baseline to Week 12 (n=20)	-18 (± 19)			
Change from Baseline to Week 24 (n=20)	-18.6 (± 20.3)			
Change from Baseline to Week 48 (n=12)	-17.3 (± 18.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients With Improved, Unchanged or Worsened Clinical Signs of Acromegaly (Arthralgia) From Baseline

End point title	Percentage of Patients With Improved, Unchanged or Worsened Clinical Signs of Acromegaly (Arthralgia) From Baseline

End point description:

The status of clinical signs of acromegaly assessed by an acromegaly symptoms questionnaire (paper form) completed by the patient at each study visit. The scoring for each clinical sign of acromegaly on the questionnaire is from 0 (no symptom) to 8 (severe, incapacitating symptom). The variation (or no variation) in scores indicate whether the clinical sign of acromegaly had improved, worsened or was unchanged.

Analysis based on the number (n) of subjects in the ITT population with a valid value.

End point type	Secondary

End point timeframe:

Week 1 (Baseline), 12, 24 and 48

End point values	Lanreotide Autogel 120 mg			
Subject group type	Reporting group			
Number of subjects analysed	89			
Units: percentage of subjects				
number (not applicable)				
Baseline to week 12 - Worsened (n=88)	9.1			
Baseline to week 12 - Unchanged (n=88)	26.1			
Baseline to week 12 - Improved (n=88)	64.8			

Baseline to week 24 - Worsened (n=81)	11.1			
Baseline to week 24 - Unchanged (n=81)	24.7			
Baseline to week 24 - Improved (n=81)	64.2			
Baseline to week 48 - Worsened (n=62)	17.7			
Baseline to week 48 - Unchanged (n=62)	22.6			
Baseline to week 48 - Improved (n=62)	59.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients With Improved, Unchanged or Worsened Clinical Signs of Acromegaly (Excessive Perspiration) From Baseline

End point title	Percentage of Patients With Improved, Unchanged or Worsened Clinical Signs of Acromegaly (Excessive Perspiration) From Baseline

End point description:

The status of clinical signs of acromegaly assessed by an acromegaly symptoms questionnaire (paper form) completed by the patient at each study visit. The scoring for each clinical sign of acromegaly on the questionnaire is from 0 (no symptom) to 8 (severe, incapacitating symptom). The variation (or no variation) in scores indicate whether the clinical sign of acromegaly had improved, worsened or was unchanged.

Analysis based on the number (n) of subjects in the ITT population with a valid value.

End point type	Secondary

End point timeframe:

Week 1 (Baseline), 12, 24 and 48

End point values	Lanreotide Autogel 120 mg			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: percentage of subjects				
number (not applicable)				
Baseline to week 12 - Worsened (n=88)	11.4			
Baseline to week 12 - Unchanged (n=88)	25			
Baseline to week 12 - Improved (n=88)	63.6			
Baseline to week 24 - Worsened (n=81)	14.8			
Baseline to week 24 - Unchanged (n=81)	21			
Baseline to week 24 - Improved (n=81)	64.2			
Baseline to week 48 - Worsened (n=62)	9.7			
Baseline to week 48 - Unchanged (n=62)	24.2			
Baseline to week 48 - Improved (n=62)	66.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients With Improved, Unchanged or Worsened Clinical Signs of Acromegaly (Fatigue) From Baseline

End point title	Percentage of Patients With Improved, Unchanged or Worsened Clinical Signs of Acromegaly (Fatigue) From Baseline

End point description:

The status of clinical signs of acromegaly assessed by an acromegaly symptoms questionnaire (paper form) completed by the patient at each study visit. The scoring for each clinical sign of acromegaly on the questionnaire is from 0 (no symptom) to 8 (severe, incapacitating symptom). The variation (or no variation) in scores indicate whether the clinical sign of acromegaly had improved, worsened or was unchanged.

Analysis based on the number (n) of subjects in the ITT population with a valid value.

End point type	Secondary

End point timeframe:

Week 1 (Baseline), 12, 24 and 48

End point values	Lanreotide Autogel 120 mg			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: percentage of subjects				
number (not applicable)				
Baseline to week 12 - Worsened (n=88)	13.6			
Baseline to week 12 - Unchanged (n=88)	25			
Baseline to week 12 - Improved (n=88)	61.4			
Baseline to week 24 - Worsened (n=81)	16			
Baseline to week 24 - Unchanged (n=81)	17.3			
Baseline to week 24 - Improved (n=81)	66.7			
Baseline to week 48 - Worsened (n=62)	14.5			
Baseline to week 48 - Unchanged (n=62)	29			
Baseline to week 48 - Improved (n=62)	56.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients With Improved, Unchanged or Worsened Clinical Signs of Acromegaly (Headache) From Baseline

End point title	Percentage of Patients With Improved, Unchanged or Worsened Clinical Signs of Acromegaly (Headache) From Baseline

End point description:

The status of clinical signs of acromegaly assessed by an acromegaly symptoms questionnaire (paper form) completed by the patient at each study visit. The scoring for each clinical sign of acromegaly on the questionnaire is from 0 (no symptom) to 8 (severe, incapacitating symptom). The variation (or no variation) in scores indicate whether the clinical sign of acromegaly had improved, worsened or was unchanged.

Analysis based on the number (n) of subjects in the ITT population with a valid value.

End point type	Secondary

End point timeframe:

Week 1 (Baseline), 12, 24 and 48

End point values	Lanreotide Autogel 120 mg			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: percentage of subjects				
number (not applicable)				
Baseline to week 12 - Worsened (n=88)	13.6			
Baseline to week 12 - Unchanged (n=88)	46.6			
Baseline to week 12 - Improved (n=88)	39.8			
Baseline to week 24 - Worsened (n=81)	11.1			
Baseline to week 24 - Unchanged (n=81)	42			
Baseline to week 24 - Improved (n=81)	46.9			
Baseline to week 48 - Worsened (n=62)	14.5			
Baseline to week 48 - Unchanged (n=62)	46.8			
Baseline to week 48 - Improved (n=62)	38.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients With Improved, Unchanged or Worsened Clinical Signs of Acromegaly (Soft Tissue Swelling) From Baseline

End point title	Percentage of Patients With Improved, Unchanged or Worsened Clinical Signs of Acromegaly (Soft Tissue Swelling) From Baseline

End point description:

The status of clinical signs of acromegaly assessed by an acromegaly symptoms questionnaire (paper form) completed by the patient at each study visit. The scoring for each clinical sign of acromegaly on the questionnaire is from 0 (no symptom) to 8 (severe, incapacitating symptom). The variation (or no variation) in scores indicate whether the clinical sign of acromegaly had improved, worsened or was unchanged.

Analysis based on the number (n) of subjects in the ITT population with a valid value.

End point type	Secondary

End point timeframe:

Week 1 (Baseline), 12, 24 and 48

End point values	Lanreotide Autogel 120 mg			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: percentage of subjects				
number (not applicable)				
Baseline to week 12 - Worsened (n=88)	10.2			
Baseline to week 12 - Unchanged (n=88)	26.1			
Baseline to week 12 - Improved (n=88)	63.6			
Baseline to week 24 - Worsened (n=81)	11.1			
Baseline to week 24 - Unchanged (n=81)	22.2			
Baseline to week 24 - Improved (n=81)	66.7			
Baseline to week 48 - Worsened (n=62)	14.5			
Baseline to week 48 - Unchanged (n=62)	19.4			
Baseline to week 48 - Improved (n=62)	66.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in the Global Acromegaly Quality of Life Assessment (AcroQoL) From Baseline

End point title	Changes in the Global Acromegaly Quality of Life Assessment (AcroQoL) From Baseline

End point description:

Acromegaly Quality of Life Assessment (AcroQoL) questionnaire response scores range from 0 to 100. Higher scores indicate best possible Quality of Life.

Analysis based on the number (n) of subjects in the ITT population with a valid value.

End point type	Secondary

End point timeframe:

Week 1 (Baseline), 12, 24 and 48

End point values	Lanreotide Autogel 120 mg			
Subject group type	Reporting group			
Number of subjects analysed	84			
Units: Units on a scale				
arithmetic mean (confidence interval 95%)				
Baseline to week 12 (n=82)	7.8 (5.7 to 9.8)			
Baseline to week 24 (n=75)	8 (5.3 to 10.8)			
Baseline to week 48 (n=59)	9.5 (6.2 to 12.8)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 28 days after the last Lanreotide Autogel injection.

Adverse event reporting additional description:

One Lanreotide Autogel subcutaneous (s.c.) injection administered every 28 days for 12 courses as primary medical treatment in newly diagnosed acromegaly patients with pituitary tumour.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Lanreotide Autogel 120 mg

Reporting group description:

Lanreotide Autogel 120 mg injection was administered subcutaneously (SC) every 28 days for 12 courses as primary medical treatment in newly diagnosed acromegaly patients with pituitary tumour.

Serious adverse events	Lanreotide Autogel 120 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 90 (14.44%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Thyroid cancer			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thyroid neoplasm			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Hypophysectomy			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Hypothermia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian cyst			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sleep apnoea syndrome			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Investigations			

Gamma-glutamyltransferase increased				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Insulin-like growth factor increased				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oxygen saturation decreased				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Intracranial hypotension				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 90 (2.22%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Eye disorders				

Visual acuity reduced				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Pneumoperitoneum				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Renal colic				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Hyperparathyroidism				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Osteoarthritis				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Lanreotide Autogel 120 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	72 / 90 (80.00%)		
General disorders and administration site conditions			
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 90 (5.56%)		
occurrences (all)	5		
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 90 (10.00%)		
occurrences (all)	16		
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	35 / 90 (38.89%)		
occurrences (all)	98		
Gastrointestinal disorder			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 90 (11.11%)		
occurrences (all)	16		
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 90 (6.67%)		
occurrences (all)	14		
Hepatobiliary disorders			
Cholelithiasis			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 90 (6.67%)		
occurrences (all)	7		
Skin and subcutaneous tissue disorders			
Alopecia			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 90 (13.33%)		
occurrences (all)	12		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 January 2009	Amendment 1: - Change in the name and address of the sponsor. - Change of timing of follow-up MRIs central readings
25 September 2009	Amendment 2: This amendment aimed to improve the scientific quality of the study. Study procedures did not change. -Inclusion and exclusion criteria amended related to visual field defect (Changes in inclusion and exclusion criteria do affect judgement of any efficacy endpoints, primary or secondary). -Extension of the recruitment period up to 33 months From a safety point of view the critical point of this amendment was to maintain the feasibility of a good visual evaluation capability, ensuring that visual defect that could result from pituitary adenoma change would be detected.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported