Clinical trial results:
A PHASE IV, OPEN-LABEL, RANDOMISED, CROSS-OVER STUDY TO ASSESS PATIENT PREFERENCE AND HEALTH ECONOMY IN PATIENTS WITH NEUROENDOCRINE TUMOURS, TREATED WITH LANREOTIDE AUTOGEL GIVEN AS SELF ADMINISTRATION

Summary

EudraCT number	2007-006514-42
Trial protocol	SE DK
Global end of trial date	16 August 2010

Results information

Result version number	v1 (current)
This version publication date	11 March 2016
First version publication date	11 March 2016

Trial information

Trial identification

Sponsor protocol code	A-99-52030-216

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Ipsen AB
Sponsor organisation address	Kista Science Tower, Farogatan 33,, Kista, Sweden, 164 51
Public contact	Medical Director, Endocrinology, Ipsen, clinical.trials@ipsen.com
Scientific contact	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	27 July 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 August 2010
Global end of trial reached?	Yes
Global end of trial date	16 August 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the patient preference of two lanreotide Autogel administration practices; self/partner or healthcare professional administration.

Protection of trial subjects:

This clinical study was designed and implemented and reported in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations (including European Directive 2001/20/EC, US Code of Federal Regulations Title 21, and Japanese Ministry of Health, Labor, and Welfare), and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	13 June 2008
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	Norway: 4
Country: Number of subjects enrolled	Sweden: 15
Country: Number of subjects enrolled	Denmark: 7
Worldwide total number of subjects	26
EEA total number of subjects	26

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	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 94 patients were entered on the screening and recruitment logs of all 10 participating sites. Date of first enrolment: 13 June 2008.

Pre-assignment

Screening details:

Out of 94 patients, 62 patients were offered participation. 32 were not eligible and 36 patients were chose not to participate mainly due to lack of motivation, satisfaction with current form of administration or fear of self-injection. 26 patients at nine sites entered the study of which 23 completed the study and 3 withdrew prematurely.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence Group 1 (Self-HCP): lanreotide Autogel

Arm description:

lanreotide Autogel, 90 or 120 mg in a pre-filled syringe given as a deep subcutaneous injection. The study with a training period where the patient or partner performed two or three training injections under supervision of a HCP at a healthcare provider facility. The training injections were followed by a self-administration block of three subsequent unsupervised injections every 28th day at the patient's home.

Arm type	Experimental
Investigational medicinal product name	lanreotide Autogel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The study drug administered was lanreotide Autogel, 90 or 120 mg in a pre-filled syringe given as a deep subcutaneous injection either in the upper external quadrant of the buttock or in the upper outer thigh.

Arm title	Sequence Group 2 (HCP-Self): lanreotide Autogel

Arm description:

lanreotide Autogel, 90 or 120 mg in a pre-filled syringe given as a deep subcutaneous injection. The study with a healthcare administration block with three HCP provided injections according to clinical routine every 28th day. A training period followed the healthcare administration block with two or three training injections performed by the patient or partner under supervision at the healthcare provider facilities.

Arm type	Experimental
Investigational medicinal product name	lanreotide Autogel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The study drug administered was lanreotide Autogel, 90 or 120 mg in a pre-filled syringe given as a deep subcutaneous injection either in the upper external quadrant of the buttock or in the upper outer thigh.

Number of subjects in period 1	Sequence Group 1 (Self-HCP): lanreotide Autogel	Sequence Group 2 (HCP-Self): lanreotide Autogel
Started	11	15
Completed	10	13
Not completed	1	2
Consent withdrawn by subject	1	-
Adverse event	-	1
Patient died	-	1

Baseline characteristics

Reporting groups

Reporting group title	Sequence Group 1 (Self-HCP): lanreotide Autogel

Reporting group description:

lanreotide Autogel, 90 or 120 mg in a pre-filled syringe given as a deep subcutaneous injection. The study with a training period where the patient or partner performed two or three training injections under supervision of a HCP at a healthcare provider facility. The training injections were followed by a self-administration block of three subsequent unsupervised injections every 28th day at the patient's home.

Reporting group title	Sequence Group 2 (HCP-Self): lanreotide Autogel

Reporting group description:

lanreotide Autogel, 90 or 120 mg in a pre-filled syringe given as a deep subcutaneous injection. The study with a healthcare administration block with three HCP provided injections according to clinical routine every 28th day. A training period followed the healthcare administration block with two or three training injections performed by the patient or partner under supervision at the healthcare provider facilities.

Reporting group values	Sequence Group 1 (Self-HCP): lanreotide Autogel	Sequence Group 2 (HCP-Self): lanreotide Autogel	Total
Number of subjects	11	15	26
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)	6	8	14
From 65-84 years	5	7	12
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	63.2	60	
standard deviation	± 6.5	± 12.7	-
Gender categorical Units: Subjects			
Female	4	8	12
Male	7	7	14
Number of patients per country Units: Subjects			
Denmark	3	4	7
Norway	1	3	4
Sweden	7	8	15

End points

End points reporting groups

Reporting group title	Sequence Group 1 (Self-HCP): lanreotide Autogel

Reporting group description:

lanreotide Autogel, 90 or 120 mg in a pre-filled syringe given as a deep subcutaneous injection. The study with a training period where the patient or partner performed two or three training injections under supervision of a HCP at a healthcare provider facility. The training injections were followed by a self-administration block of three subsequent unsupervised injections every 28th day at the patient's home.

Reporting group title	Sequence Group 2 (HCP-Self): lanreotide Autogel

Reporting group description:

lanreotide Autogel, 90 or 120 mg in a pre-filled syringe given as a deep subcutaneous injection. The study with a healthcare administration block with three HCP provided injections according to clinical routine every 28th day. A training period followed the healthcare administration block with two or three training injections performed by the patient or partner under supervision at the healthcare provider facilities.

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All randomised patients with at least one dose of study medication and with a preference assessment recorded.

Subject analysis set title	Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

Baseline refers to the last non-study visit at the clinic.

Subject analysis set title	Group 1 Self or Partner First Then HCP Administration
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Self or Partner Administration followed by HCP Administration.

Subject analysis set title	Group 2 HCP Then Self or Partner Administration
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Administration by HCP then Self or Partner Administration.

Subject analysis set title	Training Period
Subject analysis set type	Full analysis

Subject analysis set description:

The training period was where the subject or partner performed two or three training injections under supervision of a HCP at a healthcare provider facility.

Subject analysis set title	Self or Partner Administration
Subject analysis set type	Full analysis

Subject analysis set description:

The self or partner administration block (after training period) included three unsupervised injections every 28th day at the subject's home.

Subject analysis set title	HCP Administration
Subject analysis set type	Full analysis

Subject analysis set description:

A healthcare administration block included three HCP provided injections according to clinical routine every 28th day at the healthcare provider facility.

Primary: Subject Preference for Self or Partner Administration

End point title	Subject Preference for Self or Partner Administration[1]

End point description:

A global question was asked: 'If you could choose, which administration method would you like to use on a regular basis?' A) Healthcare professional provided injection B) Self/ partner administered injection

Analysis was performed on Intention to Treat population defined as all randomized subjects with ≥ 1 dose of study medication and with a preference assessment recorded.

End point type	Primary

End point timeframe:

Between week 30 to 34

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 provided for Subject Preference for Self or Partner Administration

End point values	Group 1 Self or Partner First Then HCP Administration	Group 2 HCP Then Self or Partner Administration		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	14		
Units: Participants				
Proportion preferring Self-partner Administration	10	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients Stating at Least One Injection Interfered With Daily Activities

End point title	Number of Patients Stating at Least One Injection Interfered With Daily Activities

End point description:

The subject was asked: 'Does the treatment administration used today interfere with your daily activities?'.

Analysis was performed on Intention to Treat population defined as all randomized subjects with ≥ 1 dose of study medication and with a preference assessment recorded.

End point type	Secondary

End point timeframe:

Between baseline to week 32, after each injection (8-9 injections).

End point values	Training Period	Self or Partner Administration	HCP Administration	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	25	25	25	
Units: participants				
Patients with atleast 1 Injection Interference	6	2	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients Stating at Least One Injection Negatively Interfered With Psychological Wellbeing

End point title	Number of Patients Stating at Least One Injection Negatively Interfered With Psychological Wellbeing

End point description:

The subject was asked: 'Does the treatment administration used today negatively interfere with your psychological wellbeing?'

Analysis was performed on Intention to Treat population defined as all randomized subjects with ≥ 1 dose of study medication and with a preference assessment recorded.

-vely = Negatively, inj = Injection

End point type	Secondary

End point timeframe:

Between baseline to week 32, after each injection (8-9 injections)

End point values	Training Period	Self or Partner Administration	HCP Administration	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	25	25	25	
Units: participants				
Patients Stating at Least One Inj -vely Interfered	4	2	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Days Sick Leave

End point title	Days Sick Leave

End point description:

Health care and patient costs associated with the treatment of carcinoid symptoms in subjects treated with lanreotide Autogel were assessed through recording loss of production for subject through total number of days sick leave of the employed patients (n=6).

Safety population: all randomized subjects with at least one dose of study medication. Two of the six subjects reported sick leave during the study. One subject was absent for one day due to unknown reason, the other was absent for 22 days due to surgery of metastasis.

End point type	Secondary

End point timeframe:

Group 1 - between week 8 to 20 (self or partner administration), between week 20 to 32 (HCP administration). Group 2 - between week 20 to 32 (self or partner administration), between week 0 to week 12 (HCP administration).

End point values	Self or Partner Administration	HCP Administration		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: days	23	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Number of Visits to HCP Due to Carcinoid Symptoms

End point title	Total Number of Visits to HCP Due to Carcinoid Symptoms

End point description:

Health care and patient costs associated with the treatment of carcinoid symptoms in subjects treated with lanreotide Autogel were assessed by recording the total number of visits made by participants (n=12) to HCP due to carcinoid symptoms.

Safety population: all randomized subjects with at least one dose of study medication.

End point type	Secondary

End point timeframe:

Group 1 - between week 8 to 20 (self or partner administration), between week 20 to 32 (HCP administration). Group 2 - between week 20 to 32 (self or partner administration), between week 0 to week 12 (HCP administration).

End point values	Self or Partner Administration	HCP Administration		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	12		
Units: visits	17	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Perceived Symptom Control Evaluation in Respect to Episodes of Flushing

End point title	Perceived Symptom Control Evaluation in Respect to Episodes of Flushing

End point description:

Participants were asked how they perceived the symptoms in respect to episodes of flushing since the last injection. Participants included in the study were previously treated with lanreotide Autogel and therefore the assessment at baseline was made in comparison to their previous injection outside of the study protocol.

Analysis was performed on Intention to Treat population defined as all randomized subjects with ≥ 1 dose of study medication and with a preference assessment recorded.

End point type	Secondary

End point timeframe:

Group 1 - baseline, week 16 to 20 (self or partner administration) and week 30 to 34 (HCP administration). Group 2 - baseline, week 12 (HCP administration) and week 30 (self or partner administration).

End point values	Baseline	Self or Partner Administration	HCP Administration	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	25	25	25	
Units: participants				
Worsened	0	1	1	
Similar	24	21	20	
Improved	1	2	4	
Missing	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Perceived Symptom Control Evaluation in Respect to Episodes of Diarrhoea

End point title	Perceived Symptom Control Evaluation in Respect to Episodes of Diarrhoea

End point description:

Participants were asked how they perceived the symptoms in respect to episodes of diarrhoea since the last injection. Participants included in the study were previously treated with lanreotide autogel and therefore the assessment at baseline was made in comparison to previous injection outside of the study protocol.

Analysis was performed on Intention to Treat population defined as all randomized subjects with ≥ 1 dose of study medication and with a preference assessment recorded.

End point type	Secondary

End point timeframe:

Group 1 - baseline, week 16 to 20 (self or partner administration) and week 30 to 34 (HCP administration). Group 2 - baseline, week 12 to 16 (HCP administration) and week 30 to 34 (self or partner administration).

End point values	Baseline	Self or Partner Administration	HCP Administration	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	25	25	25	
Units: participants				
Worsened	1	4	0	
Similar	22	17	24	
Improved	2	3	1	
Missing	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Chromogranin A Levels

End point title	Chromogranin A Levels

End point description:

Biochemical control was assessed by analyzing chromogranin A levels at each site visit, which was mandatory for all subjects.

'Before self or partner administration' was assessed at baseline for group 1 and at week 12 for group 2.

'After self or partner administration' was assessed at week 16 to 20 for group 1 and at week 12 for group 2.

'Before HCP administration' was assessed at week 16 to 20 for group 1 and at baseline for group 2.

'After HCP administration' was assessed at week 30 to 34 for group 1 and week 12 for group 2.

ITT population that had hormone levels assessed at each administration block.

End point type	Secondary

End point timeframe:

Group 1 - Baseline, week 16 to 20 and 30 to 34. Group 2 - Baseline, week 12 and 30 to 34.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: nmol/l				
arithmetic mean (standard deviation)				
Before Self or Partner Administration	37.48 (± 58.35)			
After Self or Partner Administration	47.85 (± 74.89)			
Before HCP Administration	42.05 (± 70.74)			
After HCP Administration	37.42 (± 57.96)			

Statistical analyses

No statistical analyses for this end point

Secondary: 5-hydroxyindoleacetic Acid (5-HIAA) Levels

End point title	5-hydroxyindoleacetic Acid (5-HIAA) Levels

End point description:

Biochemical control was assessed by analysing 5-HIAA levels at each site visit, which was judged as necessary by the investigator at each site.

'Before self or partner administration' was assessed at baseline for group 1 and at week 12 for group 2.

'After self or partner administration' was assessed at week 16 to 20 for group 1 and at week 12 for group 2.

'Before HCP administration' was assessed at week 16 to 20 for group 1 and at baseline for group 2.

'After HCP administration' was assessed at week 30 to 34 for group 1 and week 12 for group 2.

5-HIAA were assessed as judged necessary by the investigator at each site.

End point type	Secondary

End point timeframe:

Group 1 - Baseline, week 16 to 20 and 30 to 34. Group 2 - Baseline, week 12 and 30 to 34.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: nmol/l				
arithmetic mean (standard deviation)				
Before Self or Partner Administration	220.17 (± 238.32)			
After Self or Partner Administration	219.17 (± 227.64)			
Before HCP Administration	217.08 (± 244.32)			
After HCP Administration	219.58 (± 218.51)			

Statistical analyses

No statistical analyses for this end point

Secondary: Healthcare Professionals With Positive Response to Specified Questions on Self or Partner Administration Method

End point title	Healthcare Professionals With Positive Response to Specified Questions on Self or Partner Administration Method

End point description:

Assessed by the number of HCP with a positive response 'yes' to two questions:
1.Based on your experience during this trial, did you feel confident in the safety of your patients?
2.Based on your experience during this trial, would you recommend suitable patients to try self or partner administration?

One HCP from each site who enrolled participants replied to the question and the method used is Self or

Partner Administration Method.

End point type	Secondary

End point timeframe:

Between week 30 to 34.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: participants				
HCP With +ve Response to Specified Questions	9			

Statistical analyses

No statistical analyses for this end point

Secondary: Telephone Contacts with Study Site Staff

End point title	Telephone Contacts with Study Site Staff

End point description:

Health care and patient costs associated with the treatment of carcinoid symptoms in subjects treated with lanreotide Autogel were assessed by recording the time, taken for telephone contacts with study site staff.

End point type	Secondary

End point timeframe:

Group 1 - between week 8 to 20 (self or partner administration), between week 20 to 32 (HCP administration). Group 2 - between week 20 to 32 (self or partner administration), between week 0 to week 12 (HCP administration).

End point values	Self or Partner Administration	HCP Administration		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	25		
Units: Minutes				
Time spent for telephone contacts with Study staff	205	312		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to visit 3	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups	
Reporting group title	Training Period
Reporting group description:	
The training period was where the subject or partner performed two or three training injections under supervision of a HCP at a healthcare provider facility.	
Reporting group title	Self or Partner Administration
Reporting group description:	
The self or partner administration block (after training period) included three unsupervised injections every 28th day at the subject's home.	
Reporting group title	HCP Administration
Reporting group description:	
A healthcare administration block included three HCP provided injections according to clinical routine every 28th day at the healthcare provider facility.	

Serious adverse events	Training Period	Self or Partner Administration	HCP Administration
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 26 (15.38%)	4 / 26 (15.38%)	3 / 26 (11.54%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0
Injury, poisoning and procedural complications			
Post procedural fistula			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 26 (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

General disorders and administration site conditions			
Death			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Disease progression			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 26 (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
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 26 (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
Ileus			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritoneal cyst			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Cholangitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 26 (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
Infections and infestations			
Biliary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Training Period	Self or Partner Administration	HCP Administration
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 26 (26.92%)	4 / 26 (15.38%)	7 / 26 (26.92%)
Vascular disorders			
Flushing			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	2 / 26 (7.69%)
occurrences (all)	0	2	2
Nervous system disorders			

Headache			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 26 (11.54%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	4	1	0
General disorders and administration site conditions			
Disease progression			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	2 / 26 (7.69%)
occurrences (all)	0	2	2
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 26 (15.38%)	1 / 26 (3.85%)	3 / 26 (11.54%)
occurrences (all)	4	3	6
Gastrointestinal disorders			
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 26 (11.54%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	4	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 February 2008	Local Danish Amendment: In Denmark, the following changes were made to the initial protocol following a request from the Ethics Committee in Region Midtjylland: • A section to describe how the patients were recruited into the study was added. • A section to describe potential risks and side effects were added. • A section to describe the ethical aspects of the study was added. • An appendix to define the financial situation was added, including details of who initiated the study, who the sponsor is, details of the financial agreement and information regarding the financial relationship between the Principal Investigator (PI) in Denmark and the sponsor. • A section to clearly state that all results, whether positive or negative will be published was added. • A more detailed section regarding the Informed Consent process was added.
13 March 2008	Amendment 1: In amendment 1, dated 13 March 2008, the following changes were made to the initial protocol: • Patients with previous experience of self and/or partner-administered lanreotide Autogel should not be allowed to participate in the study due to the risk of receiving biased data. • An inconsistency concerning the time between Visit 1 and 2 for Group 1 was corrected to 20-24 weeks throughout the protocol. • The randomisation process was incorporated into the eCRF instead of being performed manually by the Clinical Study Coordinator at Ipsen. This change was made to minimise the risk of human randomisation errors, as well as to increase the availability. • Patient initials were removed from the patient coding process. Only patient number was used as patient identification. Amendment 1 was submitted to all participating countries after initial approval.
12 November 2008	Amendment 2: In amendment 2, dated 12 November 2008, the following changes were made to the protocol: • A misprint of the emergency phone number on the cover page was corrected. • The recruitment period was extended by 6 months, from 6 to 12 months in order to reach the inclusion target. • The maximum number of patients allowed per site was increased from 5 to 10 patients to allow high-recruiting sites to include more than 5 patients. • The responsibility for data entry of laboratory values was transferred from study personnel to central laboratory personnel. Amendment 2 was submitted to Swedish and Norwegian regulatory authorities and Ethics Committees in Nov/Dec 2008. A modified version of amendment 2 was submitted to Danish regulatory authorities and Ethics Committees in April 2009 as local Danish amendment 2.
06 April 2009	Local Danish Amendment 2: In local Danish amendment 2, dated 06 April 2009, the following changes were made to the protocol: • A misprint of the emergency phone number on the cover page was corrected. • Recruitment period was extended by 12 months, from 6 to 18 months. • Maximum number of patients allowed per site was increased from 5 to 10 patients. • Compensation to high-recruiting sites was increased to compensate for time spent pre-screening patients. Local Danish amendment 2 was submitted to Danish authorities as stated above.
29 January 2010	Amendment 3: The following changes were made to the protocol: • The number of patients required for inclusion was reduced from 42 to 26 due to slow recruitment and a higher proportion of patients preferring self-partner administration compared to the value used in sample size calculations. Amendment 3 was submitted to regulatory authorities and ethics committees in all participating countries.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported