



Clinical trial results:

Phase II, open, single group, multicentre study to evaluate the efficacy and safety of Lanreotide Autogel® (120 mg) administered every 4 weeks by deep subcutaneous injection in the tumour's growth stabilization of patients with progressive neuroendocrine tumours who are not eligible to be treated with either surgery or chemotherapy

Summary

EudraCT number	2004-002871-18
Trial protocol	ES
Global end of trial date	06 November 2009

Results information

Result version number	v1 (current)
This version publication date	14 May 2016
First version publication date	14 May 2016

Trial information

Trial identification

Sponsor protocol code	A-92-52030-166
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Ipsen Pharma
Sponsor organisation address	65, Quai Georges Gorse, Boulogne-Billancourt Cedex, France, 92650
Public contact	Medical Director, Neurosurgery., Ipsen Pharma, clinical.trials@ipsen.com
Scientific contact	Medical Director, Neurosurgery., Ipsen Pharma, 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 December 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 November 2009
Global end of trial reached?	Yes
Global end of trial date	06 November 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of Somatulina Autogel® in tumour growth stabilisation, in patients with progressive neuroendocrine tumours who are not eligible to be treated with either surgery or chemotherapy at the time of their inclusion in the study.

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 with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 May 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	22 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	17
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Thirty patients from 17 Spanish investigational centres were included in this study, with a maximum of four patients recruited by each of three centres.

Pre-assignment

Screening details:

Thirty patients were screened and all thirty were included in the study.

Period 1

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

Arms

Arm title	All Subjects
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Arm description:

Lanreotide Autogel 120mg

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:

Lanreotide Autogel 120 mg single deep subcutaneous (s.c.) injection every 4 week (28±5 days) intervals up to 23 doses

Number of subjects in period 1	All Subjects
Started	30
Completed	3
Not completed	27
Patient decision	1
Disease progression	21
Adverse Event	2
Death	1
Not Specified	1
Protocol deviation	1

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial
Reporting group description:	
Lanreotide Autogel 120 mg single deep subcutaneous (s.c.) injection every 4 week (28±5 days) intervals up to 23 doses	

Reporting group values	Overall Trial	Total	
Number of subjects	30	30	
Age categorical			
Units: Subjects			

Age continuous			
Intent-To-Treat (ITT) population are patients who have received at least one dose of lanreotide Autogel®.			
Units: years			
arithmetic mean	62.4		
standard deviation	± 10.3	-	
Gender categorical			
ITT population			
Units: Subjects			
Female	15	15	
Male	15	15	
Race			
ITT population			
Units: Subjects			
Caucasian	30	30	
Body Mass Index (BMI)			
ITT population			
Units: kg/m ²			
arithmetic mean	25.51		
standard deviation	± 5.64	-	
Longest diameter of the Target Lesions at baseline			
Units: cm			
arithmetic mean	11.46		
standard deviation	± 10.05	-	
Urinary 5-HIAA			
5-HIAA (5-hydroxyindole acetic acid)			
N=19			
Units: NA			
arithmetic mean	291.99		
standard deviation	± 462.52	-	

End points

End points reporting groups

Reporting group title	All Subjects
Reporting group description:	
Lanreotide Autogel 120mg	

Primary: Median time to disease progression

End point title	Median time to disease progression ^[1]
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End point description:

Time until disease progression according to the Response Evaluation Criteria in Solid Tumors (RECIST) 1.0 criteria. Disease progression was defined as the occurrence, while on treatment with lanreotide Autogel, of one or more new lesions; a $\geq 20\%$ increase in the sum of the maximum diameters of the "target lesions", taking as reference the lowest sum of maximum diameters recorded since the start of the study; or unequivocal progression of "nontarget lesions"

ITT population

End point type	Primary
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End point timeframe:

Time between study inclusion until disease progression (Up to Visit 24)

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: Data reported for single arm, due to system limitation, statistical analysis details cannot be reported

End point values	All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: Months				
median (confidence interval 95%)				
Progressive Disease	12.9 (7.9 to 16.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of reduction of the Serum Chromogranin A as compared to the baseline

End point title	Percentage of reduction of the Serum Chromogranin A as compared to the baseline
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End point description:

Patients with Normalised and/or Decrease $\geq 30\%$ in Serum Chromogranin A (CgA) Concentration at Each Visit

ITT population

Mc Nemar's Test p values: week 8 (Visit 3) = 0.0002, week 20 (Visit 6) = 0.0027, week 32 (Visit 9) = 0.0082, week 44 (Visit 12) = 0.0253, week 56 (Visit 15) = 0.0253, week 68 (Visit 18) = 0.0455, week

80 (Visit 21) = 0.0833 and week 92 (Visit 24) = 0.1573

End point type	Secondary
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End point timeframe:

At Baseline (Visit 0), week 8, 20, 32, 44, 56, 68, 80 and 92

End point values	All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage of subjects				
number (confidence interval 95%)				
At Visit 3	70.4 (53.1 to 87.6)			
At Visit 6	60.9 (40.9 to 80.8)			
At Visit 9	63.2 (41.5 to 84.8)			
At Visit 12	53.3 (28.1 to 78.6)			
At Visit 15	61.5 (35.1 to 88)			
At Visit 18	60 (29.6 to 90.4)			
At Visit 21	57.1 (20.5 to 93.8)			
At Visit 24	66.7 (13.3 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Factors Predictive of Tumour Growth Control for Cox regression

End point title	Factors Predictive of Tumour Growth Control for Cox regression
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End point description:

To identify the factors predictive of tumour growth control on treatment with lanreotide Autogel ®

ITT population

The values reported are Hazard ratio (95% confidence interval)

func (functionality)

Cox regression p values: Age = 0.8267, Sex = 0.7232, Presence or absence of tumour functionality = 0.0354, ECOG scale = 0.9453, Tumour origin - FOREGUT (REF:UNKNOWN) = 0.0809, Tumour origin - MIDGUT (REF:UNKNOWN) = 0.0323, Tumour origin - MIDGUT (REF:FOREGUT) = 0.4457, Time between tumour diagnosis and study inclusion = 0.2562, Ki-67 index rank = 0.0890, Initial tumour mass = 0.3639, Previous treatment of the tumour: Chemotherapy = 0.9019, Previous treatment of the tumour: Interferon = 0.8273, Previous treatment of the tumour: Radiotherapy = 0.7576, Previous treatment of the tumour: Somatostatin = 0.8946, Previous treatment of the tumour: Surgery = 0.9727, Lanreotide serum levels = 0.7470, CgA response (ref: Yes) = 0.5869

End point type	Secondary
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End point timeframe:

Duration between study inclusion and the date of the last assessment with a response at "stable

End point values	All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Hazard ratio				
number (confidence interval 95%)				
Age	0.995 (0.95 to 1.04)			
Sex (ref: MALE)	1.156 (0.52 to 2.59)			
Presence/absence-tumour func (ref: Functional)	2.529 (1.07 to 6)			
ECOG scale	1.03 (0.45 to 2.36)			
Tumour origin - FOREGUT (REF:UNKNOWN)	0.277 (0.07 to 1.17)			
Tumour origin - MIDGUT (REF:UNKNOWN)	0.198 (0.04 to 0.87)			
Tumour origin - MIDGUT (REF:FOREGUT)	0.713 (0.3 to 1.7)			
Time between tumour diagnosis and study inclusion	1 (1 to 1)			
Ki-67 index rank	1.096 (0.99 to 1.22)			
Initial tumour mass	1.019 (0.98 to 1.06)			
Previous treatment of tumour:Chemotherapy(ref:Yes)	1.054 (0.46 to 2.42)			
Previous treatment of tumour: Interferon(ref:Yes)	0.886 (0.3 to 2.64)			
Previous treatment of tumour:Radiotherapy(ref:Yes)	1.375 (0.18 to 10.4)			
Previous treatment of tumour:Somatostatin(ref:Yes)	0.934 (0.34 to 2.55)			
Previous treatment of tumour: Surgery(ref:Yes)	1.016 (0.42 to 2.47)			
Lanreotide serum levels	0.968 (0.79 to 1.18)			
CgA response (ref: Yes)	0.772 (0.3 to 1.96)			

Statistical analyses

No statistical analyses for this end point

Secondary: Factors Predictive of Progression Free Survival for Cox regression

End point title	Factors Predictive of Progression Free Survival for Cox regression
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End point description:

To identify the factors predictive of PFS on treatment with lanreotide Autogel ®

ITT population

The values reported are Hazard ratio (95% confidence interval)

func (functionality)

Cox regression p values: Age = 0.3669, Sex = 0.4633, Presence or absence of tumour functionality = 0.1214, ECOG scale = 0.1961, Time between tumour diagnosis and study inclusion = 0.3968, Ki-67 index rank = 0.0178, Initial tumour mass = 0.9933, Previous treatment of the tumour: Chemotherapy = 0.3175, Previous treatment of the tumour: Interferon = 0.7742, Previous treatment of the tumour: Radiotherapy = 0.7733, Previous treatment of the tumour: Somatostatin = 0.8288, Previous treatment of the tumour: Surgery = 0.9416, Lanreotide serum levels = 0.5550, CgA response (ref: Yes) = 0.9959, Tumour origin - FOREGUT (REF:UNKNOWN) = 0.1457, Tumour origin - MIDGUT (REF:UNKNOWN) = 0.0694, Tumour origin - MIDGUT (REF:FOREGUT) = 0.5111

End point type	Secondary
End point timeframe:	
Duration between study inclusion and the date of disease progression (Up to Visit 24)	

End point values	All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Hazard ratio				
number (confidence interval 95%)				
Age	0.981 (0.94 to 1.02)			
Sex (ref: MALE)	0.718 (0.3 to 1.74)			
Presence/absence of tumour func(ref: Functional)	2.036 (0.83 to 5.01)			
ECOG scale	1.659 (0.77 to 3.57)			
Tumour origin - FOREGUT (REF:UNKNOWN)	0.352 (0.09 to 1.44)			
Tumour origin - MIDGUT (REF:UNKNOWN)	0.257 (0.06 to 1.11)			
Tumour origin - MIDGUT (REF:FOREGUT)	0.73 (0.29 to 1.87)			
Time between tumour diagnosis and study inclusion	1 (1 to 1)			
Ki-67 index rank	1.17 (1.03 to 1.33)			
Initial tumour mass	1 (0.95 to 1.05)			
Previous treatment tumour:Chemotherapy (ref: Yes)	1.623 (0.63 to 4.2)			
Previous treatment tumour:Interferon (ref: Yes)	0.852 (0.29 to 2.54)			
Previous treatment tumour:Radiotherapy (ref:Yes)	1.347 (0.18 to 10.2)			
Previous treatment tumour:Somatostatin (ref:Yes)	0.886 (0.3 to 2.64)			
Previous treatment tumour:Surgery (ref:Yes)	0.965 (0.37 to 2.49)			
Lanreotide serum levels	0.933 (0.74 to 1.18)			
CgA response (ref: Yes)	1.003 (0.38 to 2.63)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Partial or Complete Response of the Tumoural Lesions

End point title	Number of subjects with Partial or Complete Response of the Tumoural Lesions
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End point description:

ITT population

Complete response (CR): Disappearance of all "target lesions" and "nontarget lesions", and normalisation of tumour marker concentrations.

Partial response (PR): A reduction of at least 30% of the sum of maximum diameters of the "target lesions" taking as reference the baseline maximum diameters, and/or disappearance of all the "target lesions" with persistence of one or more "nontarget lesions" and/or tumour markers over the limits of the disease.

End point type	Secondary
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End point timeframe:

Up to Visit 24 (Week 92)

End point values	All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Number of subjects				
Partial Response	0			
Complete Response	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline of sum of the Longest Diameter of the target lesions

End point title	Mean Change from Baseline of sum of the Longest Diameter of the target lesions
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End point description:

ITT population

End point type	Secondary
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End point timeframe:

At Baseline (Visit 0), week 8, 20, 32, 44, 56, 68, 80 and 92

End point values	All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: cm				
arithmetic mean (standard deviation)				
Week 8 (N=27)	0.14 (± 1.06)			
Week 20 (n=23)	0.34 (± 2.02)			
Week 32 (N=19)	-0.25 (± 1.36)			
Week 44 (N=15)	-0.19 (± 1.9)			
Week 56 (N=12)	-0.31 (± 0.78)			
week 68 (N=11)	-0.17 (± 0.52)			
Week 80 (N=7)	0.6 (± 1.31)			
Week 92 (N=3)	-0.2 (± 0.17)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline of Maximum Decrease or Minimum Increase of the Longest Diameter of the target lesions

End point title	Mean change from Baseline of Maximum Decrease or Minimum Increase of the Longest Diameter of the target lesions
End point description:	
ITT population	
End point type	Secondary
End point timeframe:	
At Baseline (Visit 0) and week 92 (visit 24)	

End point values	All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: cm				
arithmetic mean (standard deviation)				
MAXIMUM DECREASE OR MINIMUM INCREASE FROM BASELINE	-0.35 (± 1.58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage Change from Baseline of Other Tumour Markers: Urinary 5-HIAA

End point title	Mean Percentage Change from Baseline of Other Tumour Markers: Urinary 5-HIAA
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End point description:

ITT population

5-HIAA (5- hydroxyindole acetic acid)

Student's test values: week 8 (Visit 3) = 0.0006, week 20 (Visit 6) = 0.0005, week 56 (Visit 15) = 0.0220, week 68 (Visit 18) = 0.5820;

Wilcoxon's test values: week 32 (Visit 9) = 0.4697, week 44 (Visit 12) = 0.3223;

Within-group test Not done at week 80 (Visit 21) and week 92 (Visit 24)

End point type	Secondary
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End point timeframe:

At Baseline (Visit 0), week 8, 20, 32, 44, 56, 68, 80 and 92

End point values	All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage change				
arithmetic mean (standard deviation)				
Week 8 (N=17)	-30.1 (± 29.3)			
Week 20 (N=12)	-33.8 (± 24.4)			
Week 32 (N=12)	-9.6 (± 66.9)			
Week 44 (N=10)	-11.4 (± 63.1)			
Week 56 (N=8)	-36.6 (± 35.3)			
week 68 (N=8)	-10.9 (± 53.5)			
Week 80 (N=6)	-34.8 (± 46.9)			
Week 92 (N=3)	-62.9 (± 16.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Mean And Change in Mean of QLQ-C30 by Five Functional Scale

End point title	Baseline Mean And Change in Mean of QLQ-C30 by Five Functional Scale
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End point description:

The QLQ-C30 is composed of both multi-item scales and single item measures. These include five functional scales (physical [PF], role [RF], emotional [EF], cognitive [CF] and social [SF])

QLQ-C30 (Quality of Life Questionnaire)

ITT population

End point type	Secondary
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End point timeframe:

At Baseline (Visit 0), week 8, 20, 32, 44, 56, 68, 80 and 92

End point values	All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Physical Functioning: Baseline (N=27)	90.37 (± 12.59)			
Physical Functioning: Week 8 (N=15)	-4.22 (± 15.14)			
Physical Functioning: Week 20 (N=15)	-8.89 (± 22.35)			
Physical Functioning: Week 32 (N=11)	0.61 (± 3.6)			
Physical Functioning: Week 44 (N=9)	0.74 (± 5.21)			
Physical Functioning: Week 56 (N=8)	4.17 (± 7.07)			
Physical Functioning: Week 68 (N=8)	0.83 (± 6.61)			
Physical Functioning: Week 80 (N=3)	-8.89 (± 15.4)			
Physical Functioning: Week 92 (N=1)	0 (± 0)			
Role Functioning: Baseline (N=27)	87.04 (± 21.35)			
Role Functioning: Week 8 (N=15)	1.11 (± 14.73)			
Role Functioning: Week 20 (N=15)	2.22 (± 12.39)			
Role Functioning: Week 32 (N=11)	6.06 (± 15.41)			
Role Functioning: Week 44 (N=9)	5.56 (± 16.67)			
Role Functioning: Week 56 (N=8)	2.08 (± 5.89)			
Role Functioning: Week 68 (N=8)	-6.25 (± 12.4)			
Role Functioning: Week 80 (N=3)	-22.22 (± 38.49)			
Role Functioning: Week 92 (N=1)	0 (± 0)			
Cognitive Functioning: Baseline (N=28)	84.52 (± 22.19)			
Cognitive Functioning: Week 8 (N=16)	3.13 (± 23.74)			
Cognitive Functioning: Week 20 (N=16)	-6.25 (± 17.08)			
Cognitive Functioning: Week 32 (N=11)	0 (± 16.67)			
Cognitive Functioning: Week 44 (N=10)	1.67 (± 18.34)			
Cognitive Functioning: Week 56 (N=9)	1.85 (± 26.93)			
Cognitive Functioning: Week 68 (N=9)	7.41 (± 23.73)			
Cognitive Functioning: Week 80 (N=4)	8.33 (± 28.87)			
Cognitive Functioning: Week 92 (N=1)	0 (± 0)			
Emotional Functioning: Baseline (N=28)	72.02 (± 26.47)			
Emotional Functioning: Week 8 (N=16)	4.69 (± 21.29)			
Emotional Functioning: Week 20 (N=16)	3.65 (± 28.86)			
Emotional Functioning: Week 32 (N=11)	3.03 (± 15.49)			
Emotional Functioning: Week 44 (N=10)	8.33 (± 23.57)			
Emotional Functioning: Week 56 (N=9)	11.11 (± 17.68)			
Emotional Functioning: Week 68 (N=9)	1.85 (± 35.79)			
Emotional Functioning: Week 80 (N=4)	22.92 (± 29.17)			
Emotional Functioning: Week 92 (N=1)	8.33 (± 0)			

Social Functioning: Baseline (N=28)	90.48 (± 17.23)			
Social Functioning: Week 8 (N=16)	-1.04 (± 21.49)			
Social Functioning: Week 20 (N=16)	0 (± 20.18)			
Social Functioning: Week 32 (N=11)	-7.58 (± 20.23)			
Social Functioning: Week 44 (N=10)	-10 (± 14.05)			
Social Functioning: Week 56 (N=9)	-5.56 (± 20.41)			
Social Functioning: Week 68 (N=9)	-7.41 (± 26.5)			
Social Functioning: Week 80 (N=4)	4.17 (± 20.97)			
Social Functioning: Week 92 (N=1)	0 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Mean And Change in Mean of QLQ-C30 Three Symptom Scale

End point title	Baseline Mean And Change in Mean of QLQ-C30 Three Symptom Scale
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End point description:

The QLQ-C30 is composed of both multi-item scales and single item measures. These include three symptom scales (fatigue [FA], nausea and vomiting[NV], and pain [PA]).

QLQ-C30 (Quality of Life Questionnaire)

ITT population

End point type	Secondary
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End point timeframe:

At Baseline (Visit 0), week 8, 20, 32, 44, 56, 68, 80 and 92

End point values	All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Fatigue: Baseline (N=27)	16.46 (± 19.09)			
Fatigue: Week 8 (N=15)	5.93 (± 17.75)			
Fatigue: Week 20 (N=15)	2.96 (± 17.04)			
Fatigue: Week 32 (N=11)	5.05 (± 12.54)			
Fatigue: Week 44 (N=9)	6.17 (± 14.81)			
Fatigue: Week 56 (N=8)	-2.78 (± 23.57)			
Fatigue: Week 68 (N=8)	19.44 (± 27.7)			
Fatigue: Week 80 (N=3)	7.41 (± 12.83)			
Fatigue: Week 92 (N=1)	0 (± 0)			
Nausea And Vomiting: Baseline (N=28)	9.52 (± 20.5)			

Nausea And Vomiting: Week 8 (N=16)	-6.25 (± 17.08)			
Nausea And Vomiting: Week 20 (N=16)	-3.13 (± 12.5)			
Nausea And Vomiting: Week 32 (N=11)	0 (± 0)			
Nausea And Vomiting: Week 44 (N=10)	0 (± 0)			
Nausea And Vomiting: Week 56 (N=9)	-5.56 (± 23.57)			
Nausea And Vomiting: Week 68 (N=9)	-7.41 (± 22.22)			
Nausea And Vomiting: Week 80 (N=4)	-16.67 (± 33.33)			
Nausea And Vomiting: Week 92 (N=1)	0 (± 0)			
Pain Scale: Baseline (N=28)	20.24 (± 26.59)			
Pain Scale: Week 8 (N=16)	6.25 (± 30.35)			
Pain Scale: Week 20 (N=16)	2.08 (± 17.08)			
Pain Scale: Week 32 (N=11)	0 (± 16.67)			
Pain Scale: Week 44 (N=10)	8.33 (± 25.15)			
Pain Scale: Week 56 (N=9)	-5.56 (± 22.05)			
Pain Scale: Week 68 (N=9)	3.7 (± 34.13)			
Pain Scale: Week 80 (N=4)	-16.67 (± 30.43)			
Pain Scale: Week 92 (N=1)	-33.33 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Mean And Change in Mean of QLQ-C30 Six Single Scale

End point title	Baseline Mean And Change in Mean of QLQ-C30 Six Single Scale
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End point description:

The QLQ-C30 is composed of both multi-item scales and single item measures. These include six single items (dyspnoea [DY], insomnia/sleep disturbance [SL], appetite loss [AP], constipation [CO], diarrhoea [DI] and financial difficulties [FI]).

QLQ-C30 (Quality of Life Questionnaire)

ITT population

End point type	Secondary
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End point timeframe:

At Baseline (Visit 0), week 8, 20, 32, 44, 56, 68, 80 and 92

End point values	All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Dyspnoea: Baseline (N=27)	1.23 (± 6.42)			

Dyspnoea: Week 8 (N=15)	4.44 (± 11.73)			
Dyspnoea: Week 20 (N=15)	4.44 (± 11.73)			
Dyspnoea: Week 32 (N=11)	3.03 (± 10.05)			
Dyspnoea: Week 44 (N=9)	0 (± 0)			
Dyspnoea: Week 56 (N=8)	0 (± 0)			
Dyspnoea: Week 68 (N=8)	0 (± 0)			
Dyspnoea: Week 80 (N=3)	22.22 (± 38.49)			
Dyspnoea: Week 92 (N=1)	0 (± 0)			
Insomnia: Baseline (N=27)	25.93 (± 33.76)			
Insomnia: Week 8 (N=15)	6.67 (± 18.69)			
Insomnia: Week 20 (N=15)	-2.22 (± 23.46)			
Insomnia: Week 32 (N=11)	0 (± 29.81)			
Insomnia: Week 44 (N=9)	11.11 (± 16.67)			
Insomnia: Week 56 (N=8)	16.67 (± 25.2)			
Insomnia: Week 68 (N=8)	16.67 (± 30.86)			
Insomnia: Week 80 (N=3)	0 (± 0)			
Insomnia: Week 92 (N=1)	0 (± 0)			
Appetite Loss: Baseline (N=27)	8.64 (± 19.81)			
Appetite Loss: Week 8 (N=15)	11.11 (± 24.12)			
Appetite Loss: Week 20 (N=15)	8.89 (± 19.79)			
Appetite Loss: Week 32 (N=11)	3.03 (± 10.05)			
Appetite Loss: Week 44 (N=9)	7.41 (± 22.22)			
Appetite Loss: Week 56 (N=8)	-4.17 (± 11.79)			
Appetite Loss: Week 68 (N=8)	8.33 (± 29.55)			
Appetite Loss: Week 80 (N=3)	-11.11 (± 19.25)			
Appetite Loss: Week 92 (N=1)	0 (± 0)			
Cosntipation Scale: Baseline (N=28)	9.52 (± 19.99)			
Cosntipation Scale: Week 8 (N=16)	12.5 (± 36.26)			
Cosntipation Scale: Week 20 (N=16)	6.25 (± 13.44)			
Cosntipation Scale: Week 32 (N=11)	-6.06 (± 13.48)			
Cosntipation Scale: Week 44 (N=10)	-6.67 (± 14.05)			
Cosntipation Scale: Week 56 (N=9)	-3.7 (± 20.03)			
Cosntipation Scale: Week 68 (N=9)	-11.11 (± 23.57)			
Cosntipation Scale: Week 80 (N=4)	-16.67 (± 33.33)			
Cosntipation Scale: Week 92 (N=1)	33.33 (± 0)			
Diarrhoea Scale: Baseline (N=28)	27.38 (± 30.16)			
Diarrhoea Scale: Week 8 (N=16)	-10.42 (± 20.07)			
Diarrhoea Scale: Week 20 (N=16)	-6.25 (± 38.91)			
Diarrhoea Scale: Week 32 (N=11)	-6.06 (± 29.13)			
Diarrhoea Scale: Week 44 (N=10)	-3.33 (± 18.92)			

Diarrhoea Scale: Week 56 (N=9)	-7.41 ($\pm$ 22.22)			
Diarrhoea Scale: Week 68 (N=9)	7.41 ($\pm$ 22.22)			
Diarrhoea Scale: Week 80 (N=4)	0 ($\pm$ 38.49)			
Diarrhoea Scale: Week 92 (N=1)	33.33 ($\pm$ 0)			
Financial Difficulties: Baseline (N=28)	8.33 ($\pm$ 23.35)			
Financial Difficulties: Week 8 (N=16)	-2.08 ($\pm$ 30.96)			
Financial Difficulties: Week 20 (N=16)	-10.42 ($\pm$ 26.44)			
Financial Difficulties: Week 32 (N=11)	0 ($\pm$ 0)			
Financial Difficulties: Week 44 (N=10)	3.33 ($\pm$ 18.92)			
Financial Difficulties: Week 56 (N=9)	0 ($\pm$ 28.87)			
Financial Difficulties: Week 68 (N=9)	11.11 ($\pm$ 37.27)			
Financial Difficulties: Week 80 (N=4)	16.67 ($\pm$ 33.33)			
Financial Difficulties: Week 92 (N=1)	0 ($\pm$ 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Mean And Change in Mean of QLQ-C30 Global Quality Of Life Scale

End point title	Baseline Mean And Change in Mean of QLQ-C30 Global Quality Of Life Scale
End point description: The QLQ-C30 is composed of both multi-item scales and single item measures.	
ITT population	
End point type	Secondary
End point timeframe: At Baseline (Visit 0), week 8, 20, 32, 44, 56, 68, 80 and 92	

End point values	All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Global Health Status: Baseline (N=28)	69.05 ($\pm$ 22.32)			
Global Health Status: Week 8 (N=16)	1.56 ($\pm$ 18.06)			
Global Health Status: Week 20 (N=16)	2.6 ($\pm$ 22.92)			
Global Health Status: Week 32 (N=11)	-4.55 ($\pm$ 19.49)			
Global Health Status: Week 44 (N=10)	2.5 ($\pm$ 15.24)			
Global Health Status: Week 56 (N=9)	8.33 ($\pm$ 17.18)			
Global Health Status: Week 68 (N=9)	-19.44 ($\pm$ 26.68)			

Global Health Status: Week 80 (N=4)	6.25 ($\pm$ 14.23)			
Global Health Status: Week 92 (N=1)	0 ($\pm$ 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Symptomatic Control related to Neuroendocrine Tumours During The Treatment Period

End point title	Number of Subjects With Symptomatic Control related to Neuroendocrine Tumours During The Treatment Period
End point description: Evaluation of the symptom control	
ITT population	
NET (Neuroendocrine tumours)	
End point type	Secondary
End point timeframe: Up to Visit 24 (Week 92)	

End point values	All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Number of subjects				
Symptoms related to NET	6			
Diarrhoea	6			
Asthenia	1			
Flushes	1			
Suffocations with tachycardia	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to visit 24

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	11.1
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Reporting groups

Reporting group title	All Subjects
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Reporting group description:

Safety population: includes all patients who have received at least one dose of Somatuline Autogel® (same definition as ITT population)

Serious adverse events	All Subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 30 (20.00%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	2		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	1 / 1		
Hepatobiliary disorders			
Gallbladder fistula			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	1 / 1		
Skin and subcutaneous tissue disorders			
Skin ulcer			

subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 30 (3.33%)		
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	All Subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 30 (83.33%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	7		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	8 / 30 (26.67%)		
occurrences (all)	20		
Injection site pain			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	8		
Injection site nodule			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Blood and lymphatic system disorders			

Anaemia subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 4		
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	13 / 30 (43.33%) 30		
Abdominal pain subjects affected / exposed occurrences (all)	4 / 30 (13.33%) 7		
Flatulence subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 3		
Constipation subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 3		
Vomiting subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Skin and subcutaneous tissue disorders			
Pruritus subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 3		
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 6		
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 3		
Arthralgia subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 30 (13.33%) 4		
Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 February 2006	Two new centers has been incorporated. To do faster the procedure to assign randomization codes to radiological copies.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported