# 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 |

**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 |

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/m2 | | | |
| 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] |
|---|---|

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 ≥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 |
|---|---|

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 |
|---|---|

End point description:

Patients with Normalised and/or Decrease ≥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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

End point description:

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: 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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |

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 |

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 (± 22.22) | | | |
| Diarrhoea Scale: Week 68 (N=9) | 7.41 (± 22.22) | | | |
| Diarrhoea Scale: Week 80 (N=4) | 0 (± 38.49) | | | |
| Diarrhoea Scale: Week 92 (N=1) | 33.33 (± 0) | | | |
| Financial Difficulties: Baseline (N=28) | 8.33 (± 23.35) | | | |
| Financial Difficulties: Week 8 (N=16) | -2.08 (± 30.96) | | | |
| Financial Difficulties: Week 20 (N=16) | -10.42 (± 26.44) | | | |
| Financial Difficulties: Week 32 (N=11) | 0 (± 0) | | | |
| Financial Difficulties: Week 44 (N=10) | 3.33 (± 18.92) | | | |
| Financial Difficulties: Week 56 (N=9) | 0 (± 28.87) | | | |
| Financial Difficulties: Week 68 (N=9) | 11.11 (± 37.27) | | | |
| Financial Difficulties: Week 80 (N=4) | 16.67 (± 33.33) | | | |
| Financial Difficulties: 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 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 (± 22.32) | | | |
| Global Health Status: Week 8 (N=16) | 1.56 (± 18.06) | | | |
| Global Health Status: Week 20 (N=16) | 2.6 (± 22.92) | | | |
| Global Health Status: Week 32 (N=11) | -4.55 (± 19.49) | | | |
| Global Health Status: Week 44 (N=10) | 2.5 (± 15.24) | | | |
| Global Health Status: Week 56 (N=9) | 8.33 (± 17.18) | | | |
| Global Health Status: Week 68 (N=9) | -19.44 (± 26.68) | | | |

| | | | | |
|---|---|---|---|---|
| Global Health Status: Week 80 (N=4) | 6.25 (± 14.23) | | | |
| Global Health Status: Week 92 (N=1) | 0 (± 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 |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 11.1 |

| Reporting groups | |
|---|---|
| Reporting group title | All Subjects |

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

| | | | |
|---|---|---|---|
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 4 / 30 (13.33%)<br>4 | | |
| Metabolism and nutrition disorders<br>Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all) | 3 / 30 (10.00%)<br>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.<br>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