Clinical trial results:
A PHASE II, MULTICENTRE, RANDOMIZED CONTROLLED STUDY EVALUATING THE QUALITY OF LIFE IN PATIENTS WITH INOPERABLE MALIGNANT BOWEL OBSTRUCTION TREATED WITH LANREOTIDE AUTOGEL 120 MG IN COMBINATION WITH STANDARD CARE VS. STANDARD CARE ALONE (QOL IN IMBO STUDY)

Summary

EudraCT number	2013-003176-12
Trial protocol	IT
Global end of trial date	16 January 2018

Results information

Result version number	v1 (current)
This version publication date	29 June 2019
First version publication date	29 June 2019

Trial information

Trial identification

Sponsor protocol code	A-93-52030-279

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02365584
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ipsen SpA
Sponsor organisation address	Via del Bosco Rinnovato, 6, Milano Fiori Nord, Palazzo U7, Milano, Italy, 20090 Assago
Public contact	Medical Director, Ipsen SpA, clinical.trials@ipsen.com
Scientific contact	Medical Director, Ipsen SpA, 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	16 January 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 January 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the impact on Quality of Life (Edmonton Symptom Assessment System [ESAS] total score) of lanreotide Autogel 120 milligrams (mg) in combination with standard care, in comparison to standard care alone, in patients affected by inoperable malignant bowel obstruction.

Protection of trial subjects:

The study was conducted under the provisions of the Declaration of Helsinki, in accordance with the International Conference on Harmonisation Consolidated Guideline on Good Clinical Practice and in compliance with Independent Ethics Committees / Institutional Review Boards and informed consent regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 January 2015
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	Italy: 43
Worldwide total number of subjects	43
EEA total number of subjects	43

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)	29
From 65 to 84 years	12
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Recruitment to this prospective, randomised, parallel arm, open-label study began on 14 Jan 2015. Patients with a documented diagnosis of inoperable malignant bowel obstruction who had a nasogastric tube (NGT) or presented with ≥ 3 vomiting episodes/day in the last consecutive 48 hours at time of enrolment were recruited to 14 centres in Italy.

Pre-assignment

Screening details:

Overall, 43 patients were enrolled and treated in this phase II study. Planned study period duration was 28 days.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Standard Care

Arm description:

Patients received standard care only according to site clinical practice.

Arm type	Standard Care

No investigational medicinal product assigned in this arm

Arm title	Standard Care + Lanreotide Autogel

Arm description:

Patients received standard care according to site clinical practice and a single administration of Lanreotide Autogel 120 mg by deep subcutaneous injection on Day 1.

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

Dosage and administration details:

Lanreotide Autogel was administered by deep subcutaneous injection in the upper outer quadrant of the buttock. Administration of Lanreotide Autogel was to occur in conjunction with or on the same day of standard care therapy administration. The administrations were supervised by the Investigator, or designee.

Number of subjects in period 1	Standard Care	Standard Care + Lanreotide Autogel
Started	21	22
Completed	9	8
Not completed	12	14
Consent withdrawn by subject	1	-
Adverse event, non-fatal	2	2

Disease Progression	9	12

Baseline characteristics

Reporting groups	
Reporting group title	Standard Care
Reporting group description:	
Patients received standard care only according to site clinical practice.	
Reporting group title	Standard Care + Lanreotide Autogel
Reporting group description:	
Patients received standard care according to site clinical practice and a single administration of Lanreotide Autogel 120 mg by deep subcutaneous injection on Day 1.	

Reporting group values	Standard Care	Standard Care + Lanreotide Autogel	Total
Number of subjects	21	22	43
Age categorical Units: Subjects			
Age continuous Units: Years arithmetic mean standard deviation	 61.8 ± 9.6	 62.8 ± 12.3	 -
Gender categorical Units: Subjects			
Female	14	19	33
Male	7	3	10
Race/Ethnicity, Customized Units: Subjects			
Caucasian / White	21	22	43

End points

End points reporting groups

Reporting group title	Standard Care
Reporting group description:	
Patients received standard care only according to site clinical practice.	
Reporting group title	Standard Care + Lanreotide Autogel
Reporting group description:	
Patients received standard care according to site clinical practice and a single administration of Lanreotide Autogel 120 mg by deep subcutaneous injection on Day 1.	

Primary: Mean Area Under Curve (AUC) of Edmonton Symptom Assessment System (ESAS) Total Scores Collected for the First 7 Days; Full Analysis Set (FAS)

End point title	Mean Area Under Curve (AUC) of Edmonton Symptom Assessment System (ESAS) Total Scores Collected for the First 7 Days; Full Analysis Set (FAS)
End point description:	
Quality of Life was assessed using ESAS, evaluating 9 common symptoms in cancer patients: pain, activity, nausea, depression, anxiety, drowsiness, appetite, well-being and shortness of breath. Symptom severity is rated 0-10 on a numerical scale (0=symptom absent; 10=worst severity). ESAS total score is sum of the 9 items (max score=90). Low scores indicate good quality of life; high scores indicate strong discomfort. Questionnaire assessments by the patient or by nurse/caregiver in case of patient's physical inability. AUC is area under the line which joins the points defined by plotting ESAS total score on vertical axis and time values on horizontal axis, computed using trapezoidal rule. Primary endpoint was analysed using the FAS which included all randomised patients who received study therapy, fulfilled the ESAS questionnaire at baseline and had ≥ 5 post-treatment assessments during first 7 days. Mean AUC of ESAS total scores during first 7 days is presented.	
End point type	Primary
End point timeframe:	
Baseline (Day 1, before randomisation), Days 2, 3, 4, 5, 6 and 7.	

End point values	Standard Care	Standard Care + Lanreotide Autogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: Scores on a scale x time (day)				
least squares mean (standard error)	179 (± 12.4)	190 (± 12.4)		

Statistical analyses

Statistical analysis title	ESAS AUC: treatment comparison
Statistical analysis description:	
Analysis of covariance (ANCOVA), where the AUC was the dependent and the independent was the baseline ESAS total score.	
Comparison groups	Standard Care v Standard Care + Lanreotide Autogel

Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.5396
Method	ANCOVA
Parameter estimate	Adjusted Least Square Mean Difference
Point estimate	-11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-47
upper limit	25
Variability estimate	Standard error of the mean
Dispersion value	17.7

Notes:

[1] - The assumptions required for the analysis of covariance (ANCOVA) were to be tested as follows:
• The equality of variances was to verified using the Levene's test. If it was significant AUC values were to be properly transformed.
• The linear relationship of AUC with the basal total score within treatment group was to be tested by a regression analysis.
• The parallelism of the regression lines between groups and the slope non zero value with the appropriate F tests.

Secondary: Mean Change From Baseline in ESAS Total Score; FAS

End point title	Mean Change From Baseline in ESAS Total Score; FAS

End point description:

Quality of Life was assessed using ESAS, evaluating 9 common symptoms in cancer patients: pain, activity, nausea, depression, anxiety, drowsiness, appetite, well-being and shortness of breath. Symptom severity is rated 0-10 on a numerical scale (0=symptom absent; 10=worst severity). ESAS total score is sum of the 9 items (max score=90). Low scores indicate good quality of life; high scores indicate strong discomfort. Questionnaire assessments by the patient or by nurse/caregiver in case of patient's physical inability.
Secondary endpoints were analysed using the ITT population but to permit following the FAS which was used for primary endpoint analysis, ESAS total score results are reported for both the ITT and the FAS. Mean change from baseline of ESAS total score at Days 7, 14 and 28 is presented here for the FAS; a positive change indicates a worsening condition. 'n' in category title indicates number of patients analysed at each time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1, before randomisation) and Days 7, 14 and 28.

End point values	Standard Care	Standard Care + Lanreotide Autogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Change at Day 7 (n=18, 19)	-5.1 (± 15.7)	1.9 (± 18.4)		
Change at Day 14 (n=16, 14)	-1.3 (± 21.4)	-7.3 (± 16.7)		
Change at Day 28 (n=8, 8)	-6.8 (± 15.2)	-10.3 (± 16.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in ESAS Total Score; Intention To Treat (ITT) Population

End point title	Mean Change From Baseline in ESAS Total Score; Intention To Treat (ITT) Population

End point description:

Quality of Life was assessed using ESAS, evaluating 9 common symptoms in cancer patients: pain, activity, nausea, depression, anxiety, drowsiness, appetite, well-being and shortness of breath. Symptom severity is rated 0-10 on a numerical scale (0=symptom absent; 10=worst severity). ESAS total score is sum of the 9 items (max score=90). Low scores indicate good quality of life; high scores indicate strong discomfort. Questionnaire assessments by the patient or by nurse/caregiver in case of patient's physical inability.
Secondary endpoints were analysed using the ITT population but to permit following the FAS which was used for primary endpoint analysis, ESAS total score results are reported for both the ITT and the FAS. Mean change from baseline of ESAS total score at Days 7, 14 and 28 is presented here for the ITT population (all randomised patients); a positive change indicates a worsening condition. 'n' in category title indicates number of patients analysed at each time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1, before randomisation) and Days 7, 14 and 28.

End point values	Standard Care	Standard Care + Lanreotide Autogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	22		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Change at Day 7 (n=18, 20)	-5.1 (± 15.7)	1.5 (± 18.1)		
Change at Day 14 (n=16, 14)	-1.3 (± 21.4)	-7.3 (± 16.7)		
Change at Day 28 (n=8, 8)	-6.8 (± 15.2)	-10.3 (± 16.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Single ESAS Items Symptom Scores; ITT Population

End point title	Mean Change From Baseline in Single ESAS Items Symptom Scores; ITT Population

End point description:

Quality of Life was assessed using ESAS, evaluating 9 common symptoms in cancer patients: pain, activity, nausea, depression, anxiety, drowsiness, appetite, well-being and shortness of breath. Symptom severity is rated 0-10 on a numerical scale (0=symptom absent; 10=worst severity). Low scores indicate good quality of life; high scores indicate strong discomfort. Questionnaire assessments by the patient or by nurse/caregiver in case of patient's physical inability.
Mean change from baseline of each individual ESAS item score at Days 7, 14 and 28 is presented for the ITT population (all randomised patients); a positive change indicates a worsening condition. 'n' in category title indicates number of patients analysed at each time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1, before randomisation) and Days 7, 14 and 28.

End point values	Standard Care	Standard Care + Lanreotide Autogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	22		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Change at Day 7: Pain (n=18, 20)	-1.8 (± 3.6)	0.1 (± 3.4)		
Change at Day 14: Pain (n=16, 13)	-1.3 (± 3.6)	-1.9 (± 2.9)		
Change at Day 28: Pain (n=7, 6)	-3.0 (± 3.1)	-1.3 (± 4.2)		
Change at Day 7: Activity (n=18, 20)	-0.3 (± 2.6)	0.7 (± 2.6)		
Change at Day 14: Activity (n=16, 13)	-0.3 (± 3.3)	-0.7 (± 3.0)		
Change at Day 28: Activity (n=7, 6)	-1.4 (± 2.8)	-0.3 (± 3.2)		
Change at Day 7: Nausea (n=18, 20)	0.5 (± 3.2)	0.9 (± 3.2)		
Change at Day 14: Nausea (n=16, 13)	0.1 (± 3.8)	0.5 (± 4.1)		
Change at Day 28: Nausea (n=7, 6)	-0.6 (± 4.6)	0.0 (± 3.9)		
Change at Day 7: Depression (n=18, 20)	-1.8 (± 3.5)	-1.1 (± 3.7)		
Change at Day 14 Depression (n=16, 13)	-1.9 (± 3.5)	-2.4 (± 3.2)		
Change at Day 28: Depression (n=7, 6)	-2.6 (± 1.9)	-3.7 (± 4.0)		
Change at Day 7: Anxiety (n=18, 20)	0.0 (± 2.7)	-0.2 (± 3.2)		
Change at Day 14: Anxiety (n=16, 13)	0.4 (± 3.3)	-2.7 (± 3.8)		
Change at Day 28: Anxiety (n=7, 6)	-1.1 (± 1.9)	-1.5 (± 1.0)		
Change at Day 7: Drowsiness (n=18, 20)	-0.7 (± 2.7)	0.4 (± 3.1)		
Change at Day 14: Drowsiness (n=16, 13)	-0.1 (± 3.5)	-0.6 (± 2.6)		
Change at Day 28: Drowsiness (n=7, 6)	-1.9 (± 3.1)	-1.5 (± 1.5)		
Change at Day 7: Appetite (n=18, 20)	-0.2 (± 3.1)	0.5 (± 3.2)		
Change at Day 14: Appetite (n=16, 13)	0.9 (± 3.0)	0.4 (± 3.9)		
Change at Day 28: Appetite (n=7, 6)	0.4 (± 3.1)	-2.0 (± 2.3)		
Change at Day 7: Well-being (n=18, 20)	-0.8 (± 2.6)	-0.4 (± 3.1)		
Change at Day 14: Well-being (n=16, 13)	0.4 (± 2.5)	-0.5 (± 4.3)		
Change at Day 28: Well-being (n=7, 6)	0.4 (± 2.4)	-2.3 (± 2.9)		
Change at Day 7: Shortness of breath (n=18, 20)	-0.1 (± 2.3)	0.7 (± 2.6)		
Change at Day 14: Shortness of breath (n=16, 13)	0.6 (± 3.4)	0.7 (± 2.9)		

Change at Day 28: Shortness of breath (n=7, 6)	-0.4 (± 2.0)	-0.2 (± 3.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Performing General Activity (Karnofsky Performance Status [KPS]); ITT Population

End point title	Mean Change From Baseline in Performing General Activity (Karnofsky Performance Status [KPS]); ITT Population

End point description:

The KPS allows patients to be classified as to their functional impairment and was used to assess general activity. KPS scores range from 0 (dead) to 100 (normal/no disease) and are classified as 0-40 = unable to care for self; 50-70 = unable to work; 80-100 = able to work. The lower the KPS score, the worse the survival for most serious illnesses. Scores were recorded on the patient's medical file at each study visit (Days 1, 7, 14 and 28).
Mean change from baseline of KPS score at Days 7, 14 and 28 is presented for the ITT population (all randomised patients); a negative change indicates a worsening condition. 'n' in category title indicates number of patients analysed at each time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1, before randomisation) and Days 7, 14 and 28.

End point values	Standard Care	Standard Care + Lanreotide Autogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	22		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Change at Day 7 (n=18, 19)	-2.8 (± 12.3)	-3.7 (± 6.8)		
Change at Day 14 (n=16, 13)	-5.6 (± 11.5)	-5.4 (± 12.7)		
Change at Day 28 (n=8, 7)	-5.0 (± 16.0)	-7.1 (± 20.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Daily Intensity of Abdominal Pain Score (Visual Analogue Scale [VAS]); ITT Population

End point title	Mean Change From Baseline in Daily Intensity of Abdominal Pain Score (Visual Analogue Scale [VAS]); ITT Population

End point description:

Abdominal pain was assessed using the VAS numeric pain distress scale which is a 100-millimetre (10-centimetre) scoring scale on which patients mark their perceived level of pain. Scores range from 0 to 100 where 0=no pain and 100=unbearable pain. Higher scores indicate a worse outcome. Scores were

recorded on the Patient Diary daily until the end of study (Day 28), by the patient or filled in by the nurse/caregiver in case of patient's physical inability.
Mean change from baseline of VAS for abdominal pain at Days 7, 14 and 28 is presented for the ITT population (all randomised patients); a positive change indicates a worsening condition. 'n' in category title indicates number of patients analysed at each time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1, before randomisation) and Days 7, 14 and 28.

End point values	Standard Care	Standard Care + Lanreotide Autogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	22		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Change at Day 7 (n=19, 19)	-22.0 (± 32.5)	-9.6 (± 30.8)		
Change at Day 14 (n=16, 14)	-15.6 (± 34.9)	-27.7 (± 28.8)		
Change at Day 28 (n=7, 7)	-32.0 (± 31.5)	-17.0 (± 34.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients Experiencing ≤ 2 Vomiting Episodes/Day During at Least 3 Consecutive Days, in Patients Without NGT

End point title	Number of Patients Experiencing ≤ 2 Vomiting Episodes/Day During at Least 3 Consecutive Days, in Patients Without NGT

End point description:

Vomiting episodes and NGT presence were recorded on the Patient Diary daily until the end of study (Day 28), by the patient or filled in by the nurse/caregiver in case of patient's physical inability. Number of patients experiencing ≤ 2 vomiting episodes/day during at least 3 consecutive days, in patients without NGT, is presented for the ITT population (all randomised patients). Number of patients without NGT for each of the specified time points is also presented. Patients without NGT were defined as patients without the insertion of NGT for the whole study period.

End point type	Secondary

End point timeframe:

From Baseline (Day 1, before randomisation) to Days 7, 14 and 28.

End point values	Standard Care	Standard Care + Lanreotide Autogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	22		
Units: Participants				
From Day 1 to Day 7: ≤ 2 vomiting episodes/day	5	4		

From Day 1 to Day 7: patients without NGT	6	8		
From Day 1 to Day 14: ≤ 2 vomiting episodes/day	4	4		
From Day 1 to Day 14: patients without NGT	5	7		
From Day 1 to Day 28: ≤ 2 vomiting episodes/day	4	4		
From Day 1 to Day 28: patients without NGT	5	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Daily NGT Secretion Volume, in Patients With a NGT

End point title	Mean Daily NGT Secretion Volume, in Patients With a NGT

End point description:

NGT presence and related secretion volume were recorded on the Patient Diary daily until the end of study (Day 28), by the patient or filled in by the nurse/caregiver in case of patient's physical inability. Mean daily secretion volumes, in patients with NGT, is presented. Only in patients with NGT were included in the analysis (Standard Care arm: n=11, 15, 16 and 16 at Baseline, Days 7, 14 and 28, respectively; Standard Care + Lanreotide Autogel arm: n=14, 14, 15 and 15 at Baseline, Days 7, 14 and 28, respectively). 'n' in category title indicates number of patients with data available for analysis at each time point; 999999 denotes a data value as non-calculable.

End point type	Secondary

End point timeframe:

Baseline (Day 1, before randomisation) and Days 7, 14 and 28.

End point values	Standard Care	Standard Care + Lanreotide Autogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	22		
Units: millilitres				
arithmetic mean (standard deviation)				
Baseline (n=1, 2)	200.0 (± 999999)	700.0 (± 141.4)		
Day 7 (n=4, 2)	4875.0 (± 4023.6)	1025.0 (± 813.2)		
Day 14 (n=2, 6)	12675.0 (± 2863.8)	7090.8 (± 2433.9)		
Day 28 (n=10, 7)	27501.0 (± 27081.8)	18301.4 (± 11657.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Number of Daily Vomiting Episodes; ITT Population

End point title	Mean Change From Baseline in Number of Daily Vomiting Episodes; ITT Population

End point description:

Vomiting episodes were recorded on the Patient Diary daily until the end of study (Day 28), by the patient or filled in by the nurse/caregiver in case of patient's physical inability. Mean change from baseline in number of daily vomiting episodes for the periods Day 1 to Day 7, Day 1 to Day 14 and Day 1 to Day 28 is presented for the ITT population (all randomised patients). 'n' in category title indicates number of patients with data available for analysis at each time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1, before randomisation) and Days 7, 14 and 28.

End point values	Standard Care	Standard Care + Lanreotide Autogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	22		
Units: Episodes (daily)				
arithmetic mean (standard deviation)				
Change Day 1 to Day 7 (n=21, 20)	5.7 (± 6.2)	6.0 (± 9.9)		
Change Day 1 to Day 14 (n=21, 20)	10.6 (± 12.7)	10.4 (± 15.8)		
Change Day 1 to Day 28 (n=21, 20)	16.5 (± 19.9)	14.1 (± 20.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Passage of Stools; ITT Population

End point title	Assessment of Passage of Stools; ITT Population

End point description:

Passage of stools assessments (Yes/No) were recorded on the Patient Diary daily until the end of study (Day 28), by the patient or filled in by the nurse/caregiver in case of patient's physical inability.
The ITT population included all randomised patients.

End point type	Secondary

End point timeframe:

From Baseline (Day 1, before randomisation) to Day 28.

End point values	Standard Care	Standard Care + Lanreotide Autogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	22		
Units: Subjects				
Day 1: Yes	2	2		
Day 1: No	19	20		

Day 2: Yes	6	3		
Day 2: No	13	16		
Day 3: Yes	4	3		
Day 3: No	15	17		
Day 4: Yes	4	2		
Day 4: No	15	18		
Day 5: Yes	6	3		
Day 5: No	13	17		
Day 6: Yes	4	2		
Day 6: No	15	17		
Day 7: Yes	3	3		
Day 7: No	16	16		
Day 8: Yes	6	3		
Day 8: No	12	17		
Day 9: Yes	4	5		
Day 9: No	13	14		
Day 10: Yes	3	1		
Day 10: No	13	15		
Day 11: Yes	5	1		
Day 11: No	10	14		
Day 12: Yes	4	1		
Day 12: No	11	11		
Day 13: Yes	3	1		
Day 13: No	12	13		
Day 14: Yes	5	1		
Day 14: No	10	14		
Day 15: Yes	2	2		
Day 15: No	12	10		
Day 16: Yes	3	2		
Day 16: No	11	9		
Day 17: Yes	2	3		
Day 17: No	12	9		
Day 18: Yes	3	2		
Day 18: No	11	8		
Day 19: Yes	3	2		
Day 19: No	8	8		
Day 20: Yes	2	2		
Day 20: No	9	8		
Day 21: Yes	2	2		
Day 21: No	9	7		
Day 22: Yes	2	2		
Day 22: No	9	6		
Day 23: Yes	3	2		
Day 23: No	7	5		
Day 24: Yes	3	2		
Day 24: No	7	6		
Day 25: Yes	2	2		
Day 25: No	7	5		
Day 26: Yes	2	2		
Day 26: No	6	6		
Day 27: Yes	1	2		
Day 27: No	7	4		

Day 28: Yes	3	2		
Day 28: No	4	5		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From baseline (Day 1) until end of study (Day 28).	
Adverse event reporting additional description:	
Treatment emergent adverse events are reported for the safety population which included all patients who received at least one dose of study therapy.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Standard Care
Reporting group description:	
Patients received standard care only according to site clinical practice.	
Reporting group title	Standard Care + Lanreotide Autogel
Reporting group description:	
Patients received standard care according to site clinical practice and a single administration of Lanreotide Autogel 120 mg by deep subcutaneous injection on Day 1.	

Serious adverse events	Standard Care	Standard Care + Lanreotide Autogel	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 21 (9.52%)	2 / 22 (9.09%)	
number of deaths (all causes)	2	2	
number of deaths resulting from adverse events	2	2	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myocardial infarction			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	

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

Non-serious adverse events	Standard Care	Standard Care + Lanreotide Autogel	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 21 (23.81%)	5 / 22 (22.73%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 21 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 21 (9.52%)	1 / 22 (4.55%)	
occurrences (all)	2	1	
Infections and infestations			
Pharyngitis			
subjects affected / exposed	0 / 21 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	3 / 21 (14.29%)	0 / 22 (0.00%)	
occurrences (all)	3	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study was terminated early due to insufficient recruitment. As a consequence, the results of the analyses should be interpreted cautiously and no conclusions should be made.

Notes: