EU Clinical Trials Register

Clinical trial results:
A phase IIIb multicenter, open-label, single arm study to evaluate the efficacy and safety of pasireotide in patients with acromegaly inadequately controlled with first generation somatostatin analogues

Summary

EudraCT number	2014-002630-31
Trial protocol	HU BE PT IT FR BG
Global end of trial date	27 September 2018

Results information

Result version number	v1 (current)
This version publication date	12 October 2019
First version publication date	12 October 2019

Trial information

Trial identification

Sponsor protocol code	CSOM230C2413

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02354508
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma, AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Study Director, Novartis Pharma, AG, +41 613241111, novartis.email@novartis.com
Scientific contact	Study Director, Novartis Pharma, AG, +41 613241111, novartis.email@novartis.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 September 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of pasireotide LAR in patients with acromegaly who are inadequately controlled with maximal approved doses of currently available somatostatin analogues, as measured by the proportion of patients with GH <1μg/L and IGF-1 <ULN at week 36

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 March 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	Argentina: 1
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Brazil: 10
Country: Number of subjects enrolled	Bulgaria: 4
Country: Number of subjects enrolled	China: 7
Country: Number of subjects enrolled	Colombia: 2
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Malaysia: 4
Country: Number of subjects enrolled	Mexico: 22
Country: Number of subjects enrolled	Portugal: 7
Country: Number of subjects enrolled	Romania: 9
Country: Number of subjects enrolled	Turkey: 12
Worldwide total number of subjects	123
EEA total number of subjects	65

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)	115
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Planned 112 subjects and analyzed 123 subjects.

For Disposition/Baseline Characteristics Tables, TOTAL = subjects in the Pasireotide LAR arm.

Pre-assignment

Screening details:

Subjects were allocated to Group 1 or Group 2 based on previously received first generation Somatostatin analog (SSA).

Period 1

Period 1 title	Period 1 - Core Phase
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Lanreotide 120 mg

Arm description:

Participants were treated with lanreotide 120mg and assigned to Group 2 (before starting on Pasireotide in the Core phase).

Arm type	Experimental
Investigational medicinal product name	Pasireotide LAR
Investigational medicinal product code	SOM230
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

microparticles powder in vials containing nominally 40
and 60 mg of pasireotide (as free base) along with solvent for suspension for injection in ampules for the reconstitution of the LAR microparticles.

Arm title	Octreotide 30 mg

Arm description:

Participants were treated with octreotide 30 mg and assigned to Group 2 (before starting on Pasireotide in the Core phase). .

Arm type	Experimental
Investigational medicinal product name	Pasireotide LAR
Investigational medicinal product code	SOM230
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

microparticles powder in vials containing nominally 40
and 60 mg of pasireotide (as free base) along with solvent for suspension for injection in ampules for the reconstitution of the LAR microparticles.

Investigational medicinal product name	Octreotide 40 mg
Investigational medicinal product code	SMS995
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

40 mg Octreotide LAR used during the run-in phase for patients in Group 1 (Octreotide LAR 30 mg group)

Arm title	Octreotide 40 mg

Arm description:

Participants were treated with octreotide 40 mg and assigned to either Group 1 (if 40mg octreotide was approved in the country) or Group 2 if 40mg octreotide was not approved in the country (before starting on Pasireotide in the Core phase).

Arm type	Experimental
Investigational medicinal product name	Pasireotide LAR
Investigational medicinal product code	SOM230
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

microparticles powder in vials containing nominally 40
and 60 mg of pasireotide (as free base) along with solvent for suspension for injection in ampules for the reconstitution of the LAR microparticles.

Number of subjects in period 1	Lanreotide 120 mg	Octreotide 30 mg	Octreotide 40 mg
Started	41	29	53
Completed	39	27	47
Not completed	2	2	6
Consent withdrawn by subject	-	1	2
Adverse event, non-fatal	1	1	2
Unsatisfactory therapeutic effect	1	-	2

Period 2

Period 2 title	Period 2 - Extension Phase
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Lanreotide 120 mg

Arm description:

Participants were treated with lanreotide 120mg and assigned to Group 2 (before starting on Pasireotide in the Core phase).

Arm type	Experimental

Investigational medicinal product name	Pasireotide LAR
Investigational medicinal product code	SOM230
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

microparticles powder in vials containing nominally 40
and 60 mg of pasireotide (as free base) along with solvent for suspension for injection in ampules for
the reconstitution of the LAR microparticles.

Arm title	Octreotide 30 mg

Arm description:

Participants were treated with octreotide 30 mg and assigned to Group 2 (before starting on Pasireotide
in the Core phase). .

Arm type	Experimental
Investigational medicinal product name	Pasireotide LAR
Investigational medicinal product code	SOM230
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

microparticles powder in vials containing nominally 40
and 60 mg of pasireotide (as free base) along with solvent for suspension for injection in ampules for
the reconstitution of the LAR microparticles.

Investigational medicinal product name	Octreotide 40 mg
Investigational medicinal product code	SMS995
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

40 mg Octreotide LAR used during the run-in phase for patients in Group 1 (Octreotide LAR 30 mg
group)

Arm title	Octreotide 40 mg

Arm description:

Participants were treated with octreotide 40 mg and assigned to either Group 1 (if 40mg octreotide was
approved in the country) or Group 2 if 40mg octreotide was not approved in the country (before starting
on Pasireotide in the Core phase).

Arm type	Experimental
Investigational medicinal product name	Pasireotide LAR
Investigational medicinal product code	SOM230
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

microparticles powder in vials containing nominally 40
and 60 mg of pasireotide (as free base) along with solvent for suspension for injection in ampules for
the reconstitution of the LAR microparticles.

Number of subjects in period 2[1]	Lanreotide 120 mg	Octreotide 30 mg	Octreotide 40 mg
Started	26	23	39
Completed	20	19	36
Not completed	6	4	3
Physician decision	5	-	1
Consent withdrawn by subject	-	1	-
Unsatisfactory therapeutic effect	1	3	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: No statistical analysis was planned for this endpoint.

Period 3

Period 3 title	Period 3 - Post-treatment follow-up
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Lanreotide 120 mg

Arm description:

Participants were treated with lanreotide 120mg and assigned to Group 2 (before starting on Pasireotide in the Core phase).

Arm type	Experimental
Investigational medicinal product name	Pasireotide LAR
Investigational medicinal product code	SOM230
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

microparticles powder in vials containing nominally 40
and 60 mg of pasireotide (as free base) along with solvent for suspension for injection in ampules for the reconstitution of the LAR microparticles.

Arm title	Octreotide 30 mg

Arm description:

Participants were treated with octreotide 30 mg and assigned to Group 2 (before starting on Pasireotide in the Core phase). .

Arm type	Experimental
Investigational medicinal product name	Pasireotide LAR
Investigational medicinal product code	SOM230
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

microparticles powder in vials containing nominally 40
and 60 mg of pasireotide (as free base) along with solvent for suspension for injection in ampules for the reconstitution of the LAR microparticles.

Investigational medicinal product name	Octreotide 40 mg
Investigational medicinal product code	SMS995
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

40 mg Octreotide LAR used during the run-in phase for patients in Group 1 (Octreotide LAR 30 mg group)

Arm title	Octreotide 40 mg

Arm description:

Participants were treated with octreotide 40 mg and assigned to either Group 1 (if 40mg octreotide was approved in the country) or Group 2 if 40mg octreotide was not approved in the country (before starting on Pasireotide in the Core phase).

Arm type	Experimental
Investigational medicinal product name	Pasireotide LAR
Investigational medicinal product code	SOM230
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

microparticles powder in vials containing nominally 40
and 60 mg of pasireotide (as free base) along with solvent for suspension for injection in ampules for
the reconstitution of the LAR microparticles.

Number of subjects in period 3	Lanreotide 120 mg	Octreotide 30 mg	Octreotide 40 mg
Started	20	19	36
Completed	18	17	33
Not completed	4	3	3
Physician decision	3	-	1
Consent withdrawn by subject	-	1	-
Unsatisfactory therapeutic effect	1	2	2
Joined	2	1	0
followed for safety	2	1	-

Baseline characteristics

Reporting groups

Reporting group title	Lanreotide 120 mg
Reporting group description:	
Participants were treated with lanreotide 120mg and assigned to Group 2 (before starting on Pasireotide in the Core phase).	
Reporting group title	Octreotide 30 mg
Reporting group description:	
Participants were treated with octreotide 30 mg and assigned to Group 2 (before starting on Pasireotide in the Core phase). .	
Reporting group title	Octreotide 40 mg
Reporting group description:	
Participants were treated with octreotide 40 mg and assigned to either Group 1 (if 40mg octreotide was approved in the country) or Group 2 if 40mg octreotide was not approved in the country (before starting on Pasireotide in the Core phase).	

Reporting group values	Lanreotide 120 mg	Octreotide 30 mg	Octreotide 40 mg
Number of subjects	41	29	53
Age categorical			
Units: Subjects			
Adults (18-64 years)	40	28	47
From 65-84 years	1	1	6
Age Continuous			
Units: years			
arithmetic mean	41.8	41.6	46.6
standard deviation	± 10.02	± 12.89	± 11.63
Sex: Female, Male			
Units: Subjects			
Female	19	18	25
Male	22	11	28
Race/Ethnicity, Customized			
Units: Subjects			
Caucasian	34	14	30
Black	0	1	0
Asian	1	7	3
Native American	2	0	1
Other	4	7	19

Reporting group values	Total		
Number of subjects	123		
Age categorical			
Units: Subjects			
Adults (18-64 years)	115		
From 65-84 years	8		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		

Sex: Female, Male			
Units: Subjects			
Female	62		
Male	61		
Race/Ethnicity, Customized			
Units: Subjects			
Caucasian	78		
Black	1		
Asian	11		
Native American	3		
Other	30		

Subject analysis sets

Subject analysis set title	Pasireotide LAR overall
Subject analysis set type	Full analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg.

Subject analysis set title	Up-titrated to Pasireotide LAR 60 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the subset of participants in the FAS who started treatment with 40 mg pasireotide LAR in the core phase and were up-titrated to pasireotide LAR 60 mg.

Subject analysis set title	Pasireotide LAR overall
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg.

Subject analysis set title	Pasireotide LAR monotherapy
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received pasireotide LAR only

Subject analysis set title	Pasireotide with concomitant medication
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received pasireotide along with other concomitant medications.or octreotide 40 mg.

Subject analysis set title	Pasireotide LAR overall
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg.

Subject analysis set title	Up-titrated to Pasireotide LAR 60 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the subset of participants in the Extension FAS who started treatment with 40 mg pasireotide LAR in the extension phase and were up-titrated to pasireotide LAR 60 mg.

Subject analysis set title	Pasireotide LAR (run-in phase)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who were part of the run-in phase, i.e. group 1)

Subject analysis set title	GH: ≥ 1 - ≤ 2.5 µg/L at screening
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These Participants had this GH level at screening

Subject analysis set title	GH: > 2.5 µg/L at screening
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These Participants had this GH level at screening

Subject analysis set title	GH: Missing
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These Participants were missing GH levels at screening

Subject analysis set title	Pasireotide LAR overall
Subject analysis set type	Full analysis

Subject analysis set description:

This is the total sum of participants with at screening with various or missing GH levels

Subject analysis set title	Diabetic
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who were diabetic in the Pasireotide LAR overall group

Subject analysis set title	Pasireotide LAR overall - AcroQOL total scores
Subject analysis set type	Full analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg.

Subject analysis set title	Pasireotide LAR overall - AcroQOL physical sub-scores
Subject analysis set type	Full analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg

Subject analysis set title	Pasireotide LAR overall - AcroQOL psychological sub-scores
Subject analysis set type	Full analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg.

Subject analysis set title	Pasireotide LAR overall - AcroQOL psycho/appearance sub-scores
Subject analysis set type	Full analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg

Subject analysis set title	Pasireotide LAR overall-AcroQOL psycho/pers relatns sub-scores
Subject analysis set type	Full analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg

Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Headache
Subject analysis set type	Full analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg.

Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Fatigue
Subject analysis set type	Full analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg

Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Perspiration
Subject analysis set type	Full analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg.

Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Osteoarthralgia
Subject analysis set type	Full analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg

Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Paresthesiae
Subject analysis set type	Full analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg

Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Paresthsiae
Subject analysis set type	Full analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg

Subject analysis set title	Up-titrated to Pasireotide LAR 60 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the subset of participants in the FAS who started treatment with 40 mg pasireotide LAR in the core phase and were up-titrated to pasireotide LAR 60 mg.

Subject analysis set title	Pasireotide LAR overall
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These are the participants in the extension phase who received Pasireotide LAR

Subject analysis set title	Pasireotide LAR monotherapy
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These Participants were treated with pasireotide LAR only in the extension phase

Subject analysis set title	Pasireotide with concomitant mediaction
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These Participants were treated with pasireotide LAR as well as other concomitant medications in the extension phase

Subject analysis set title	Pasireotide LAR overall
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase

Subject analysis set title	Pasireotide LAR overall - AcroQOL total scores
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase

Subject analysis set title	Pasireotide LAR overall - AcroQOL physical sub-scores
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase

Subject analysis set title	Pasireotide LAR overall - AcroQOL psychological sub-scores
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase

Subject analysis set title	Pasireotide LAR overall - AcroQOL psycho/appearance sub-scores
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase

Subject analysis set title	Pasireotide LAR overall-AcroQOL psycho/pers relatns sub-scores
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase

Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Headache
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase

Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Fatigue
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase

Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Perspiration
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase

Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Osteoarthralgia
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase

Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Paresthesiae
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase

Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Paresthsiae
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase

Subject analysis set title	Pre-diabetic
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who were pre-diabetic in the Pasireotide LAR overall group

Subject analysis set title	Non-diabetic
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who were non-diabetic in the Pasireotide LAR overall group

Reporting group values	Pasireotide LAR overall	Up-titrated to Pasireotide LAR 60 mg	Pasireotide LAR overall
Number of subjects	123	90	102
Age categorical			
Units: Subjects			
Adults (18-64 years)			
From 65-84 years			
Age Continuous			
Units: years			
arithmetic mean	14.6	6.7	15.7
standard deviation	±	±	±
Sex: Female, Male			
Units: Subjects			
Female			
Male			
Race/Ethnicity, Customized			
Units: Subjects			
Caucasian			
Black			
Asian			
Native American			
Other			

Reporting group values	Pasireotide LAR monotherapy	Pasireotide with concomitant medication	Pasireotide LAR overall
Number of subjects	76	12	88
Age categorical			
Units: Subjects			
Adults (18-64 years)			
From 65-84 years			
Age Continuous			
Units: years			
arithmetic mean	17.1	0.0	14.8
standard deviation	±	±	±
Sex: Female, Male			
Units: Subjects			
Female			
Male			
Race/Ethnicity, Customized			
Units: Subjects			
Caucasian			
Black			
Asian			
Native American			
Other			

Reporting group values	Up-titrated to Pasireotide LAR 60 mg	Pasireotide LAR (run-in phase)	GH: ≥ 1 - ≤ 2.5 µg/L at screening
Number of subjects	70	17	28

Age categorical Units: Subjects			
Adults (18-64 years)			
From 65-84 years			
Age Continuous Units: years			
arithmetic mean	5.9		
standard deviation	±	±	±
Sex: Female, Male Units: Subjects			
Female			
Male			
Race/Ethnicity, Customized Units: Subjects			
Caucasian			
Black			
Asian			
Native American			
Other			

Reporting group values	GH: > 2.5 µg/L at screening	GH: Missing	Pasireotide LAR overall
Number of subjects	94	1	123
Age categorical Units: Subjects			
Adults (18-64 years)			
From 65-84 years			
Age Continuous Units: years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male Units: Subjects			
Female			
Male			
Race/Ethnicity, Customized Units: Subjects			
Caucasian			
Black			
Asian			
Native American			
Other			

Reporting group values	Diabetic	Pasireotide LAR overall - AcroQOL total scores	Pasireotide LAR overall - AcroQOL physical sub-scores
Number of subjects	52	123	123
Age categorical Units: Subjects			
Adults (18-64 years)			
From 65-84 years			

Age Continuous			
Units: years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male			
Units: Subjects			
Female			
Male			
Race/Ethnicity, Customized			
Units: Subjects			
Caucasian			
Black			
Asian			
Native American			
Other			

Reporting group values	Pasireotide LAR overall - AcroQOL psychological sub-scores	Pasireotide LAR overall - AcroQOL psycho/appearance sub-scores	Pasireotide LAR overall-AcroQOL psycho/pers relatns sub-scores
Number of subjects	123	123	123
Age categorical			
Units: Subjects			
Adults (18-64 years)			
From 65-84 years			
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male			
Units: Subjects			
Female			
Male			
Race/Ethnicity, Customized			
Units: Subjects			
Caucasian			
Black			
Asian			
Native American			
Other			

Reporting group values	Pasireotide LAR overall - Acromegaly symptom: Headache	Pasireotide LAR overall - Acromegaly symptom: Fatigue	Pasireotide LAR overall - Acromegaly symptom: Perspiration
Number of subjects	123	123	123
Age categorical			
Units: Subjects			
Adults (18-64 years)			
From 65-84 years			
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	±	±	±

Sex: Female, Male Units: Subjects			
Female			
Male			
Race/Ethnicity, Customized Units: Subjects			
Caucasian			
Black			
Asian			
Native American			
Other			

Reporting group values	Pasireotide LAR overall - Acromegaly symptom: Osteoarthralgia	Pasireotide LAR overall - Acromegaly symptom: Paresthesiae	Pasireotide LAR overall - Acromegaly symptom: Paresthsiae
Number of subjects	123	123	123
Age categorical Units: Subjects			
Adults (18-64 years)			
From 65-84 years			
Age Continuous Units: years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male Units: Subjects			
Female			
Male			
Race/Ethnicity, Customized Units: Subjects			
Caucasian			
Black			
Asian			
Native American			
Other			

Reporting group values	Up-titrated to Pasireotide LAR 60 mg	Pasireotide LAR overall	Pasireotide LAR monotherapy
Number of subjects	70	88	76
Age categorical Units: Subjects			
Adults (18-64 years)			
From 65-84 years			
Age Continuous Units: years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male Units: Subjects			
Female			
Male			

Race/Ethnicity, Customized Units: Subjects			
Caucasian			
Black			
Asian			
Native American			
Other			

Reporting group values	Pasireotide with concomitant mediaction	Pasireotide LAR overall	Pasireotide LAR overall - AcroQOL total scores
Number of subjects	12	88	88
Age categorical Units: Subjects			
Adults (18-64 years)			
From 65-84 years			
Age Continuous Units: years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male Units: Subjects			
Female			
Male			
Race/Ethnicity, Customized Units: Subjects			
Caucasian			
Black			
Asian			
Native American			
Other			

Reporting group values	Pasireotide LAR overall - AcroQOL physical sub-scores	Pasireotide LAR overall - AcroQOL psychological sub-scores	Pasireotide LAR overall - AcroQOL psycho/appearance sub-scores
Number of subjects	88	88	88
Age categorical Units: Subjects			
Adults (18-64 years)			
From 65-84 years			
Age Continuous Units: years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male Units: Subjects			
Female			
Male			
Race/Ethnicity, Customized Units: Subjects			
Caucasian			
Black			

Asian			
Native American			
Other			

Reporting group values	Pasireotide LAR overall-AcroQOL psycho/pers relatns sub-scores	Pasireotide LAR overall - Acromegaly symptom: Headache	Pasireotide LAR overall - Acromegaly symptom: Fatigue
Number of subjects	88	88	88
Age categorical			
Units: Subjects			
Adults (18-64 years)			
From 65-84 years			
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male			
Units: Subjects			
Female			
Male			
Race/Ethnicity, Customized			
Units: Subjects			
Caucasian			
Black			
Asian			
Native American			
Other			

Reporting group values	Pasireotide LAR overall - Acromegaly symptom: Perspiration	Pasireotide LAR overall - Acromegaly symptom: Osteoarthralgia	Pasireotide LAR overall - Acromegaly symptom: Paresthesiae
Number of subjects	88	88	88
Age categorical			
Units: Subjects			
Adults (18-64 years)			
From 65-84 years			
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male			
Units: Subjects			
Female			
Male			
Race/Ethnicity, Customized			
Units: Subjects			
Caucasian			
Black			
Asian			
Native American			
Other			

Reporting group values	Pasireotide LAR overall - Acromegaly symptom: Paresthsiae	Pre-diabetic	Non-diabetic
Number of subjects	88	60	11
Age categorical Units: Subjects			
Adults (18-64 years) From 65-84 years			

Age Continuous
Units: years
    arithmetic mean
    standard deviation
	±	±	±

Sex: Female, Male Units: Subjects			
Female Male			
Race/Ethnicity, Customized Units: Subjects			

Caucasian
    Black
    Asian
    Native American
    Other			

End points

End points reporting groups

Reporting group title	Lanreotide 120 mg
Reporting group description:	
Participants were treated with lanreotide 120mg and assigned to Group 2 (before starting on Pasireotide in the Core phase).	
Reporting group title	Octreotide 30 mg
Reporting group description:	
Participants were treated with octreotide 30 mg and assigned to Group 2 (before starting on Pasireotide in the Core phase). .	
Reporting group title	Octreotide 40 mg
Reporting group description:	
Participants were treated with octreotide 40 mg and assigned to either Group 1 (if 40mg octreotide was approved in the country) or Group 2 if 40mg octreotide was not approved in the country (before starting on Pasireotide in the Core phase).	
Reporting group title	Lanreotide 120 mg
Reporting group description:	
Participants were treated with lanreotide 120mg and assigned to Group 2 (before starting on Pasireotide in the Core phase).	
Reporting group title	Octreotide 30 mg
Reporting group description:	
Participants were treated with octreotide 30 mg and assigned to Group 2 (before starting on Pasireotide in the Core phase). .	
Reporting group title	Octreotide 40 mg
Reporting group description:	
Participants were treated with octreotide 40 mg and assigned to either Group 1 (if 40mg octreotide was approved in the country) or Group 2 if 40mg octreotide was not approved in the country (before starting on Pasireotide in the Core phase).	
Reporting group title	Lanreotide 120 mg
Reporting group description:	
Participants were treated with lanreotide 120mg and assigned to Group 2 (before starting on Pasireotide in the Core phase).	
Reporting group title	Octreotide 30 mg
Reporting group description:	
Participants were treated with octreotide 30 mg and assigned to Group 2 (before starting on Pasireotide in the Core phase). .	
Reporting group title	Octreotide 40 mg
Reporting group description:	
Participants were treated with octreotide 40 mg and assigned to either Group 1 (if 40mg octreotide was approved in the country) or Group 2 if 40mg octreotide was not approved in the country (before starting on Pasireotide in the Core phase).	
Subject analysis set title	Pasireotide LAR overall
Subject analysis set type	Full analysis
Subject analysis set description:	
This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg.	
Subject analysis set title	Up-titrated to Pasireotide LAR 60 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
This is the subset of participants in the FAS who started treatment with 40 mg pasireotide LAR in the core phase and were up-titrated to pasireotide LAR 60 mg.	
Subject analysis set title	Pasireotide LAR overall
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg.

Subject analysis set title	Pasireotide LAR monotherapy
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received pasireotide LAR only

Subject analysis set title	Pasireotide with concomitant medication
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received pasireotide along with other concomitant medications.or octreotide 40 mg.

Subject analysis set title	Pasireotide LAR overall
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg.

Subject analysis set title	Up-titrated to Pasireotide LAR 60 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This is the subset of participants in the Extension FAS who started treatment with 40 mg pasireotide LAR in the extension phase and were up-titrated to pasireotide LAR 60 mg.

Subject analysis set title	Pasireotide LAR (run-in phase)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who were part of the run-in phase, i.e. group 1)

Subject analysis set title	GH: ≥ 1 - ≤ 2.5 µg/L at screening
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These Participants had this GH level at screening

Subject analysis set title	GH: > 2.5 µg/L at screening
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These Participants had this GH level at screening

Subject analysis set title	GH: Missing
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These Participants were missing GH levels at screening

Subject analysis set title	Pasireotide LAR overall
Subject analysis set type	Full analysis

Subject analysis set description:

This is the total sum of participants with at screening with various or missing GH levels

Subject analysis set title	Diabetic
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who were diabetic in the Pasireotide LAR overall group

Subject analysis set title	Pasireotide LAR overall - AcroQOL total scores
Subject analysis set type	Full analysis

Subject analysis set description:

This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg.

Subject analysis set title	Pasireotide LAR overall - AcroQOL physical sub-scores
Subject analysis set type	Full analysis

Subject analysis set description:	
This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg	
Subject analysis set title	Pasireotide LAR overall - AcroQOL psychological sub-scores
Subject analysis set type	Full analysis

Subject analysis set description:	
This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg.	
Subject analysis set title	Pasireotide LAR overall - AcroQOL psycho/appearance sub-scores
Subject analysis set type	Full analysis

Subject analysis set description:	
This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg	
Subject analysis set title	Pasireotide LAR overall-AcroQOL psycho/pers relatns sub-scores
Subject analysis set type	Full analysis

Subject analysis set description:	
This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg	
Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Headache
Subject analysis set type	Full analysis

Subject analysis set description:	
This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg.	
Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Fatigue
Subject analysis set type	Full analysis

Subject analysis set description:	
This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg	
Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Perspiration
Subject analysis set type	Full analysis

Subject analysis set description:	
This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg.	
Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Osteoarthralgia
Subject analysis set type	Full analysis

Subject analysis set description:	
This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg	
Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Paresthesiae
Subject analysis set type	Full analysis

Subject analysis set description:	
This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg	
Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Paresthsiae
Subject analysis set type	Full analysis

Subject analysis set description:	
This is the sum total of participants in under the previous treatments: lanreotide 120 mg, octreotide 30 mg or octreotide 40 mg	
Subject analysis set title	Up-titrated to Pasireotide LAR 60 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:	
This is the subset of participants in the FAS who started treatment with 40 mg pasireotide LAR in the core phase and were up-titrated to pasireotide LAR 60 mg.	
Subject analysis set title	Pasireotide LAR overall

Subject analysis set type	Sub-group analysis
Subject analysis set description:	
These are the participants in the extension phase who received Pasireotide LAR	
Subject analysis set title	Pasireotide LAR monotherapy
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
These Participants were treated with pasireotide LAR only in the extension phase	
Subject analysis set title	Pasireotide with concomitant mediaction
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
These Participants were treated with pasireotide LAR as well as other concomitant medications in the extension phase	
Subject analysis set title	Pasireotide LAR overall
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase	
Subject analysis set title	Pasireotide LAR overall - AcroQOL total scores
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase	
Subject analysis set title	Pasireotide LAR overall - AcroQOL physical sub-scores
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase	
Subject analysis set title	Pasireotide LAR overall - AcroQOL psychological sub-scores
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase	
Subject analysis set title	Pasireotide LAR overall - AcroQOL psycho/appearance sub-scores
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase	
Subject analysis set title	Pasireotide LAR overall-AcroQOL psycho/pers relatns sub-scores
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase	
Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Headache
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase	
Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Fatigue
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase	
Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Perspiration

Subject analysis set type	Sub-group analysis
Subject analysis set description:	
This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase	
Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Osteoarthralgia
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase	
Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Paresthesiae
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase	
Subject analysis set title	Pasireotide LAR overall - Acromegaly symptom: Paresthsiae
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
This is the sum total of participants who were treated with at least one dose of pasireotide LAR in the extension phase	
Subject analysis set title	Pre-diabetic
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who were pre-diabetic in the Pasireotide LAR overall group	
Subject analysis set title	Non-diabetic
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who were non-diabetic in the Pasireotide LAR overall group	

Primary: Core phase: Proportion of participants with mean GH < 1 g/L and IGF–1 < ULN at Week 36 by previous treatment and overall

End point title	Core phase: Proportion of participants with mean GH < 1 g/L and IGF-1 < ULN at Week 36 by previous treatment and overall[1]
End point description:	
Proportion of participants who achieved biochemical control defined as GH <1µg/L and IGF-1 <ULN at week 36.	
End point type	Primary
End point timeframe:	
Week 36	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint.

End point values	Lanreotide 120 mg	Octreotide 30 mg	Octreotide 40 mg	Pasireotide LAR overall
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	41	29	53	123
Units: Percentage of participants				
number (confidence interval 95%)	14.6 (5.57 to 29.17)	13.8 (3.89 to 31.66)	15.1 (6.75 to 27.59)	14.6 (8.91 to 22.14)

Statistical analyses

No statistical analyses for this end point

Primary: Core phase: Proportion of participants with mean GH < 1 g/L and IGF-1 < ULN at Week 36 for participants up-titrated to pasireotide LAR 60 mg

End point title	Core phase: Proportion of participants with mean GH < 1 g/L and IGF-1 < ULN at Week 36 for participants up-titrated to pasireotide LAR 60 mg[2]

End point description:

Proportion of participants who achieved biochemical control defined as GH <1μg/L and IGF-1 <ULN at week 36, for participants who had been up-titrated with pasireotide LAR 60 mg.

End point type	Primary

End point timeframe:

Week 36

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint.

End point values	Up-titrated to Pasireotide LAR 60 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	90			
Units: Percentage of participants				
number (confidence interval 95%)	6.7 (2.49 to 13.95)			

Statistical analyses

No statistical analyses for this end point

Primary: Core phase: Proportion of participants with mean GH < 1 g/L and IGF-1 < ULN at Week 36

End point title	Core phase: Proportion of participants with mean GH < 1 g/L and IGF-1 < ULN at Week 36[3]

End point description:

Proportion of participants who achieved biochemical control defined as GH <1μg/L and IGF-1 <ULN at week 36.

End point type	Primary

End point timeframe:

Wek 36

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint.

End point values	Pasireotide LAR overall			
Subject group type	Subject analysis set			
Number of subjects analysed	102			
Units: Percentage of participants				
number (confidence interval 95%)	15.7 (9.24 to 24.22)			

Statistical analyses

No statistical analyses for this end point

Primary: Core phase: Proportion of participants with mean GH < 1 g/L and IGF-1 < ULN at Week 36

End point title	Core phase: Proportion of participants with mean GH < 1 g/L and IGF-1 < ULN at Week 36[4]

End point description:

Proportion of patients who achieved biochemical control defined as GH <1µg/L and IGF-1 <ULN at week 36, by previous treatment, type of therapy and overall.

End point type	Primary

End point timeframe:

Week 36

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint.

End point values	Lanreotide 120 mg	Octreotide 30 mg	Octreotide 40 mg	Pasireotide LAR monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	26	23	39	76
Units: Percentage of participants				
number (confidence interval 95%)	7.7 (0.95 to 25.13)	13.0 (2.78 to 33.59)	20.5 (9.30 to 36.46)	17.1 (9.43 to 27.47)

End point values	Pasireotide with concomitant medication	Pasireotide LAR overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	88		
Units: Percentage of participants				
number (confidence interval 95%)	0.0 (0.00 to 26.46)	14.8 (8.11 to 23.94)		

Statistical analyses

No statistical analyses for this end point

Primary: Core phase: Proportion of participants with mean GH < 1 g/L and IGF-1 < ULN at Week 36 for participants up-titrated to pasireotide LAR 60 mg

End point title	Core phase: Proportion of participants with mean GH < 1 g/L and IGF-1 < ULN at Week 36 for participants up-titrated to pasireotide LAR 60 mg[5]

End point description:

Proportion of participants who achieved biochemical control defined as GH <1µg/L and IGF-1 <ULN at week 36, for participants who had been up-titrated with pasireotide LAR 60 mg.

End point type	Primary

End point timeframe:

Week 36

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint.

End point values	Up-titrated to Pasireotide LAR 60 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	70			
Units: Percentage of participants				
number (confidence interval 95%)	5.9 (1.63 to 14.38)			

Statistical analyses

No statistical analyses for this end point

Primary: Core phase: Proportion of participants with mean GH < 1 g/L and IGF-1 < ULN at Week 36 overall by baseline diabetic status

End point title	Core phase: Proportion of participants with mean GH < 1 g/L and IGF-1 < ULN at Week 36 overall by baseline diabetic status[6]

End point description:

Proportion of participants who achieved biochemical control defined as GH <1µg/L and IGF-1 <ULN at week 36, overall by baseline diabetic status.

End point type	Primary

End point timeframe:

Week 36

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint.

End point values	Pasireotide LAR overall			
Subject group type	Subject analysis set			
Number of subjects analysed	88			
Units: Percentage of participants				
number (confidence interval 95%)				
Diabetic	14.0 (5.30 to 27.93)			
Pre-diabetic	19.4 (8.19 to 36.02)			
Non-diabetic	0.0 (0.00 to 33.63)			

Statistical analyses

No statistical analyses for this end point

Primary: Core phase: Proportion of participants with mean GH < 1 g/L and IGF-1 < ULN at Week 36 by previous treatment and overall - LOCF

End point title	Core phase: Proportion of participants with mean GH < 1 g/L and IGF-1 < ULN at Week 36 by previous treatment and overall - LOCF[7]

End point description:

Proportion of participants who achieved biochemical control defined as GH <1µg/L and IGF-1 <ULN at week 36, by previous treatment and overall - last observation carried forward (LOCF)

End point type	Primary

End point timeframe:

Week 36

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint.

End point values	Lanreotide 120 mg	Octreotide 30 mg	Octreotide 40 mg	Pasireotide LAR overall
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	41	29	53	123
Units: Percentage of participants				
number (confidence interval 95%)	14.6 (5.57 to 29.17)	13.8 (3.89 to 31.66)	17.0 (8.07 to 29.80)	15.4 (9.56 to 23.07)

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Change in mean Growth Hormone (GH) values from baseline to week 36

End point title	Core phase: Change in mean Growth Hormone (GH) values from baseline to week 36

End point description:

Core phase - Changes in mean GH from study baseline to week 36.

End point type	Secondary
End point timeframe:	
baseline, week 36	

End point values	Lanreotide 120 mg	Octreotide 30 mg	Octreotide 40 mg	Pasireotide LAR overall
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	41	29	53	123
Units: percentage				
arithmetic mean (standard error)	-7.7 (± 19.51)	-8.5 (± 24.41)	-39.8 (± 54.87)	-6.0 (± 17.10)

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Change in standardized IGF-1 values from baseline to Week 36

End point title	Core phase: Change in standardized IGF-1 values from baseline to Week 36
End point description:	
Core phase - Changes in standardized IGF-1 from study baseline to week 36.	
End point type	Secondary
End point timeframe:	
baseline, week 36	

End point values	Lanreotide 120 mg	Octreotide 30 mg	Octreotide 40 mg	Pasireotide LAR overall
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	41	29	53	123
Units: percentage				
arithmetic mean (standard deviation)	-1.1 (± 1.8)	-0.8 (± 0.78)	-1.1 (± 1.39)	-1.0 (± 1.18)

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Proportion of participants with mean GH <1 µg/L and IGF-1 <ULN

End point title	Core phase: Proportion of participants with mean GH <1 µg/L and IGF-1 <ULN
End point description:	

Proportion of participants achieving GH <1 µg/L and IGF-1 <ULN at weeks 12 and 24 overall and by GH

level at screening.

End point type	Secondary

End point timeframe:
Week 12, Week 24

End point values	Pasireotide LAR overall	Pasireotide LAR (run-in phase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	123	17		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 12: GH: ≥ 1 - ≤ 2.5 µg/L at screening	28.6 (13.22 to 48.67)	25.0 (0.63 to 80.59)		
Week 24: GH: ≥ 1 - ≤ 2.5 µg/L at screening	39.3 (21.50 to 59.42)	25.0 (0.63 to 80.59)		
Week 12: GH: > 2.5 µg/L at screening	5.3 (1.75 to 11.98)	7.7 (0.19 to 36.03)		
Week 24: GH: > 2.5 µg/L at screening	5.3 (1.75 to 11.98)	7.7 (0.19 to 36.03)		
Week 12: GH: Missing	0.0 (0.00 to 97.50)	0.0 (0.00 to 0.00)		
Week 24: GH: Missing	0.0 (0.00 to 97.50)	0.0 (0.00 to 0.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Proportion of participants with IGF-1 <ULN overall by GH level at screening

End point title	Core phase: Proportion of participants with IGF-1 <ULN overall by GH level at screening

End point description:
Proportion of participants achieving IGF-1 <ULN at weeks 12, 24 & 36.

End point type	Secondary

End point timeframe:
Weeks 12, 24 & 36

End point values	Pasireotide LAR overall	GH: ≥ 1 - ≤ 2.5 µg/L at screening	GH: > 2.5 µg/L at screening	GH: Missing
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	123	28	94	1
Units: Percentage of participants				
number (confidence interval 95%)				
Week 12	20.3 (13.61 to 28.52)	35.7 (18.64 to 55.93)	16.0 (9.22 to 24.95)	0.0 (0.00 to 97.50)

Week 24	27.6 (19.96 to 36.43)	42.9 (24.46 to 62.82)	23.4 (15.29 to 33.26)	0.0 (0.00 to 97.50)
Week 36	30.9 (22.88 to 39.86)	50.0 (30.65 to 69.35)	25.5 (17.09 to 35.57)	0.0 (0.00 to 97.50)

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Proportion of participants with mean GH <1 µg/L and IGF-1 <ULN overall by baseline diabetic status

End point title	Core phase: Proportion of participants with mean GH <1 µg/L and IGF-1 <ULN overall by baseline diabetic status
End point description:	
Core phase - Proportion of patients achieving GH <1µg/L at week 12, 24, 36 overall and by GH level at screening.	
End point type	Secondary
End point timeframe:	
Weeks 12, 24 & 36	

End point values	Diabetic	Pre-diabetic	Non-diabetic	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	52	60	11	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 12	13.5 (5.59 to 25.79)	10.0 (3.76 to 20.51)	0.0 (0.00 to 28.49)	
Week 24	13.5 (5.59 to 25.79)	13.3 (5.94 to 24.59)	9.1 (0.23 to 41.28)	
Week 36	15.4 (6.88 to 28.08)	16.7 (8.29 to 28.52)	0.0 (0.00 to 28.49)	

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Change from baseline in scores as measured by Acromegaly Quality of Life (AcroQoL)

End point title	Core phase: Change from baseline in scores as measured by Acromegaly Quality of Life (AcroQoL)
End point description:	

Evaluation of effect of pasireotide LAR on Health Related Quality of Life (HRQoL) was assessed using AcroQoL, an acromegaly-specific quality of life instrument. The AcroQol instrument is comprised of 22 questions divided into two scales: one evaluating physical aspects (8 items) and the other that addresses psychological aspects (14 items). The psychological scale can also be further divided into subscale that evaluates physical appearance and the other subscale focused on the impact of the disease on personal relationships of the patient (7 items each). Each of the questions has a 5-item Likert scale. The instrument was developed with input from both physicians and patients to assess those

dimensions of health-related quality of life most relevant and bothersome to patients with this disease.

End point type	Secondary

End point timeframe:
Weeks 12, 24 & 36

End point values	Pasireotide LAR overall - AcroQOL total scores	Pasireotide LAR overall - AcroQOL physical sub-scores	Pasireotide LAR overall - AcroQOL psychological sub-scores	Pasireotide LAR overall - AcroQOL psycho/appearance sub-scores
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	123	123	123	123
Units: scores on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=120, 120, 120, 120, 118)	4.5 (± 9.52)	5.3 (± 12.93)	4.1 (± 10.05)	6.5 (± 12.43)
Week 24 (n=118, 118, 118, 118, 117)	4.7 (± 9.88)	5.8 (± 12.26)	4.0 (± 10.72)	7.2 (± 14.44)
Week 36 (n=110, 110, 109, 110, 108)	4.6 (± 10.14)	5.4 (± 13.00)	4.3 (± 11.02)	7.0 (± 15.33)

End point values	Pasireotide LAR overall- AcroQOL psycho/pers relatns sub-scores			
Subject group type	Subject analysis set			
Number of subjects analysed	123			
Units: scores on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=120, 120, 120, 120, 118)	1.9 (± 12.04)			
Week 24 (n=118, 118, 118, 118, 117)	0.9 (± 10.70)			
Week 36 (n=110, 110, 109, 110, 108)	1.8 (± 10.69)			

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Percentage of participants reporting levels 1 - 5 by dimensions of acromegaly symptoms

End point title	Core phase: Percentage of participants reporting levels 1 - 5 by dimensions of acromegaly symptoms

End point description:

Symptoms of acromegaly were collected at various visits. Ring size was measured with a gauge using the fourth digit of the non-dominant hand. In the case a patient had a fourth digit size exceeding the highest size; the fifth digit of that hand was used for initial and follow-up investigation. The measurement was to be provided on a scale of 1-15 including half sizes. Investigators also asked the participants to score the following symptoms of acromegaly: headache, fatigue, perspiration, paresthesias, osteoarthralgia according to a five-point score scale (0=absent, 1=mild, 2=moderate, 3=severe, 4=very severe).

End point type	Secondary
End point timeframe: Weeks 12, 24 & 36	

End point values	Pasireotide LAR overall - Acromegaly symptom: Headache	Pasireotide LAR overall - Acromegaly symptom: Fatigue	Pasireotide LAR overall - Acromegaly symptom: Perspiration	Pasireotide LAR overall - Acromegaly symptom: Osteoarthralgia
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	123	123	123	123
Units: Percentage of participants				
number (not applicable)				
Week 12: Non/absent (n=119, 119, 119, 119, 119)	56.9	37.4	56.9	43.1
Week 12: Mild (n=119, 119, 119, 119, 119)	24.4	26.8	26.8	27.6
Week 12: Moderate (n=119, 119, 119, 119, 119)	14.6	18.7	8.1	14.6
Week 12: Severe (n=119, 119, 119, 119, 119)	0.8	8.9	3.3	8.9
Week 12: Very severe (n=119, 119, 119, 119, 119)	0.0	4.9	1.6	2.4
Week 12: Not done (n=119, 119, 119, 119, 119)	0.0	0.0	0.0	0.0
Week 24: Non/absent (n=119, 119, 119, 119, 119)	59.3	46.3	64.2	47.2
Week 24: Mild (n=119, 119, 119, 119, 119)	27.6	20.3	21.1	26.8
Week 24: Moderate (n=119, 119, 119, 119, 119)	8.1	17.9	8.9	14.6
Week 24: Severe (n=119, 119, 119, 119, 119)	1.6	7.3	1.6	3.3
Week 24: Very severe (n=119, 119, 119, 119, 119)	0.0	4.9	0.8	4.9
Week 24: Not done (n=119, 119, 119, 119, 119)	0.0	0.0	0.0	0.0
Week 36: Non/absent (n=113, 113, 113, 113, 113)	63.4	47.2	61.8	47.2
Week 36: Mild (n=113, 113, 113, 113, 113)	17.1	23.6	18.7	26.8
Week 36: Moderate (n=113, 113, 113, 113, 113)	9.8	13.0	7.3	12.2
Week 36: Severe (n=113, 113, 113, 113, 113)	1.6	4.9	4.1	3.3
Week 36: Very severe (n=113, 113, 113, 113, 113)	0.0	3.3	0.0	2.4
Week 36: Not done (n=113, 113, 113, 113, 113)	0.0	0.0	0.0	0.0

End point values	Pasireotide LAR overall - Acromegaly symptom:			

	Paresthesiae			
Subject group type	Subject analysis set			
Number of subjects analysed	123			
Units: Percentage of participants				
number (not applicable)				
Week 12: Non/absent (n=119, 119, 119, 119, 119)	69.1			
Week 12: Mild (n=119, 119, 119, 119, 119)	15.4			
Week 12: Moderate (n=119, 119, 119, 119, 119)	5.7			
Week 12: Severe (n=119, 119, 119, 119, 119)	4.9			
Week 12: Very severe (n=119, 119, 119, 119, 119)	1.6			
Week 12: Not done (n=119, 119, 119, 119, 119)	0.0			
Week 24: Non/absent (n=119, 119, 119, 119, 119)	72.4			
Week 24: Mild (n=119, 119, 119, 119, 119)	13.8			
Week 24: Moderate (n=119, 119, 119, 119, 119)	7.3			
Week 24: Severe (n=119, 119, 119, 119, 119)	0.8			
Week 24: Very severe (n=119, 119, 119, 119, 119)	2.4			
Week 24: Not done (n=119, 119, 119, 119, 119)	0.0			
Week 36: Non/absent (n=113, 113, 113, 113, 113)	69.1			
Week 36: Mild (n=113, 113, 113, 113, 113)	14.6			
Week 36: Moderate (n=113, 113, 113, 113, 113)	5.7			
Week 36: Severe (n=113, 113, 113, 113, 113)	1.6			
Week 36: Very severe (n=113, 113, 113, 113, 113)	0.8			
Week 36: Not done (n=113, 113, 113, 113, 113)	0.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Percentage of participants with Acromegaly shift symptoms from baseline to most extreme post-baseline

End point title	Core phase: Percentage of participants with Acromegaly shift symptoms from baseline to most extreme post-baseline

End point description:

Symptoms of acromegaly were collected at various visits. Ring size was measured with a gauge using the fourth digit of the non-dominant hand. In the case a patient had a fourth digit size exceeding the highest size; the fifth digit of that hand was used for initial and follow-up investigation. The measurement was to be provided on a scale of 1-15 including half sizes. Investigators also asked the participants to score the following symptoms of acromegaly: headache, fatigue, perspiration, paresthesias, osteoarthralgia according to a five-point score scale (0=absent, 1=mild, 2=moderate,

3=severe, 4=very severe).

End point type	Secondary
End point timeframe: Weeks 12, 24 & 36	

End point values	Pasireotide LAR overall - Acromegaly symptom: Headache	Pasireotide LAR overall - Acromegaly symptom: Fatigue	Pasireotide LAR overall - Acromegaly symptom: Perspiration	Pasireotide LAR overall - Acromegaly symptom: Osteoarthralgia
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	123	123	123	123
Units: Percentage of participants				
number (not applicable)				
Baseline (BL): Non/absent	41.5	36.6	43.1	33.3
BL: Mild	25.2	17.8	25.2	21.1
BL: Moderate	18.7	26.0	18.7	26.0
BL: Severe	8.9	13.8	8.9	16.3
BL: Very severe	5.7	4.9	4.1	3.3
BL: Not done	0.0	0.0	0.0	0.0
BL: Total	100.0	100.0	100.0	100.0
Most extreme post-BL: total Non/absent	36.6	26.0	37.4	26.8
Most extreme post-BL: total Mild	30.9	22.8	29.3	26.0
Most extreme post-BL: total Moderate	20.3	22.8	20.3	24.4
Most extreme post-BL: total Severe	9.8	15.4	7.3	14.6
Most extreme post-BL: total Very severe	2.4	13.0	5.7	8.1
Most extreme post-BL: total Not done	0.0	0.0	0.0	0.0

End point values	Pasireotide LAR overall - Acromegaly symptom: Paresthsiae			
Subject group type	Subject analysis set			
Number of subjects analysed	123			
Units: Percentage of participants				
number (not applicable)				
Baseline (BL): Non/absent	54.5			
BL: Mild	25.2			
BL: Moderate	10.6			
BL: Severe	8.9			
BL: Very severe	0.8			
BL: Not done	0.0			
BL: Total	100.0			
Most extreme post-BL: total Non/absent	47.2			
Most extreme post-BL: total Mild	27.6			
Most extreme post-BL: total Moderate	13.0			
Most extreme post-BL: total Severe	9.8			

Most extreme post-BL: total Very severe	2.4
Most extreme post-BL: total Not done	0.0

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Change from baseline in EQ-5D-5L index scores

End point title	Core phase: Change from baseline in EQ-5D-5L index scores

End point description:

Evaluation of effect of pasireotide LAR on health status, measured by EQ-5D-5L, a valid and reliable instrument for measuring general health status. The EQ-5D-5L consists of 2 pages – the descriptive system and the EQ visual analogue scale (EQ VAS). The descriptive system comprises 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each with 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. The EQ VAS records the respondent's self-rated health on a 20-cm vertical, visual analogue scale with endpoints labeled 'the best health you can imagine' and 'the worst health you can imagine'.

End point type	Secondary

End point timeframe:

Weeks 12, 24 & 36

End point values	Pasireotide LAR overall			
Subject group type	Subject analysis set			
Number of subjects analysed	123			
Units: scores on a scale				
arithmetic mean (standard deviation)				
Week 12 (n= 119)	0.0 (± 0.15)			
Week 24 (n = 118)	0.0 (± 0.15)			
Week 36 (n = 111)	0.0 (± 0.15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Change from baseline in EQ-5D-5L VAS assessment

End point title	Core phase: Change from baseline in EQ-5D-5L VAS assessment

End point description:

Evaluation of effect of pasireotide LAR on health status, measured by EQ-5D-5L, a valid and reliable instrument for measuring general health status. The EQ-5D-5L consists of 2 pages – the descriptive system and the EQ visual analogue scale (EQ VAS). The descriptive system comprises 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each with 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. The EQ VAS records the respondent's self-rated health on a 20-cm vertical, visual analogue scale with endpoints labeled 'the best health you can imagine' and 'the worst health you can imagine'.

End point type	Secondary

End point timeframe:

Weeks 12, 24 & 36

End point values	Pasireotide LAR overall			
Subject group type	Subject analysis set			
Number of subjects analysed	123			
Units: scores on a scale				
arithmetic mean (standard deviation)				
Week 12 (n= 119)	4.1 (± 14.91)			
Week 24 (n = 118)	3.4 (± 13.49)			
Week 36 (n = 111)	4.9 (± 15.24)			

Statistical analyses

No statistical analyses for this end point

Secondary: Extension phase: Proportion of participants with mean GH < 1 µg/L and IGF-1 < ULN at Weeks 48, 60 & 72

End point title	Extension phase: Proportion of participants with mean GH < 1 µg/L and IGF-1 < ULN at Weeks 48, 60 & 72
End point description:	
Proportion of patients achieving IGF-1 <ULN at weeks 48, 60 & 72 for participants with up-titrated to Pasireotide LAR 60 mg mg	
End point type	Secondary
End point timeframe:	
Weeks 48, 60 & 72	

End point values	Up-titrated to Pasireotide LAR 60 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	70			
Units: Percentage of participants				
number (confidence interval 95%)				
Week 48	5.8 (1.60 to 14.18)			
Week 60	7.1 (2.36 to 15.89)			
Week 72	5.7 (1.58 to 13.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Extension phase: Proportion of participants with mean GH < 1 µg/L and IGF-1 < ULN at Weeks 48, 60 and 72

End point title	Extension phase: Proportion of participants with mean GH < 1 µg/L and IGF-1 < ULN at Weeks 48, 60 and 72
End point description:	
Proportion of participants achieving IGF-1 <ULN at week 46, 60 and 72 overall by baseline diabetic status	
End point type	Secondary
End point timeframe:	
Weeks 48, 60, 72	

End point values	Pasireotide LAR overall			
Subject group type	Subject analysis set			
Number of subjects analysed	88			
Units: Percentage of participants				
number (confidence interval 95%)				
Week 48: Diabetic	11.6 (3.89 to 25.08)			
Week 60: Diabetic	11.6 (3.89 to 25.08)			
Week 72: Diabetic	11.6 (3.89 to 25.08)			
Week 48: Pre-diabetic	11.1 (3.11 to 26.06)			
Week 60: Pre-diabetic	16.7 (6.37 to 32.81)			
Week 72: Pre-diabetic	8.3 (1.75 to 22.47)			
Week 48: Non-diabetic	22.2 (2.81 to 60.01)			
Week 60: Non-diabetic	22.2 (2.81 to 60.01)			
Week 72: Non-diabetic	22.2 (2.81 to 60.01)			

Statistical analyses

No statistical analyses for this end point

Secondary: Extension phase: Proportion of participants with mean GH < 1 µg/L at Weeks 48, 60 and 72, overall, Pasireotide montherapy and Pasireotide with concomittant medication and by GH level at screening

End point title	Extension phase: Proportion of participants with mean GH < 1 µg/L at Weeks 48, 60 and 72, overall, Pasireotide montherapy and Pasireotide with concomittant medication and by GH level at screening
End point description:	
Proportion of patients achieving GH <1 µg/L and IGF-1 <ULN at week 48 by treatment with pasireotide	

LAR alone or with concomitant medications used to treat acromegaly

End point type	Secondary

End point timeframe:

Weeks 48, 60, 72

End point values	Pasireotide LAR monotherapy	Pasireotide LAR overall	Pasireotide with concomitant mediaction	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	88	12	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 48: GH: >= 1 - <= 2.5 μg/L at screening	76.5 (50.10 to 93.19)	65.0 (40.78 to 84.61)	0.0 (0.00 to 70.76)	
Week 60: GH: >= 1 - <= 2.5 μg/L at screening	70.6 (44.04 to 89.69)	60.0 (36.05 to 80.88)	0.0 (0.00 to 70.76)	
Week 72: GH: >= 1 - <= 2.5 μg/L at screening	64.7 (38.33 to 85.79)	55.0 (31.53 to 76.94)	0.0 (0.00 to 70.76)	
Week 48: GH: > 2.5 μg/L at screening	11.9 (4.91 to 22.93)	11.8 (5.22 to 21.87)	11.1 (0.28 to 48.25)	
Week 60: GH: > 2.5 μg/L at screening	11.9 (4.91 to 22.93)	10.3 (4.24 to 20.07)	0.0 (0.00 to 33.63)	
Week 72: GH: > 2.5 μg/L at screening	11.9 (4.91 to 22.93)	10.3 (4.24 to 20.07)	0.0 (0.00 to 33.63)	
Week 48: Pasireotide LAR overall	26.3 (16.87 to 37.68)	23.9 (15.42 to 34.14)	8.3 (0.21 to 38.48)	
Week 60: Pasireotide LAR overall	25.0 (15.77 to 36.26)	21.6 (13.53 to 31.65)	0.0 (0.00 to 26.46)	
Week 72: Pasireotide LAR overall	23.7 (14.68 to 34.82)	20.5 (12.60 to 30.39)	0.0 (0.00 to 26.46)	

Statistical analyses

No statistical analyses for this end point

Secondary: Extension phase: Change from baseline in scores as measured by Acromegaly Quality of Life (AcroQoL)

End point title	Extension phase: Change from baseline in scores as measured by Acromegaly Quality of Life (AcroQoL)

End point description:

Evaluation of effect of pasireotide LAR on Health Related Quality of Life (HRQoL) was assessed using AcroQoL, an acromegaly-specific quality of life instrument. The AcroQol instrument is comprised of 22 questions divided into two scales: one evaluating physical aspects (8 items) and the other that addresses psychological aspects (14 items). The psychological scale can also be further divided into subscale that evaluates physical appearance and the other subscale focused on the impact of the disease on personal relationships of the patient (7 items each). Each of the questions has a 5-item Likert scale. The instrument was developed with input from both physicians and patients to assess those dimensions of health-related quality of life most relevant and bothersome to patients with this disease.

End point type	Secondary

End point timeframe:

Weeks 48, 60 & 72

End point values	Pasireotide LAR overall - AcroQOL total scores	Pasireotide LAR overall - AcroQOL physical sub-scores	Pasireotide LAR overall - AcroQOL psychological sub-scores	Pasireotide LAR overall - AcroQOL psycho/appearance sub-scores
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	88	88	88	88
Units: scores on a scale				
arithmetic mean (standard deviation)				
Week 60 (n = 1, 1, 1, 1, 1)	-4.5 (± 0.0)	0.0 (± 0.00)	-7.1 (± 0.00)	-3.6 (± 0.00)
Week 72 (n = 74, 74, 73, 74, 72)	1.6 (± 9.72)	0.9 (± 10.61)	1.8 (± 10.60)	0.8 (± 12.82)

End point values	Pasireotide LAR overall- AcroQOL psycho/pers relatns sub-scores			
Subject group type	Subject analysis set			
Number of subjects analysed	88			
Units: scores on a scale				
arithmetic mean (standard deviation)				
Week 60 (n = 1, 1, 1, 1, 1)	-10.7 (± 0.00)			
Week 72 (n = 74, 74, 73, 74, 72)	2.9 (± 11.82)			

Statistical analyses

No statistical analyses for this end point

Secondary: Extension phase: Percentage of participants reporting levels 1 - 5 by dimensions of acromegaly symptoms

End point title	Extension phase: Percentage of participants reporting levels 1 - 5 by dimensions of acromegaly symptoms

End point description:

Symptoms of acromegaly were collected at various visits. Ring size was measured with a gauge using the fourth digit of the non-dominant hand. In the case a patient had a fourth digit size exceeding the highest size; the fifth digit of that hand was used for initial and follow-up investigation. The measurement was to be provided on a scale of 1-15 including half sizes. Investigators also asked the participants to score the following symptoms of acromegaly: headache, fatigue, perspiration, paresthesias, osteoarthralgia according to a five-point score scale (0=absent, 1=mild, 2=moderate, 3=severe, 4=very severe).

End point type	Secondary

End point timeframe:

Weeks 48, 60 & 72

End point values	Pasireotide LAR overall - Acromegaly symptom: Headache	Pasireotide LAR overall - Acromegaly symptom: Fatigue	Pasireotide LAR overall - Acromegaly symptom: Perspiration	Pasireotide LAR overall - Acromegaly symptom: Osteoarthralgia
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	88	88	88	88
Units: Percentage of participants				
number (not applicable)				
Week 48: None/absent (n= 81, 81, 81, 81, 81)	63.6	59.1	69.3	53.4
Week 48: Mild (n= 81, 81, 81, 81, 81)	19.3	17.0	13.6	25.0
Week 48: Moderate (n= 81, 81, 81, 81, 81)	8.0	12.5	9.1	9.1
Week 48: Severe (n= 81, 81, 81, 81, 81)	1.1	3.4	0.0	3.4
Week 48: Very severe (n= 81, 81, 81, 81, 81)	0.0	0.0	0.0	1.1
Week 48: Not done (n= 81, 81, 81, 81, 81)	0.0	0.0	0.0	0.0
Week 60: None/absent (n = 77, 77, 77, 77, 77)	60.2	48.9	60.2	56.8
Week 60: Mild (n = 77, 77, 77, 77, 77)	17.0	20.5	20.5	14.8
Week 60: Moderate (n = 77, 77, 77, 77, 77)	6.8	13.6	6.8	11.4
Week 60: Severe (n = 77, 77, 77, 77, 77)	3.4	4.5	0.0	3.4
Week 60: Very severe (n = 77, 77, 77, 77, 77)	0.0	0.0	0.0	1.1
Week 60: Not done (n = 77, 77, 77, 77, 77)	0.0	0.0	0.0	0.0
Week 72: None/absent (n = 74, 74, 74, 74, 74)	56.8	44.3	61.4	51.1
Week 72: Mild (n = 74, 74, 74, 74, 74)	17.0	23.9	15.9	20.5
Week 72: Moderate (n = 74, 74, 74, 74, 74)	8.0	10.2	6.8	10.2
Week 72: Severe (n = 74, 74, 74, 74, 74)	2.3	4.5	0.0	1.1
Week 72: Very severe (n = 74, 74, 74, 74, 74)	0.0	1.1	0.0	1.1
Week 72: Not done (n = 74, 74, 74, 74, 74)	0.0	0.0	0.0	0.0

End point values	Pasireotide LAR overall - Acromegaly symptom: Paresthesiae			
Subject group type	Subject analysis set			
Number of subjects analysed	88			
Units: Percentage of participants				
number (not applicable)				

Week 48: None/absent (n= 81, 81, 81, 81, 81)	71.6
Week 48: Mild (n= 81, 81, 81, 81, 81)	14.8
Week 48: Moderate (n= 81, 81, 81, 81, 81)	4.5
Week 48: Severe (n= 81, 81, 81, 81, 81)	0.0
Week 48: Very severe (n= 81, 81, 81, 81, 81)	1.1
Week 48: Not done (n= 81, 81, 81, 81, 81)	0.0
Week 60: None/absent (n = 77, 77, 77, 77, 77)	70.5
Week 60: Mild (n = 77, 77, 77, 77, 77)	10.2
Week 60: Moderate (n = 77, 77, 77, 77, 77)	4.5
Week 60: Severe (n = 77, 77, 77, 77, 77)	1.1
Week 60: Very severe (n = 77, 77, 77, 77, 77)	1.1
Week 60: Not done (n = 77, 77, 77, 77, 77)	0.0
Week 72: None/absent (n = 74, 74, 74, 74, 74)	67.0
Week 72: Mild (n = 74, 74, 74, 74, 74)	11.4
Week 72: Moderate (n = 74, 74, 74, 74, 74)	5.7
Week 72: Severe (n = 74, 74, 74, 74, 74)	0.0
Week 72: Very severe (n = 74, 74, 74, 74, 74)	0.0
Week 72: Not done (n = 74, 74, 74, 74, 74)	0.0

Statistical analyses

No statistical analyses for this end point

Secondary: Extension phase: Percentage of participants with Acromegaly shift symptoms from extension baseline to most extreme post-extension baseline

End point title	Extension phase: Percentage of participants with Acromegaly shift symptoms from extension baseline to most extreme post-extension baseline

End point description:

Symptoms of acromegaly were collected at various visits. Ring size was measured with a gauge using the fourth digit of the non-dominant hand. In the case a patient had a fourth digit size exceeding the highest size; the fifth digit of that hand was used for initial and follow-up investigation. The measurement was to be provided on a scale of 1-15 including half sizes. Investigators also asked the participants to score the following symptoms of acromegaly: headache, fatigue, perspiration, paresthesias, osteoarthralgia according to a five-point score scale (0=absent, 1=mild, 2=moderate, 3=severe, 4=very severe).

End point type	Secondary

End point timeframe:

Weeks 48, 60 & 72

End point values	Pasireotide LAR overall - Acromegaly symptom: Headache	Pasireotide LAR overall - Acromegaly symptom: Fatigue	Pasireotide LAR overall - Acromegaly symptom: Perspiration	Pasireotide LAR overall - Acromegaly symptom: Osteoarthralgia
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	88	88	88	88
Units: Percentage of participants				
number (not applicable)				
Extension (Ext.)Baseline (BL): Non/absent	69.3	56.8	68.2	52.3
Ext. BL: Mild	20.5	23.9	20.5	30.7
Ext. BL: Moderate	9.1	12.5	10.2	12.5
Ext. BL: Severe	1.1	4.5	1.1	3.4
Ext. BL: Very severe	0.0	2.3	0.0	1.1
Ext. BL: Not done	0.0	0.0	0.0	0.0
Ext. BL: Total	100.0	100.0	100.0	100.0
Most extreme post-BL: total Non/absent	46.6	51.1	54.5	43.2
Most extreme post-BL: total Mild	29.5	22.7	26.1	33.0
Most extreme post-BL: total Moderate	18.2	18.2	14.8	13.6
Most extreme post-BL: total Severe	3.4	6.8	4.5	8.0
Most extreme post-BL: total Very severe	2.3	1.1	0.0	2.3
Most extreme post-BL: total Not done	0.0	0.0	0.0	0.0

End point values	Pasireotide LAR overall - Acromegaly symptom: Paresthsiae			
Subject group type	Subject analysis set			
Number of subjects analysed	88			
Units: Percentage of participants				
number (not applicable)				
Extension (Ext.)Baseline (BL): Non/absent	79.5			
Ext. BL: Mild	13.6			
Ext. BL: Moderate	5.7			
Ext. BL: Severe	0.0			
Ext. BL: Very severe	1.1			
Ext. BL: Not done	0.0			
Ext. BL: Total	100.0			
Most extreme post-BL: total Non/absent	67.0			
Most extreme post-BL: total Mild	22.7			
Most extreme post-BL: total Moderate	6.8			
Most extreme post-BL: total Severe	2.3			
Most extreme post-BL: total Very severe	1.1			
Most extreme post-BL: total Not done	0.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Extension phase: Change from baseline in EQ-5D-5L index scores

End point title	Extension phase: Change from baseline in EQ-5D-5L index scores
End point description:	

Evaluation of effect of pasireotide LAR on health status, measured by EQ-5D-5L, a valid and reliable instrument for measuring general health status. The EQ-5D-5L consists of 2 pages – the descriptive system and the EQ visual analogue scale (EQ VAS). The descriptive system comprises 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each with 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. The EQ VAS records the respondent's self-rated health on a 20-cm vertical, visual analogue scale with endpoints labeled 'the best health you can imagine' and 'the worst health you can imagine'.

End point type	Secondary
End point timeframe:	

Weeks 48, 60 & 72

End point values	Pasireotide LAR overall			
Subject group type	Subject analysis set			
Number of subjects analysed	88			
Units: scores on a scale				
arithmetic mean (standard deviation)				
Week 60 (n = 1)	-0.1 (± 0.00)			
Week 72 (n = 73)	0.0 (± 0.08)			

Statistical analyses

No statistical analyses for this end point

Secondary: Extension phase: Change from baseline in EQ-5D-5L VAS assessment

End point title	Extension phase: Change from baseline in EQ-5D-5L VAS assessment
End point description:	

Evaluation of effect of pasireotide LAR on health status, measured by EQ-5D-5L, a valid and reliable instrument for measuring general health status. The EQ-5D-5L consists of 2 pages – the descriptive system and the EQ visual analogue scale (EQ VAS). The descriptive system comprises 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each with 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. The EQ VAS records the respondent's self-rated health on a 20-cm vertical, visual analogue scale with endpoints labeled 'the best health you can imagine' and 'the worst health you can imagine'.

End point type	Secondary

End point timeframe:

Weeks 48, 60 & 72

End point values	Pasireotide LAR overall			
Subject group type	Subject analysis set			
Number of subjects analysed	88			
Units: scores on a scale				
arithmetic mean (standard deviation)				
Week 60 (n = 1)	-10.0 (± 0.0)			
Week 72 (n = 73)	1.6 (± 9.14)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from first dose of study treatment until end of study treatment plus 84 days post treatment, up to maximum duration of 76 weeks.

Adverse event reporting additional description:

AE is any sign or symptom that occurs during the study treatment plus the 84 days post treatment

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Pasireotide LAR overall
Reporting group description:	
Pasireotide LAR overall	
Reporting group title	Up-titrated to Pasireotide LAR 60 mg
Reporting group description:	
Up-titrated to Pasireotide LAR 60 mg	

Serious adverse events	Pasireotide LAR overall	Up-titrated to Pasireotide LAR 60 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 123 (9.76%)	6 / 92 (6.52%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 123 (0.81%)	1 / 92 (1.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatofibrosarcoma protuberans			
subjects affected / exposed	1 / 123 (0.81%)	1 / 92 (1.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Stress cardiomyopathy			

subjects affected / exposed	1 / 123 (0.81%)	0 / 92 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		

Blood and lymphatic system disorders

Neutropenia

subjects affected / exposed	1 / 123 (0.81%)	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		

Gastrointestinal disorders

Abdominal pain

subjects affected / exposed	1 / 123 (0.81%)	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		

Diarrhoea

subjects affected / exposed	1 / 123 (0.81%)	0 / 92 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		

Hepatobiliary disorders

Bile duct stone

subjects affected / exposed	1 / 123 (0.81%)	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		

Biliary dilatation

subjects affected / exposed	1 / 123 (0.81%)	0 / 92 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		

Cholelithiasis

subjects affected / exposed	2 / 123 (1.63%)	0 / 92 (0.00%)		
occurrences causally related to treatment / all	2 / 2	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		

Endocrine disorders

Adrenal insufficiency

subjects affected / exposed	2 / 123 (1.63%)	2 / 92 (2.17%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Nose deformity			
subjects affected / exposed	1 / 123 (0.81%)	1 / 92 (1.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Tonsillitis			
subjects affected / exposed	1 / 123 (0.81%)	0 / 92 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 123 (0.81%)	0 / 92 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ketoacidosis			
subjects affected / exposed	1 / 123 (0.81%)	0 / 92 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Pasireotide LAR overall	Up-titrated to Pasireotide LAR 60 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	112 / 123 (91.06%)	83 / 92 (90.22%)	
Investigations			
Blood glucose increased			
subjects affected / exposed	8 / 123 (6.50%)	7 / 92 (7.61%)	
occurrences (all)	11	10	
Cardiac disorders			

Sinus bradycardia			
subjects affected / exposed	9 / 123 (7.32%)	8 / 92 (8.70%)	
occurrences (all)	21	19	
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 123 (11.38%)	11 / 92 (11.96%)	
occurrences (all)	19	15	
Paraesthesia			
subjects affected / exposed	6 / 123 (4.88%)	6 / 92 (6.52%)	
occurrences (all)	6	6	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	13 / 123 (10.57%)	11 / 92 (11.96%)	
occurrences (all)	13	11	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	7 / 123 (5.69%)	4 / 92 (4.35%)	
occurrences (all)	12	9	
Fatigue			
subjects affected / exposed	8 / 123 (6.50%)	4 / 92 (4.35%)	
occurrences (all)	8	4	
Injection site pain			
subjects affected / exposed	4 / 123 (3.25%)	2 / 92 (2.17%)	
occurrences (all)	4	2	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	6 / 123 (4.88%)	6 / 92 (6.52%)	
occurrences (all)	6	6	
Abdominal pain			
subjects affected / exposed	12 / 123 (9.76%)	10 / 92 (10.87%)	
occurrences (all)	22	19	
Diarrhoea			
subjects affected / exposed	22 / 123 (17.89%)	16 / 92 (17.39%)	
occurrences (all)	35	28	
Nausea			

subjects affected / exposed	7 / 123 (5.69%)	5 / 92 (5.43%)	
occurrences (all)	8	5	

Hepatobiliary disorders
   Cholelithiasis

subjects affected / exposed	10 / 123 (8.13%)	8 / 92 (8.70%)	
occurrences (all)	12	10	

   Hepatic steatosis

subjects affected / exposed	7 / 123 (5.69%)	7 / 92 (7.61%)	
occurrences (all)	7	7	

Skin and subcutaneous tissue disorders
   Alopecia

subjects affected / exposed	11 / 123 (8.94%)	8 / 92 (8.70%)	
occurrences (all)	11	8	

Musculoskeletal and connective tissue disorders
   Arthralgia

subjects affected / exposed	7 / 123 (5.69%)	6 / 92 (6.52%)	
occurrences (all)	8	7	

   Back pain

subjects affected / exposed	6 / 123 (4.88%)	4 / 92 (4.35%)	
occurrences (all)	6	4	

   Muscle spasms

subjects affected / exposed	6 / 123 (4.88%)	5 / 92 (5.43%)	
occurrences (all)	7	6	

   Osteoarthritis

subjects affected / exposed	2 / 123 (1.63%)	0 / 92 (0.00%)	
occurrences (all)	2	0	

   Pain in extremity

subjects affected / exposed	8 / 123 (6.50%)	8 / 92 (8.70%)	
occurrences (all)	11	11	

   Tendonitis

subjects affected / exposed	4 / 123 (3.25%)	2 / 92 (2.17%)	
occurrences (all)	4	2	

Infections and infestations
   Bronchitis

subjects affected / exposed	5 / 123 (4.07%)	3 / 92 (3.26%)	
occurrences (all)	6	3	

Cystitis			
subjects affected / exposed	2 / 123 (1.63%)	0 / 92 (0.00%)	
occurrences (all)	5	0	
Influenza			
subjects affected / exposed	11 / 123 (8.94%)	7 / 92 (7.61%)	
occurrences (all)	13	8	
Upper respiratory tract infection			
subjects affected / exposed	8 / 123 (6.50%)	7 / 92 (7.61%)	
occurrences (all)	16	15	
Viral upper respiratory tract infection			
subjects affected / exposed	11 / 123 (8.94%)	7 / 92 (7.61%)	
occurrences (all)	14	7	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	29 / 123 (23.58%)	22 / 92 (23.91%)	
occurrences (all)	35	27	
Hyperglycaemia			
subjects affected / exposed	56 / 123 (45.53%)	39 / 92 (42.39%)	
occurrences (all)	76	52	
Hypoglycaemia			
subjects affected / exposed	13 / 123 (10.57%)	10 / 92 (10.87%)	
occurrences (all)	24	17	
Impaired fasting glucose			
subjects affected / exposed	7 / 123 (5.69%)	7 / 92 (7.61%)	
occurrences (all)	9	9	

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

 None reported