



## Clinical trial results:

**An open label, multicenter pasireotide roll over protocol for patients who have completed a previous Novartis sponsored pasireotide study and are judged by the investigator to benefit from continued pasireotide treatment**

### Summary

EudraCT number	2013-000267-84
Trial protocol	IT BE ES GR FR PL PT BG
Global end of trial date	25 July 2023

### Results information

Result version number	v1 (current)
This version publication date	20 February 2025
First version publication date	20 February 2025

### Trial information

#### Trial identification

Sponsor protocol code	CSOM230B2412
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01794793
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Recordati AG
Sponsor organisation address	Uferstrasse 90, , Basel, Switzerland,
Public contact	Clinical Trial Information Desk, Recordati AG, clinicaltrials.endocrinology@recordati.com
Scientific contact	Clinical Trial Information Desk, Recordati AG, clinicaltrials.endocrinology@recordati.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	29 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 July 2023
Global end of trial reached?	Yes
Global end of trial date	25 July 2023
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate long term safety data and allow continued use of pasireotide in patients who are on pasireotide treatment in a Novartis-sponsored study and are benefiting from the treatment as judged by the investigator

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 May 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 30
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Portugal: 3
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Belgium: 37
Country: Number of subjects enrolled	Bulgaria: 4
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Germany: 12
Country: Number of subjects enrolled	Greece: 2
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Argentina: 6
Country: Number of subjects enrolled	India: 20
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Japan: 6
Country: Number of subjects enrolled	Korea, Republic of: 3
Country: Number of subjects enrolled	Malaysia: 6
Country: Number of subjects enrolled	Mexico: 10
Country: Number of subjects enrolled	Peru: 16

Country: Number of subjects enrolled	Brazil: 65
Country: Number of subjects enrolled	Romania: 8
Country: Number of subjects enrolled	Russian Federation: 16
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	Türkiye: 16
Country: Number of subjects enrolled	United States: 16
Country: Number of subjects enrolled	Thailand: 15
Country: Number of subjects enrolled	Canada: 7
Worldwide total number of subjects	337
EEA total number of subjects	129

Notes:

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### **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)	305
From 65 to 84 years	32
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Eligible patients were consented and subsequently continued their treatment with pasireotide using the same formulation they were receiving in the parent study at roll-over.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Pasireotide subcutaneous

Arm description:

0.3mg, 0.6mg and 0.9mg. Doses to be taken BID or TID, dependent on parent study guidelines. Cabergoline may be combined in this arm for Cushing's Disease and Acromegaly patients.

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

Dosage and administration details:

Administered subcutaneously in strengths 0.3mg, 0.6mg and 0.9mg. Doses to be taken BID or TID, dependent on parent study guidelines.

<b>Arm title</b>	Pasireotide LAR
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Arm description:

10mg, 20mg, 40mg and 60mg. All doses to be taken q28days. Strength is dependent on parent study guidelines.

Arm type	Experimental
Investigational medicinal product name	Pasireotide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for prolonged-release suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Long Acting Release is administered by a single intramuscular (i.m.) monthly injection. The strengths are 10mg, 20mg, 40mg and 60mg. All doses to be taken q28days. Strength is dependent on parent study guidelines.

<b>Number of subjects in period 1</b>	Pasireotide subcutaneous	Pasireotide LAR
Started	38	299
Completed	22	217
Not completed	16	82
Adverse event, serious fatal	1	5
Consent withdrawn by subject	6	18
not requiring treatment	1	-
Adverse event, non-fatal	3	14
Lost to follow-up	-	7
patient not longer requiring treatment	-	13
administrative problem	1	2
Lack of efficacy	4	18
Protocol deviation	-	5

## Period 2

Period 2 title	Post-treatment Follow-up
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

## Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Pasireotide subcutaneous

### Arm description:

0.3mg, 0.6mg and 0.9mg. Doses to be taken BID or TID, dependent on parent study guidelines. Cabergoline may be combined in this arm for Cushing's Disease and Acromegaly patients.

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

### Dosage and administration details:

Administered subcutaneously in strengths 0.3mg, 0.6mg and 0.9mg. Doses to be taken BID or TID, dependent on parent study guidelines.

<b>Arm title</b>	Pasireotide LAR
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### Arm description:

Administered subcutaneously in strengths 0.3mg, 0.6mg and 0.9mg. Doses to be taken BID or TID, dependent on parent study guidelines.

Arm type	Experimental
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Investigational medicinal product name	Pasireotide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for prolonged-release suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Long Acting Release is administered by a single intramuscular (i.m.) monthly injection. The strengths are 10mg, 20mg, 40mg and 60mg. All doses to be taken q28days. Strength is dependent on parent study guidelines.

<b>Number of subjects in period 2<sup>[1]</sup></b>	Pasireotide subcutaneous	Pasireotide LAR
Started	19	130
Completed	11	99
Not completed	8	31
Consent withdrawn by subject	2	4
Adverse event, non-fatal	2	6
Lost to follow-up	-	3
administrative problem	2	3
Lack of efficacy	2	12
Protocol deviation	-	3

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: Follow-up for safety evaluation 30 days following last dose of the s.c. formulation or 84 days following last dose of the LAR formulation (based on study completion CRF). In order to be consistent with previous reports, patients who completed study treatment were also included here. The number of participants to start the follow-up Period is not equal to the number who completed previous Period as they did not continued the study.

## Baseline characteristics

### Reporting groups

Reporting group title	Treatment period
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Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	337	337	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	305	305	
From 65-84 years	32	32	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	47.6		
standard deviation	± 12.43	-	
Gender categorical			
Units: Subjects			
Female	190	190	
Male	147	147	

## End points

### End points reporting groups

Reporting group title	Pasireotide subcutaneous
Reporting group description: 0.3mg, 0.6mg and 0.9mg. Doses to be taken BID or TID, dependent on parent study guidelines. Cabergoline may be combined in this arm for Cushing's Disease and Acromegaly patients.	
Reporting group title	Pasireotide LAR
Reporting group description: 10mg, 20mg, 40mg and 60mg. All doses to be taken q28days. Strength is dependent on parent study guidelines.	
Reporting group title	Pasireotide subcutaneous
Reporting group description: 0.3mg, 0.6mg and 0.9mg. Doses to be taken BID or TID, dependent on parent study guidelines. Cabergoline may be combined in this arm for Cushing's Disease and Acromegaly patients.	
Reporting group title	Pasireotide LAR
Reporting group description: Administered subcutaneously in strengths 0.3mg, 0.6mg and 0.9mg. Doses to be taken BID or TID, dependent on parent study guidelines.	

### Primary: Incidence of adverse events to evaluate long term safety data

End point title	Incidence of adverse events to evaluate long term safety
End point description: The Safety Set included all patients who received at least one dose of study medication (pasireotide) after enrolling into the roll-over protocol	
End point type	Primary
End point timeframe: Up to approximately 10 years	

#### 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: The assessment of safety was based on the frequency and severity of AEs, adverse events of special interest (AESIs), and SAEs; summarised descriptively overall and by indication and formulation. No formal analyses were performed beyond descriptive statistics, and no hypotheses were tested.

End point values	Pasireotide subcutaneous	Pasireotide LAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	299		
Units: participants				
number (not applicable)				
AE: all grades	26	239		
AEs : Grades $\geq 3$	9	93		
Treatment-related AEs : All grades	13	114		
Treatment-related AEs : Grades $\geq 3$	2	27		
SAEs : All grades	10	81		
SAEs : Grades $\geq 3$	1	66		
Fatal SAEs : All grades	1	7		
Treatment-related fatal SAEs : All grades	0	0		

Treatment-related fatal SAEs : Grades $\geq 3$	0	0		
AEs leading to discontinuation : All grades	3	17		
AEs leading to discontinuation : Grades $\geq 3$	1	10		
TAEs leading to discontinuation: all grades	3	13		
TAEs leading to discontinuation: Grades $\geq 3$	1	6		
AEs leading to dose adjustment/interruption: All	4	35		
AEs leading to dose adjustment/interruption :G $\geq 3$	0	13		
AEs requiring additional therapy : All	17	203		
AEs requiring additional therapy : Grades $\geq 3$	4	58		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of patients with clinical benefit as assessed by the investigator

End point title	Percentage of patients with clinical benefit as assessed by the investigator
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End point description:

Efficacy was assessed by the investigator at each scheduled visit using a binary (yes/no) response confirming the investigator's judgement of clinical benefit (via the question: "Does investigator confirm that the subject continues to have clinical benefit from the study treatment"). No other measures of efficacy were used in this study.

End point type	Secondary
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End point timeframe:

up to approximately 10 years

End point values	Pasireotide subcutaneous	Pasireotide LAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	299		
Units: participants				
number (not applicable)				
month 3	29	256		
month 6	28	250		
month 12	21	234		
month 18	19	216		
month 24	17	198		
month 36	14	177		
month 48	15	162		
month 60	12	140		
month 72	12	98		
month 84	8	21		

month 96	5	1		
month 108	5	1		
month 120	0	2		

### **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Pasireotide s.c.: From start of study treatment up to 1 month after study treatment discontinuation (about 10 years) Pasireotide LAR: From start of study treatment up to 3 months after study treatment discontinuation (about 10 years)

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

### Reporting groups

Reporting group title	All participants
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Reporting group description: -

<b>Serious adverse events</b>	All participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	91 / 337 (27.00%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events	8		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colon cancer			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Leiomyoma			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pituitary tumour recurrent subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Prostate cancer metastatic subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thyroid cancer subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aortic aneurysm subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
deep vein thrombosis subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Distributive shock subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertensive emergency subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral arterial occlusive disease subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral embolism			

subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 1		
Thrombophlebitis			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Menorrhagia			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metrorrhagia			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Weight decreased			

subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Injury, poisoning and procedural complications</b>			
Femur fracture			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
joint injury			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meniscus injury			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Poisoning			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suture related complication			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper limb fracture			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Cardiac disorders</b>			
Acute myocardial infarction			
subjects affected / exposed	2 / 337 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Cardiac failure			
subjects affected / exposed	2 / 337 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Coronary artery disease			
subjects affected / exposed	2 / 337 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	2 / 337 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arrhythmia			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiorespiratory arrest			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial Ischaemia			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syringomyelia			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Epilepsy				
subjects affected / exposed	2 / 337 (0.59%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	1 / 337 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dementia				
subjects affected / exposed	1 / 337 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	1 / 337 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemic coma				
subjects affected / exposed	1 / 337 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemic seizure				
subjects affected / exposed	1 / 337 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myasthenia gravis				
subjects affected / exposed	1 / 337 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transient Ischaemic attack				
subjects affected / exposed	1 / 337 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Confusional state				

subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mental disorder			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric decompensation			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal adhesion			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal fat apron			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Anal fistula				
subjects affected / exposed	1 / 337 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	1 / 337 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 337 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Large Intestin Polyp				
subjects affected / exposed	1 / 337 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	1 / 337 (0.30%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	1 / 337 (0.30%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	1 / 337 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stasis Syndrome				
subjects affected / exposed	1 / 337 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Umbelical hernia				

subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hepatobiliary disorders</b>			
<b>Cholelithiasis</b>			
subjects affected / exposed	9 / 337 (2.67%)		
occurrences causally related to treatment / all	8 / 9		
deaths causally related to treatment / all	0 / 0		
<b>Cholecystitis</b>			
subjects affected / exposed	5 / 337 (1.48%)		
occurrences causally related to treatment / all	3 / 5		
deaths causally related to treatment / all	0 / 0		
<b>Cholangitis chronic</b>			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Cholecystitis acute</b>			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Cholecystitis chronic</b>			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hydrocholecystitis</b>			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hyperbilirubinaemia</b>			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Renal and urinary disorders</b>			

Nephrolithiasis			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperadrenocorticism			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
back pain			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Foot deformity			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Neck mass			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tendon disorder			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
subjects affected / exposed	8 / 337 (2.37%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 1		
Cellulitis			
subjects affected / exposed	4 / 337 (1.19%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	3 / 337 (0.89%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	2 / 337 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	2 / 337 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Abscess jaw			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute sinusitis			

subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronavirus infection			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea infectious			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocarditis			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Furuncle			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infected dermal cyst			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			

subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Meningitis</b>			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>peritonitis</b>			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Pneumonia pseudomonal</b>			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Pneumonia viral</b>			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
<b>Post procedural infection</b>			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Pyelonephritis acute</b>			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Sepsis</b>			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Sinusitis</b>			

subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suspected COVID-19			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	2 / 337 (0.59%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	2 / 337 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Diabetes mellitus			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diabetic ketosis			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diabetic metabolic decompensation			

subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hyperglycaemia</b>			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hyponatraemia</b>			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	All participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	220 / 337 (65.28%)		
<b>Vascular disorders</b>			
Hypertension			
subjects affected / exposed	25 / 337 (7.42%)		
occurrences (all)	25		
<b>Nervous system disorders</b>			
Headache			
subjects affected / exposed	22 / 337 (6.53%)		
occurrences (all)	22		
<b>Gastrointestinal disorders</b>			
Diarrhoea			
subjects affected / exposed	17 / 337 (5.04%)		
occurrences (all)	17		
<b>Musculoskeletal and connective tissue disorders</b>			
Back pain			
subjects affected / exposed	30 / 337 (8.90%)		
occurrences (all)	30		
<b>Infections and infestations</b>			

Nasopharyngitis subjects affected / exposed occurrences (all)	32 / 337 (9.50%) 32		
COVID-19 subjects affected / exposed occurrences (all)	20 / 337 (5.93%) 20		
Urinary tract infection subjects affected / exposed occurrences (all)	19 / 337 (5.64%) 19		
Influenza subjects affected / exposed occurrences (all)	18 / 337 (5.34%) 18		
Metabolism and nutrition disorders			
Hyperglycaemia subjects affected / exposed occurrences (all)	23 / 337 (6.82%) 23		
Diabetes mellitus subjects affected / exposed occurrences (all)	18 / 337 (5.34%) 18		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 March 2016	Clarified the main objective of this study, the previous secondary objective "To collect long-term data on serious adverse events and adverse events of special interest" was elevated to primary objective. In addition, the protocol was amended to clarify the safety monitoring guidance and to include the collection of all AEs (including non-serious AEs) and an investigator attestation of continued clinical benefit.
29 September 2017	Included language on the trial end date to meet the regulatory guidelines of the Medicine and Health Research Authority, in the United Kingdom (UK). Clarified that this trial was deemed to be a voluntary PASS by Novartis Regulatory Affairs in 2016. An interim analysis was to be performed in 2017, and every 2 years thereafter, until the final database lock. Clarified the visit schedules for patients taking pasireotide s.c. and those taking pasireotide LAR, and further highlighted the required timelines for using highly effective methods of contraception after last dose of study medication
08 March 2018	The main purpose of this amendment is to: • Update the trial selection criteria to allow patients from Novartis-sponsored trials, being treated with pasireotide alone or in combination with another treatment for Cushing's Disease and Acromegaly, to participate in this study. Several of the participating parent protocols permit for pasireotide to be administered in combination with another medical therapy. Revising the selection criteria would ensure those patients receiving clinical benefit would have continued access to the combination treatment. Combination treatment through this rollover would only be available for patients with Cushing's Disease or Acromegaly.
06 May 2020	Since Novartis had signed an agreement to transfer the worldwide rights of Signifor® and Signifor® LAR to Recordati, all applicable sections of the protocol updated to substitute the name of the current sponsor Novartis with the name of the new sponsor Recordati or of IQVIA on behalf of Recordati, as applicable.
02 November 2021	It is anticipated that pasireotide will not be commercially available and reimbursed in all participating countries at study end. In order to ensure that patients deriving clinical benefit from pasireotide will continue receiving treatment with this drug outside the frame of the clinical trial, they will be allowed to obtain pasireotide through country-specific programmes as soon as they become available – even prior to the end of the study. This will ensure treatment continuity (applicable to Brazil, France, Germany, India, Italy, Malaysia, Mexico, Peru and Thailand)

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported