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Trial record **1 of 1** for: CSOM230C2303

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Efficacy and Safety of Pasireotide Long Acting Release vs. Octreotide Long Acting Release in Patients With Metastatic Carcinoid Disease

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

Information provided by (Responsible Party):
Novartis (Novartis Pharmaceuticals)

ClinicalTrials.gov Identifier:
NCT00690430

First received: May 15, 2008
Last updated: June 25, 2013
Last verified: June 2013
History of Changes

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Results First Received: April 5, 2013

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator); Primary Purpose: Treatment
Condition:	Symptomatic Refractory Resistant Carcinoid Disease
Interventions:	Drug: Pasireotide Drug: Octreotide

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
186 patients were screened and 110 were randomized into the study.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Pasireotide LAR	Patients assigned to pasireotide LAR will receive a 60 mg dose of pasireotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 40 mg is permitted if tolerability issues arise. In addition, after 24 hours of the first LAR injections the patients were permitted to use pasireotide s.c. formulation for breakthrough symptoms as needed.
Octreotide LAR	Patients assigned to octreotide LAR will receive a 40mg dose of octreotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 30 mg is permitted if tolerability issues arise. Patients requiring a dose reduction are to return to the higher dose once the tolerability issue is resolved, if required for efficacy. In addition, after 24 hours of the first LAR injections the patients were permitted to use octreotide s.c. formulation for breakthrough symptoms as needed.
Extension: Octreotide LAR/Pasireotide LAR	After 6 month double blind core period, non-responders on Octreotide were given option to cross over to Pasireotide LAR in the Extension Phase of study.

Participant Flow for 2 periods

Period 1: Core Phase

	Pasireotide LAR	Octreotide LAR	Extension: Octreotide LAR/Pasireotide LAR
STARTED	53 [1]	57	0 [2]
COMPLETED	35	34	0
NOT COMPLETED	18	23	0
Abnormal Laboratory value	0	1	0
Adverse Event	5	1	0
Death	0	2	0
Protocol Violation	1	0	0
Withdrawal by Subject	3	3	0
Subject no longer requires study drug	1	0	0
Lack of Efficacy	8	10	0
Administrative Problems	0	1	0
Early Termination	0	5	0

[1] "Started" indicates Full Analysis Set (FAS) and Safety Set.
[2] This arm belongs to Extension Phase.

Period 2: Extension Phase

	Pasireotide LAR	Octreotide LAR	Extension: Octreotide LAR/Pasireotide LAR
STARTED	20 [1]	6 [1]	15 [1]
COMPLETED	2	1	2
NOT COMPLETED	18	5	13
Lack of Efficacy	3	1	4
Abnormal Lab Values	1	0	0
Abnormal test procedure results	1	0	0

Administrative Problems	**0**	**1**	**1**
Adverse Event	**2**	**1**	**2**
Death	**1**	**1**	**1**
Withdrawal by Subject	**0**	**0**	**2**
Early Termination	**10**	**1**	**3**

[1] Only those patients (except from UK) who received clinical benefit could extend therapy in extension

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Pasireotide LAR	Patients assigned to pasireotide LAR will receive a 60 mg dose of pasireotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 40 mg is permitted if tolerability issues arise. In addition, after 24 hours of the first LAR injections the patients were permitted to use pasireotide s.c. formulation for breakthrough symptoms as needed.
Octreotide LAR	Patients assigned to octreotide LAR will receive a 40mg dose of octreotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 30 mg is permitted if tolerability issues arise. Patients requiring a dose reduction are to return to the higher dose once the tolerability issue is resolved, if required for efficacy. In addition, after 24 hours of the first LAR injections the patients were permitted to use octreotide s.c. formulation for breakthrough symptoms as needed.
Total	Total of all reporting groups

Baseline Measures

	Pasireotide LAR	Octreotide LAR	Total
Number of Participants [units: participants]	**53**	**57**	**110**
Age [units: Years] Mean (Standard Deviation)	**61.2 (9.21)**	**62.8 (11.91)**	**62 (10.67)**
Gender [units: Participants]			
Female	**24**	**23**	**47**
Male	**29**	**34**	**63**

Outcome Measures

Hide All Outcome Measures

1. Primary: Percentage of Patients Who Achieved Clinical Symptom Improvement by Randomization Stratum and Treatment. [Time Frame: Month 6]

Measure Type	Primary
Measure Title	Percentage of Patients Who Achieved Clinical Symptom Improvement by Randomization Stratum and Treatment.
Measure Description	Percentage of patients who received clinical benefit in symptom (diarrhea and/or flushing) improvement as: Diarrhea (D)+Flushing (F): Patients with a daily mean number (#) of at least four bowel movements and a total of five or more flushing episodes. Clinical Benefit Response Criteria (CBRC): <4 daily mean bowel movements AND at least 20% reduction from Baseline in the daily mean # of bowel movements AND any reduction in the total # of flushing episodes compared with Baseline. (D) Patients with a daily mean # of at least four bowel movements and a total # of <5 flushing episodes. (CBRC) <4 daily mean bowel movements AND at least a 20% reduction from Baseline in the daily mean # of bowel movements. (F) Patients with a total # of at least 14 flushing episodes and a daily mean # of <4 bowel movements (CBRC) At least a 30% reduction from Baseline in the total # of flushing episodes.

Time Frame	Month 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Efficacy analyzable set consists of subset of FAS patients who were randomized at least six months prior to futility interim analysis data cut-off. It is for the primary efficacy analysis and secondary efficacy analysis except for tumor response assessment. Data reported was based on randomized patients at the time of the interim analysis.

Reporting Groups

	Description
Pasireotide LAR	Patients assigned to pasireotide LAR will receive a 60 mg dose of pasireotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 40 mg is permitted if tolerability issues arise. In addition, after 24 hours of the first LAR injections the patients were permitted to use pasireotide s.c. formulation for breakthrough symptoms as needed.
Octreotide LAR	Patients assigned to octreotide LAR will receive a 40mg dose of octreotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 30 mg is permitted if tolerability issues arise. Patients requiring a dose reduction are to return to the higher dose once the tolerability issue is resolved, if required for efficacy. In addition, after 24 hours of the first LAR injections the patients were permitted to use octreotide s.c. formulation for breakthrough symptoms as needed.

Measured Values

	Pasireotide LAR	**Octreotide LAR**
Number of Participants Analyzed [units: participants]	**43**	**45**
Percentage of Patients Who Achieved Clinical Symptom Improvement by Randomization Stratum and Treatment. [units: Percentage of Participants] Number (95% Confidence Interval)		

Diarrhea and Flushing (N=37, 39)	**13.5 (4.5 to 28.8)**	**28.2 (15.0 to 44.9)**
Diarrhea (N=2, 5)	**100 (15.8 to 100)**	**20.0 (0.5 to 71.6)**
Flushing (N=4, 1)	**50 (6.8 to 93.2)**	**0.0 (0.0 to 97.5)**
Overall (N=43, 45)	**20.9 (10.0 to 36.0)**	**26.7 (14.6 to 41.9)**

No statistical analysis provided for Percentage of Patients Who Achieved Clinical Symptom Improvement by Randomization Stratum and Treatment.

2. Secondary: Improvement in Daily Mean Number of Diarrhea Bowel Movement Episodes by Randomization Stratum and Treatment. [Time Frame: 6 months]

Measure Type	Secondary
Measure Title	Improvement in Daily Mean Number of Diarrhea Bowel Movement Episodes by Randomization Stratum and Treatment.
Measure Description	Percent change from Baseline in mean daily bowel movements at Month 6 were compared between the two treatment groups using ANCOVA model with treatment as the main effect and symptom levels at Baseline (e.g. mean daily bowel movement at Baseline) and randomization stratum (D+F or D) as covariates. Percentage change = (Month 6 - baseline)/baseline.
Time Frame	6 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

The Efficacy analyzable set consists of the subset of FAS patients who were randomized at least six months prior to the futility DMC data cut-off. Patients who had symptoms at baseline and at 6 months were included in this analysis.

Reporting Groups

	Description
Pasireotide LAR	Patients assigned to pasireotide LAR will receive a 60 mg dose of pasireotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 40 mg is permitted if tolerability issues arise. In addition, after 24 hours of the first LAR injections the patients were permitted to use pasireotide s.c. formulation for breakthrough symptoms as needed.
Octreotide LAR	Patients assigned to octreotide LAR will receive a 40mg dose of octreotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 30 mg is permitted if tolerability issues arise. Patients requiring a dose reduction are to return to the higher dose once the tolerability issue is resolved, if required for efficacy. In addition, after 24 hours of the first LAR injections the patients were permitted to use octreotide s.c. formulation for breakthrough symptoms as needed.

Measured Values

	Pasireotide LAR	Octreotide LAR
Number of Participants Analyzed [units: participants]	**26**	**32**
Improvement in Daily Mean Number of Diarrhea Bowel Movement Episodes by Randomization Stratum and Treatment. [units: Percentage of Episodes] Mean (Standard Deviation)		
Diarrhea and Flushing (N=24, 28)	**-23.5 (24.28)**	**-38.4 (28.74)**
Predominantly Diarrhea (D) (N=2, 4)	**-44.2 (10.26)**	**-22.9 (31.68)**
Overall (N=26, 32)	**-25.1 (24.04)**	**-36.5 (29.05)**

No statistical analysis provided for Improvement in Daily Mean Number of Diarrhea Bowel Movement Episodes by Randomization Stratum and Treatment.

3. Secondary: Improvement in Daily Mean Number of Flushing Episodes by Randomization Stratum and Treatment. [Time Frame: 6 months]

Measure Type	Secondary
Measure Title	Improvement in Daily Mean Number of Flushing Episodes by Randomization Stratum and Treatment.
Measure Description	Percent change from Baseline in total number of flushing episodes comprising Month 6 were compared between the two treatment groups using ANCOVA model with treatment as the main effect and symptom levels at Baseline (e.g. total number of flushing episodes at Baseline) and randomization stratum (D+F or F) as covariates.
Time Frame	6 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Efficacy analyzable set consists of the subset of FAS patients who were randomized at least six months prior to the futility DMC data cut-off. Patients were analyzed according the treatment they were assigned to at randomization. (ITT) principle.

Reporting Groups

	Description
Pasireotide LAR	Patients assigned to pasireotide LAR will receive a 60 mg dose of pasireotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 40 mg is permitted if tolerability issues arise. In addition, after 24 hours of the first LAR injections the patients were permitted to use pasireotide s.c. formulation for breakthrough symptoms as needed.
Octreotide LAR	Patients assigned to octreotide LAR will receive a 40mg dose of octreotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 30 mg is permitted if tolerability issues arise. Patients requiring a dose reduction are to return to the higher dose once the tolerability issue is resolved, if required for efficacy. In addition, after 24 hours of the first LAR injections the patients were permitted to use octreotide s.c. formulation for breakthrough symptoms as needed.

Measured Values

	Pasireotide LAR	Octreotide LAR
Number of Participants Analyzed [units: participants]	**28**	**29**
Improvement in Daily Mean Number of Flushing Episodes by Randomization Stratum and Treatment. [units: Percentage of Episodes] Mean (Standard Deviation)		
Diarrhea and Flushing (N=24, 28)	**-41.0 (41.06)**	**-52.8 (32.18)**
Predominately Flushing (N=4, 1)	**-48.4 (23.13)**	**47.2 [1]**
Overall (N=28, 29)	**-42.1 (38.76)**	**-49.4 (36.65)**

[1] Standard Deviation could not be calculated because there was only 1 patient analyzed.

No statistical analysis provided for Improvement in Daily Mean Number of Flushing Episodes by Randomization Stratum and Treatment.

4. Secondary: Pasireotide LAR vs. Octreotide LAR on Time to Symptom Response. [Time Frame: Month 6]

Measure Type	Secondary
Measure Title	Pasireotide LAR vs. Octreotide LAR on Time to Symptom Response.
Measure Description	No text entered.
Time Frame	Month 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or

another method. Also provides relevant details such as imputation technique, as appropriate.

This Outcome Measure was planned in the protocol but not included in the analysis due to early termination of study due to lack of efficacy in symptom control.

Reporting Groups

	Description
Pasireotide LAR	Patients assigned to pasireotide LAR will receive a 60 mg dose of pasireotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 40 mg is permitted if tolerability issues arise. In addition, after 24 hours of the first LAR injections the patients were permitted to use pasireotide s.c. formulation for breakthrough symptoms as needed.
Octreotide LAR	Patients assigned to octreotide LAR will receive a 40mg dose of octreotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 30 mg is permitted if tolerability issues arise. Patients requiring a dose reduction are to return to the higher dose once the tolerability issue is resolved, if required for efficacy. In addition, after 24 hours of the first LAR injections the patients were permitted to use octreotide s.c. formulation for breakthrough symptoms as needed.

Measured Values

	Pasireotide LAR	Octreotide LAR
Number of Participants Analyzed [units: participants]	**0**	**0**
Pasireotide LAR vs. Octreotide LAR on Time to Symptom Response.		

No statistical analysis provided for Pasireotide LAR vs. Octreotide LAR on Time to Symptom Response.

5. Secondary: Objective Tumor Response Rate Assessed by Investigator [Time Frame: Month 6]

Measure Type	Secondary
Measure Title	Objective Tumor Response Rate Assessed by Investigator

Measure Description	Baseline evaluations were to include Triphasic CT scan or MRI of the abdomen. Triphasic CT or MRIs were to be read by same radiologist at each assessment, measuring the same target and non-target lesions and accounting for all lesions that were present at Baseline. All known disease was accounted for when assessing objective tumor status. Current objective tumor status was to be captured on Tumor Assessment CRF. Objective response rate was defined by RECIST criteria: Partial response (PR) must have ≥ 30% decrease in the sum of longest diameter of all target lesions, from the baseline sum. Complete response (CR) must have disappearance of all target and non-target lesions. For CR or PR, tumor measurements must be confirmed by 2nd assessments within 4 weeks. Progression = 20% increase in the sum of longest diameter of all target lesions, from smallest sum of longest diameter of all target lesions recorded at or after baseline; or a new lesion; or progression of non-target lesions.
Time Frame	Month 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full Analysis Set (FAS) consists of all patients randomized into the study. Patients were analyzed according to the treatment they were assigned to at randomization. Patients randomized 6 months before the final clinical cutoff date were included in this analysis.

Reporting Groups

	Description
Pasireotide LAR	Patients assigned to pasireotide LAR will receive a 60 mg dose of pasireotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 40 mg is permitted if tolerability issues arise. In addition, after 24 hours of the first LAR injections the patients were permitted to use pasireotide s.c. formulation for breakthrough symptoms as needed.
Octreotide LAR	Patients assigned to octreotide LAR will receive a 40mg dose of octreotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 30 mg is permitted if tolerability issues arise. Patients requiring a dose reduction are to return to the higher dose once the tolerability issue is resolved, if required for efficacy. In addition, after 24 hours of the first LAR injections the patients were permitted to use octreotide s.c. formulation for breakthrough symptoms as needed.

Measured Values

	Pasireotide LAR	Octreotide LAR
Number of Participants Analyzed [units: participants]	**51**	**52**
Objective Tumor Response Rate Assessed by Investigator [units: Percentage of Participants] Number (95% Confidence Interval)	**2.0 (0.0 to 10.4)**	**3.8 (0.5 to 13.2)**

No statistical analysis provided for Objective Tumor Response Rate Assessed by Investigator

6. Secondary: Pasireotide LAR vs. Octreotide LAR on Disease Control Rate Based on RECIST Criteria [Time Frame: Month 6]

Measure Type	Secondary
Measure Title	Pasireotide LAR vs. Octreotide LAR on Disease Control Rate Based on RECIST Criteria
Measure Description	Disease control rate (DCR) is the proportion of patients with a best overall response of Complete Response (CR) or Partial Response (PR) or Stable Disease (SD). Complete Response (CR): Disappearance of all target lesions Partial Response (PR): At least a 30% decrease in the sum of the longest diameter of all target lesions, taking as reference the baseline sum of the longest diameters. Progressive Disease (PD): At least a 20% increase in the sum of the longest diameter of all measured target lesions, taking as reference the smallest sum of longest diameter of all target lesions recorded at or after baseline, or a new lesion; or progression of non-target lesions. Stable Disease (SD): Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for PD. Unknown (UNK) Progression has not been documented and one or more target lesions have not been assessed or have been assessed using a different method than baseline.
Time Frame	Month 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full Analysis Set (FAS) consists of all patients randomized into the study. Following the intent-to-treat principle, patients were analyzed

according to the treatment they were assigned to at randomization. Patients with analyzable data at month 6 were included in this analysis.

Reporting Groups

	Description
Pasireotide LAR	Patients assigned to pasireotide LAR will receive a 60 mg dose of pasireotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 40 mg is permitted if tolerability issues arise. In addition, after 24 hours of the first LAR injections the patients were permitted to use pasireotide s.c. formulation for breakthrough symptoms as needed.
Octreotide LAR	Patients assigned to octreotide LAR will receive a 40mg dose of octreotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 30 mg is permitted if tolerability issues arise. Patients requiring a dose reduction are to return to the higher dose once the tolerability issue is resolved, if required for efficacy. In addition, after 24 hours of the first LAR injections the patients were permitted to use octreotide s.c. formulation for breakthrough symptoms as needed.

Measured Values

	Pasireotide LAR	Octreotide LAR
Number of Participants Analyzed [units: participants]	**51**	**52**
Pasireotide LAR vs. Octreotide LAR on Disease Control Rate Based on RECIST Criteria [units: Percentage of participants] Number (95% Confidence Interval)	**62.7 (48.1 to 75.9)**	**46.2 (32.2 to 60.5)**

No statistical analysis provided for Pasireotide LAR vs. Octreotide LAR on Disease Control Rate Based on RECIST Criteria

7. Secondary: Pasireotide LAR vs. Octreotide LAR on Quality of Life Assessed by FACIT-D Questionnaire [Time Frame: Month 6]

Measure Type	Secondary
Measure Title	Pasireotide LAR vs. Octreotide LAR on Quality of Life Assessed by FACIT-D Questionnaire
Measure Description	No text entered.

Time Frame	Month 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
This Outcome Measure was planned in the protocol but not included in the analysis due to early termination of study due to lack of efficacy in symptom control.

Reporting Groups

	Description
Pasireotide LAR	Patients assigned to pasireotide LAR will receive a 60 mg dose of pasireotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 40 mg is permitted if tolerability issues arise. In addition, after 24 hours of the first LAR injections the patients were permitted to use pasireotide s.c. formulation for breakthrough symptoms as needed.
Octreotide LAR	Patients assigned to octreotide LAR will receive a 40mg dose of octreotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 30 mg is permitted if tolerability issues arise. Patients requiring a dose reduction are to return to the higher dose once the tolerability issue is resolved, if required for efficacy. In addition, after 24 hours of the first LAR injections the patients were permitted to use octreotide s.c. formulation for breakthrough symptoms as needed.

Measured Values

	Pasireotide LAR	**Octreotide LAR**
Number of Participants Analyzed [units: participants]	**0**	**0**
Pasireotide LAR vs. Octreotide LAR on Quality of Life Assessed by FACIT-D Questionnaire		

No statistical analysis provided for Pasireotide LAR vs. Octreotide LAR on Quality of Life Assessed by FACIT-D Questionnaire

8. Secondary: Pasireotide LAR vs. Octreotide LAR on Time to Symptom Progression [Time Frame: Month 6]

Measure Type	Secondary
Measure Title	Pasireotide LAR vs. Octreotide LAR on Time to Symptom Progression
Measure Description	No text entered.
Time Frame	Month 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
This Outcome Measure was planned in the protocol but not included in the analysis due to early termination of study due to lack of efficacy in symptom control.

Reporting Groups

	Description
Pasireotide LAR	Patients assigned to pasireotide LAR will receive a 60 mg dose of pasireotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 40 mg is permitted if tolerability issues arise. In addition, after 24 hours of the first LAR injections the patients were permitted to use pasireotide s.c. formulation for breakthrough symptoms as needed.
Octreotide LAR	Patients assigned to octreotide LAR will receive a 40mg dose of octreotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 30 mg is permitted if tolerability issues arise. Patients requiring a dose reduction are to return to the higher dose once the tolerability issue is resolved, if required for efficacy. In addition, after 24 hours of the first LAR injections the patients were permitted to use octreotide s.c. formulation for breakthrough symptoms as needed.

Measured Values

	Pasireotide LAR	**Octreotide LAR**

Number of Participants Analyzed [units: participants]	**0**	**0**
Pasireotide LAR vs. Octreotide LAR on Time to Symptom Progression		

No statistical analysis provided for Pasireotide LAR vs. Octreotide LAR on Time to Symptom Progression

9. Secondary: Pasireotide LAR vs. Octreotide LAR on Duration of Symptom Response [Time Frame: Month 6]

Measure Type	Secondary
Measure Title	Pasireotide LAR vs. Octreotide LAR on Duration of Symptom Response
Measure Description	No text entered.
Time Frame	Month 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
This Outcome Measure was planned in the protocol but not included in the analysis due to early termination of study due to lack of efficacy in symptom control.

Reporting Groups

	Description
Pasireotide LAR	Patients assigned to pasireotide LAR will receive a 60 mg dose of pasireotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 40 mg is permitted if tolerability issues arise. In addition, after 24 hours of the first LAR injections the patients were permitted to use pasireotide s.c. formulation for breakthrough symptoms as needed.
Octreotide LAR	Patients assigned to octreotide LAR will receive a 40mg dose of octreotide LAR i.m. depot injection once every 28 days

	(+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 30 mg is permitted if tolerability issues arise. Patients requiring a dose reduction are to return to the higher dose once the tolerability issue is resolved, if required for efficacy. In addition, after 24 hours of the first LAR injections the patients were permitted to use octreotide s.c. formulation for breakthrough symptoms as needed.

Measured Values

	Pasireotide LAR	Octreotide LAR
Number of Participants Analyzed [units: participants]	**0**	**0**
Pasireotide LAR vs. Octreotide LAR on Duration of Symptom Response		

No statistical analysis provided for Pasireotide LAR vs. Octreotide LAR on Duration of Symptom Response

10. Secondary: Assess the Proportion of Patients Who Achieved at Least a 30% Reduction in Frequency of Bowel Movements [Time Frame: Month 6]

Measure Type	Secondary
Measure Title	Assess the Proportion of Patients Who Achieved at Least a 30% Reduction in Frequency of Bowel Movements
Measure Description	No text entered.
Time Frame	Month 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
This Outcome Measure was planned in the protocol but not included in the analysis due to early termination of study due to lack of efficacy in symptom control.

Reporting Groups

	Description
Pasireotide LAR	Patients assigned to pasireotide LAR will receive a 60 mg dose of pasireotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 40 mg is permitted if tolerability issues arise. In addition, after 24 hours of the first LAR injections the patients were permitted to use pasireotide s.c. formulation for breakthrough symptoms as needed.
Octreotide LAR	Patients assigned to octreotide LAR will receive a 40mg dose of octreotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 30 mg is permitted if tolerability issues arise. Patients requiring a dose reduction are to return to the higher dose once the tolerability issue is resolved, if required for efficacy. In addition, after 24 hours of the first LAR injections the patients were permitted to use octreotide s.c. formulation for breakthrough symptoms as needed.

Measured Values

	Pasireotide LAR	Octreotide LAR
Number of Participants Analyzed [units: participants]	**0**	**0**
Assess the Proportion of Patients Who Achieved at Least a 30% Reduction in Frequency of Bowel Movements		

No statistical analysis provided for Assess the Proportion of Patients Who Achieved at Least a 30% Reduction in Frequency of Bowel Movements

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

	Description
Pasireotide LAR	Patients assigned to pasireotide LAR will receive a 60 mg dose of pasireotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 40 mg is permitted if tolerability issues arise. In addition, after 24 hours of the first LAR injections the patients were permitted to use pasireotide s.c. formulation for breakthrough symptoms as needed.
Octreotide LAR	Patients assigned to octreotide LAR will receive a 40mg dose of octreotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 30 mg is permitted if tolerability issues arise. Patients requiring a dose reduction are to return to the higher dose once the tolerability issue is resolved, if required for efficacy. In addition, after 24 hours of the first LAR injections the patients were permitted to use octreotide s.c. formulation for breakthrough symptoms as needed.
Extension Phase Pasireotide LAR	Patients assigned to pasireotide LAR will receive a 60 mg dose of pasireotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 40 mg is permitted if tolerability issues arise. In addition, after 24 hours of the first LAR injections the patients were permitted to use pasireotide s.c. formulation for breakthrough symptoms as needed.
Extension Phase Octreotide LAR	Patients assigned to octreotide LAR will receive a 40mg dose of octreotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 30 mg is permitted if tolerability issues arise. Patients requiring a dose reduction are to return to the higher dose once the tolerability issue is resolved, if required for efficacy In addition, after 24 hours of the first LAR injections the patients were permitted to use octreotide s.c. formulation for breakthrough symptoms as needed.
Crossover to Pasireotide LAR	After 6 month double blind core period, non-responders on Octreotide were given option to cross over to Pasireotide LAR in the Extension Phase of study.

Serious Adverse Events

	Pasireotide LAR	Octreotide LAR	Extension Phase Pasireotide LAR	Extension Phase Octreotide LAR	Crossover to Pasireotide LAR
Total, serious adverse events					
# participants affected / at risk	**15/53 (28.30%)**	**19/57 (33.33%)**	**9/20 (45.00%)**	**2/6 (33.33%)**	**7/15 (46.67%)**

Cardiac disorders					
Carcinoid heart disease † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Cardiac failure † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Cardiomyopathy † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Endocardial fibrosis † [1]					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Sinus bradycardia † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Tricuspid valve incompetence † [1]					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Gastrointestinal disorders					
Abdominal pain † [1]					
# participants affected / at risk	**3/53 (5.66%)**	**3/57 (5.26%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Anorectal disorder † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Colitis † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Diarrhea † [1]					
# participants affected / at risk	**4/53 (7.55%)**	**1/57 (1.75%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Ileus † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Intestinal infarction † [1]					

# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Intestinal perforation † 1					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Mesenteric vein thrombosis † 1					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Nausea † 1					
# participants affected / at risk	0/53 (0.00%)	3/57 (5.26%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Oesophageal varices haemorrhage † 1					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Pneumoperitoneum † 1					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Vomiting † 1					
# participants affected / at risk	1/53 (1.89%)	3/57 (5.26%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
General disorders					
Asthenia † 1					
# participants affected / at risk	0/53 (0.00%)	2/57 (3.51%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Chest pain † 1					
# participants affected / at risk	1/53 (1.89%)	0/57 (0.00%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Condition aggravated † 1					
# participants affected / at risk	1/53 (1.89%)	0/57 (0.00%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Device dislocation † 1					
# participants affected / at risk	0/53 (0.00%)	1/57 (1.75%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Device infusion issue † 1					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Fatigue † 1					
# participants affected / at risk	2/53 (3.77%)	2/57 (3.51%)	0/20 (0.00%)	0/6 (0.00%)	1/15 (6.67%)

General physical health deterioration † 1					
# participants affected / at risk	**1/53 (1.89%)**	**1/57 (1.75%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Localised oedema † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Malaise † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Medical device complication † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Oedema peripheral † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Hepatobiliary disorders					
Cholangitis † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Cholecystitis † 1					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Cholestasis † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Hepatic failure † 1					
# participants affected / at risk	**0/53 (0.00%)**	**2/57 (3.51%)**	**0/20 (0.00%)**	**1/6 (16.67%)**	**0/15 (0.00%)**
Hepatomegaly † 1					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Infections and infestations					
Clostridial infection † 1					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Device related infection † 1					

# participants affected / at risk	0/53 (0.00%)	1/57 (1.75%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Infectious peritonitis † 1					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Urinary tract infection † 1					
# participants affected / at risk	0/53 (0.00%)	1/57 (1.75%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Injury, poisoning and procedural complications					
Humerus fracture † 1					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Procedural pain † 1					
# participants affected / at risk	0/53 (0.00%)	1/57 (1.75%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Tendon rupture † 1					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	0/20 (0.00%)	0/6 (0.00%)	1/15 (6.67%)
Investigations					
Alanine aminotransferase increased † 1					
# participants affected / at risk	1/53 (1.89%)	0/57 (0.00%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Aspartate aminotransferase increased † 1					
# participants affected / at risk	1/53 (1.89%)	0/57 (0.00%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Blood alkaline phosphatase increased † 1					
# participants affected / at risk	0/53 (0.00%)	1/57 (1.75%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Blood bicarbonate decreased † 1					
# participants affected / at risk	1/53 (1.89%)	0/57 (0.00%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Blood creatinine increased † 1					
# participants affected / at risk	1/53 (1.89%)	1/57 (1.75%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Blood pH increased † 1					
# participants affected / at risk	1/53 (1.89%)	0/57 (0.00%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)

Gamma-glutamyltransferase increased † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Hepatic enzyme increased † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Liver function test abnormal † 1					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Troponin increased † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Weight decreased † 1					
# participants affected / at risk	**2/53 (3.77%)**	**2/57 (3.51%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Metabolism and nutrition disorders					
Decreased appetite † 1					
# participants affected / at risk	**0/53 (0.00%)**	**2/57 (3.51%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Dehydration † 1					
# participants affected / at risk	**2/53 (3.77%)**	**2/57 (3.51%)**	**1/20 (5.00%)**	**1/6 (16.67%)**	**1/15 (6.67%)**
Diabetes mellitus † 1					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Hyperglycaemia † 1					
# participants affected / at risk	**4/53 (7.55%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**1/6 (16.67%)**	**0/15 (0.00%)**
Hyperkalaemia † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Hypoglycaemia † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Hypokalaemia † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**

Hyponatraemia † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Hypovolaemia † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Malnutrition † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Metabolic acidosis † 1					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Type 2 diabetes mellitus † 1					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Musculoskeletal and connective tissue disorders					
Bone pain † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Intervertebral disc disorder † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Pain in extremity † 1					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
Carcinoid tumour † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Carcinoid tumour of the gastrointestinal tract † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Metastases to chest wall † 1					

# participants affected / at risk	0/53 (0.00%)	1/57 (1.75%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Metastatic carcinoid tumour † 1					
# participants affected / at risk	0/53 (0.00%)	1/57 (1.75%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Neoplasm malignant † 1					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Nervous system disorders					
Central nervous system lesion † 1					
# participants affected / at risk	1/53 (1.89%)	0/57 (0.00%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Hemiparesis † 1					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	0/20 (0.00%)	0/6 (0.00%)	1/15 (6.67%)
Psychiatric disorders					
Confusional state † 1					
# participants affected / at risk	0/53 (0.00%)	1/57 (1.75%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Renal and urinary disorders					
Nephritis † 1					
# participants affected / at risk	0/53 (0.00%)	1/57 (1.75%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Renal failure † 1					
# participants affected / at risk	0/53 (0.00%)	1/57 (1.75%)	0/20 (0.00%)	1/6 (16.67%)	0/15 (0.00%)
Renal failure acute † 1					
# participants affected / at risk	0/53 (0.00%)	1/57 (1.75%)	0/20 (0.00%)	0/6 (0.00%)	1/15 (6.67%)
Renal failure chronic † 1					
# participants affected / at risk	1/53 (1.89%)	0/57 (0.00%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Urinary tract disorder † 1					
# participants affected / at risk	0/53 (0.00%)	1/57 (1.75%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Respiratory, thoracic and mediastinal disorders					

Pleural effusion † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Pulmonary embolism † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Social circumstances					
Respite care † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Vascular disorders					
Flushing † 1					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Orthostatic hypotension † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Vein disorder † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Pasireotide LAR	Patients assigned to pasireotide LAR will receive a 60 mg dose of pasireotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 40 mg is permitted if tolerability issues arise. In addition, after 24 hours of the first LAR injections the patients were permitted to use pasireotide s.c. formulation for breakthrough symptoms as needed.
Octreotide LAR	Patients assigned to octreotide LAR will receive a 40mg dose of octreotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 30 mg is permitted if tolerability issues arise. Patients requiring a dose reduction are to return to the higher dose once the tolerability issue is resolved, if required for efficacy. In addition, after 24 hours of the first LAR injections the patients were permitted to use octreotide s.c. formulation for breakthrough symptoms as needed.
Extension Phase Pasireotide LAR	Patients assigned to pasireotide LAR will receive a 60 mg dose of pasireotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 40 mg is permitted if tolerability issues arise. In addition, after 24 hours of the first LAR injections the patients were permitted to use pasireotide s.c. formulation for breakthrough symptoms as needed.
Extension Phase Octreotide LAR	Patients assigned to octreotide LAR will receive a 40mg dose of octreotide LAR i.m. depot injection once every 28 days (+/- 3 days) for 6 months at visits 2, 4, 5, 6, 7 and 8. A dose reduction to 30 mg is permitted if tolerability issues arise. Patients requiring a dose reduction are to return to the higher dose once the tolerability issue is resolved, if required for efficacy In addition, after 24 hours of the first LAR injections the patients were permitted to use octreotide s.c. formulation for breakthrough symptoms as needed.
Crossover to Pasireotide LAR	After 6 month double blind core period, non-responders on Octreotide were given option to cross over to Pasireotide LAR in the Extension Phase of study.

Other Adverse Events

	Pasireotide LAR	Octreotide LAR	Extension Phase Pasireotide LAR	Extension Phase Octreotide LAR	Crossover to Pasireotide LAR
Total, other (not including serious) adverse events					

# participants affected / at risk	50/53 (94.34%)	48/57 (84.21%)	19/20 (95.00%)	5/6 (83.33%)	12/15 (80.00%)
Blood and lymphatic system disorders					
Anaemia † [1]					
# participants affected / at risk	3/53 (5.66%)	1/57 (1.75%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Leukocytosis † [1]					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Cardiac disorders					
Aortic valve sclerosis † [1]					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Atrial fibrillation † [1]					
# participants affected / at risk	0/53 (0.00%)	3/57 (5.26%)	0/20 (0.00%)	0/6 (0.00%)	0/15 (0.00%)
Bradycardia † [1]					
# participants affected / at risk	2/53 (3.77%)	1/57 (1.75%)	0/20 (0.00%)	0/6 (0.00%)	1/15 (6.67%)
Bundle branch block right † [1]					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Coronary artery disease † [1]					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Dilatation ventricular † [1]					
# participants affected / at risk	1/53 (1.89%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Mitral valve incompetence † [1]					
# participants affected / at risk	1/53 (1.89%)	1/57 (1.75%)	0/20 (0.00%)	0/6 (0.00%)	1/15 (6.67%)
Palpitations † [1]					
# participants affected / at risk	0/53 (0.00%)	5/57 (8.77%)	0/20 (0.00%)	0/6 (0.00%)	2/15 (13.33%)
Pulmonary valve incompetence † [1]					

# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Tricuspid valve incompetence † 1					
# participants affected / at risk	2/53 (3.77%)	3/57 (5.26%)	1/20 (5.00%)	0/6 (0.00%)	2/15 (13.33%)
Congenital, familial and genetic disorders					
Birth mark † 1					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	0/20 (0.00%)	0/6 (0.00%)	1/15 (6.67%)
Endocrine disorders					
Hypothyroidism † 1					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	2/20 (10.00%)	0/6 (0.00%)	0/15 (0.00%)
Eye disorders					
Conjunctivitis † 1					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Dry eye † 1					
# participants affected / at risk	2/53 (3.77%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Eye pain † 1					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Glaucoma † 1					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	0/20 (0.00%)	0/6 (0.00%)	1/15 (6.67%)
Visual impairment † 1					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Gastrointestinal disorders					
Abdominal distension † 1					
# participants affected / at risk	3/53 (5.66%)	1/57 (1.75%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Abdominal pain † 1					
# participants affected / at risk	8/53 (15.09%)	8/57 (14.04%)	1/20 (5.00%)	0/6 (0.00%)	3/15 (20.00%)

Abdominal pain lower † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Abdominal pain upper † [1]					
# participants affected / at risk	**2/53 (3.77%)**	**3/57 (5.26%)**	**2/20 (10.00%)**	**1/6 (16.67%)**	**0/15 (0.00%)**
Anal fissure † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Anal haemorrhage † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Constipation † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**4/57 (7.02%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Diarrhoea † [1]					
# participants affected / at risk	**12/53 (22.64%)**	**9/57 (15.79%)**	**4/20 (20.00%)**	**0/6 (0.00%)**	**2/15 (13.33%)**
Dry mouth † [1]					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Duodenal ulcer † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Dyspepsia † [1]					
# participants affected / at risk	**3/53 (5.66%)**	**3/57 (5.26%)**	**0/20 (0.00%)**	**1/6 (16.67%)**	**0/15 (0.00%)**
Dysphagia † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Faecal incontinence † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Flatulence † [1]					
# participants affected / at risk	**7/53 (13.21%)**	**1/57 (1.75%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**

Gastritis † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**3/20 (15.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Gastrointestinal haemorrhage † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Haematochezia † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Haemorrhoids † 1					
# participants affected / at risk	**1/53 (1.89%)**	**2/57 (3.51%)**	**4/20 (20.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Nausea † 1					
# participants affected / at risk	**10/53 (18.87%)**	**7/57 (12.28%)**	**4/20 (20.00%)**	**0/6 (0.00%)**	**3/15 (20.00%)**
Painful defaecation † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Proctalgia † 1					
# participants affected / at risk	**1/53 (1.89%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**2/15 (13.33%)**
Proctitis † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Rectal ulcer † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Short-bowel syndrome † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Varices oesophageal † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Vomiting † 1					
# participants affected / at risk	**3/53 (5.66%)**	**7/57 (12.28%)**	**4/20 (20.00%)**	**0/6 (0.00%)**	**3/15 (20.00%)**

General disorders					
Asthenia † 1					
# participants affected / at risk	**5/53 (9.43%)**	**6/57 (10.53%)**	**4/20 (20.00%)**	**1/6 (16.67%)**	**1/15 (6.67%)**
Chest pain † 1					
# participants affected / at risk	**1/53 (1.89%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**2/15 (13.33%)**
Chills † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Fatigue † 1					
# participants affected / at risk	**11/53 (20.75%)**	**8/57 (14.04%)**	**6/20 (30.00%)**	**1/6 (16.67%)**	**3/15 (20.00%)**
General physical health deterioration † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Injection site pain † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Localised oedema † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Malaise † 1					
# participants affected / at risk	**0/53 (0.00%)**	**4/57 (7.02%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Oedema peripheral † 1					
# participants affected / at risk	**9/53 (16.98%)**	**5/57 (8.77%)**	**5/20 (25.00%)**	**0/6 (0.00%)**	**3/15 (20.00%)**
Pain † 1					
# participants affected / at risk	**1/53 (1.89%)**	**1/57 (1.75%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Pyrexia † 1					
# participants affected / at risk	**0/53 (0.00%)**	**2/57 (3.51%)**	**4/20 (20.00%)**	**1/6 (16.67%)**	**2/15 (13.33%)**

Hepatobiliary disorders					
Biliary dilatation † [1]					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Cholelithiasis † [1]					
# participants affected / at risk	**4/53 (7.55%)**	**4/57 (7.02%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Hyperbilirubinaemia † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Jaundice † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Immune system disorders					
Hypersensitivity † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**1/6 (16.67%)**	**0/15 (0.00%)**
Infections and infestations					
Biliary tract infection † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Bronchitis † [1]					
# participants affected / at risk	**2/53 (3.77%)**	**1/57 (1.75%)**	**1/20 (5.00%)**	**1/6 (16.67%)**	**1/15 (6.67%)**
Candidiasis † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Clostridium difficile colitis † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Cystitis † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Ear infection † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**

Fungal infection † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Gastroenteritis † 1					
# participants affected / at risk	**0/53 (0.00%)**	**2/57 (3.51%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Gastrointestinal bacterial infection † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Incision site infection † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Infection † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Nasopharyngitis † 1					
# participants affected / at risk	**2/53 (3.77%)**	**5/57 (8.77%)**	**0/20 (0.00%)**	**1/6 (16.67%)**	**1/15 (6.67%)**
Sinusitis † 1					
# participants affected / at risk	**1/53 (1.89%)**	**1/57 (1.75%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Tooth abscess † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Tooth infection † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Upper respiratory tract infection † 1					
# participants affected / at risk	**3/53 (5.66%)**	**3/57 (5.26%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Urinary tract infection † 1					
# participants affected / at risk	**2/53 (3.77%)**	**2/57 (3.51%)**	**0/20 (0.00%)**	**1/6 (16.67%)**	**2/15 (13.33%)**
Viral infection † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Injury, poisoning and procedural complications					

Accidental overdose † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Concussion † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Humerus fracture † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Procedural pain † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Rib fracture † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Thermal burn † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Tooth fracture † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Investigations					
Alanine aminotransferase increased † 1					
# participants affected / at risk	**1/53 (1.89%)**	**3/57 (5.26%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Albumin urine present † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Aspartate aminotransferase increased † 1					
# participants affected / at risk	**2/53 (3.77%)**	**3/57 (5.26%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**2/15 (13.33%)**
Bilirubin conjugated increased † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Blood alkaline phosphatase increased † 1					
# participants affected / at risk	**2/53 (3.77%)**	**5/57 (8.77%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**2/15 (13.33%)**

Blood bilirubin increased † [1]					
# participants affected / at risk	**2/53 (3.77%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Blood calcium increased † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Blood creatine phosphokinase increased † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Blood creatinine increased † [1]					
# participants affected / at risk	**3/53 (5.66%)**	**3/57 (5.26%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Blood glucose increased † [1]					
# participants affected / at risk	**3/53 (5.66%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Blood lactate dehydrogenase increased † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Blood magnesium decreased † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Blood testosterone decreased † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Blood triglycerides increased † [1]					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**2/15 (13.33%)**
Blood urea increased † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Blood urine present † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Gamma-glutamyltransferase increased † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**3/57 (5.26%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**2/15 (13.33%)**

Glycosylated haemoglobin increased † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Haematocrit increased † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Haemoglobin decreased † 1					
# participants affected / at risk	**1/53 (1.89%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Haemoglobin increased † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Red blood cell count increased † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Weight decreased † 1					
# participants affected / at risk	**8/53 (15.09%)**	**4/57 (7.02%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Metabolism and nutrition disorders					
Acidosis † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Decreased appetite † 1					
# participants affected / at risk	**2/53 (3.77%)**	**4/57 (7.02%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Dehydration † 1					
# participants affected / at risk	**1/53 (1.89%)**	**2/57 (3.51%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Diabetes mellitus † 1					
# participants affected / at risk	**6/53 (11.32%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Glucose tolerance impaired † 1					
# participants affected / at risk	**2/53 (3.77%)**	**1/57 (1.75%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Hyperglycaemia † 1					

# participants affected / at risk	15/53 (28.30%)	3/57 (5.26%)	7/20 (35.00%)	1/6 (16.67%)	2/15 (13.33%)
Hypernatraemia † [1]					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	0/20 (0.00%)	0/6 (0.00%)	1/15 (6.67%)
Hyperuricaemia † [1]					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	0/20 (0.00%)	1/6 (16.67%)	0/15 (0.00%)
Hypoglycaemia † [1]					
# participants affected / at risk	2/53 (3.77%)	1/57 (1.75%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Hypokalaemia † [1]					
# participants affected / at risk	1/53 (1.89%)	3/57 (5.26%)	3/20 (15.00%)	0/6 (0.00%)	1/15 (6.67%)
Hypomagnesaemia † [1]					
# participants affected / at risk	1/53 (1.89%)	3/57 (5.26%)	0/20 (0.00%)	0/6 (0.00%)	1/15 (6.67%)
Hyponatraemia † [1]					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	0/20 (0.00%)	0/6 (0.00%)	1/15 (6.67%)
Increased appetite † [1]					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Malnutrition † [1]					
# participants affected / at risk	0/53 (0.00%)	3/57 (5.26%)	1/20 (5.00%)	0/6 (0.00%)	2/15 (13.33%)
Musculoskeletal and connective tissue disorders					
Arthralgia † [1]					
# participants affected / at risk	2/53 (3.77%)	1/57 (1.75%)	1/20 (5.00%)	1/6 (16.67%)	0/15 (0.00%)
Arthritis † [1]					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Back pain † [1]					
# participants affected / at risk	3/53 (5.66%)	3/57 (5.26%)	3/20 (15.00%)	0/6 (0.00%)	1/15 (6.67%)

Exostosis † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Intervertebral disc protrusion † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Muscle spasms † 1					
# participants affected / at risk	**7/53 (13.21%)**	**1/57 (1.75%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Muscular weakness † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Musculoskeletal chest pain † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Musculoskeletal pain † 1					
# participants affected / at risk	**1/53 (1.89%)**	**4/57 (7.02%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Myalgia † 1					
# participants affected / at risk	**1/53 (1.89%)**	**3/57 (5.26%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Neck pain † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Pain in extremity † 1					
# participants affected / at risk	**4/53 (7.55%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**2/15 (13.33%)**
Spinal osteoarthritis † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
Uterine leiomyoma † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Nervous system disorders					

Aphasia † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Aphonia † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Cervicobrachial syndrome † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Cognitive disorder † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Dizziness † 1					
# participants affected / at risk	**5/53 (9.43%)**	**1/57 (1.75%)**	**4/20 (20.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Dysaesthesia † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Dysgeusia † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Headache † 1					
# participants affected / at risk	**7/53 (13.21%)**	**1/57 (1.75%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Hypoaesthesia † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Lethargy † 1					
# participants affected / at risk	**3/53 (5.66%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Loss of consciousness † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Migraine † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Muscle contractions involuntary † 1					

# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Neuralgia † [1]					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	0/20 (0.00%)	0/6 (0.00%)	1/15 (6.67%)
Peripheral sensory neuropathy † [1]					
# participants affected / at risk	1/53 (1.89%)	0/57 (0.00%)	0/20 (0.00%)	0/6 (0.00%)	1/15 (6.67%)
Sciatica † [1]					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Syncope † [1]					
# participants affected / at risk	0/53 (0.00%)	2/57 (3.51%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Tremor † [1]					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	2/20 (10.00%)	0/6 (0.00%)	0/15 (0.00%)
Psychiatric disorders					
Agitation † [1]					
# participants affected / at risk	1/53 (1.89%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Anxiety † [1]					
# participants affected / at risk	3/53 (5.66%)	3/57 (5.26%)	2/20 (10.00%)	0/6 (0.00%)	1/15 (6.67%)
Confusional state † [1]					
# participants affected / at risk	1/53 (1.89%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Depression † [1]					
# participants affected / at risk	3/53 (5.66%)	1/57 (1.75%)	1/20 (5.00%)	0/6 (0.00%)	1/15 (6.67%)
Insomnia † [1]					
# participants affected / at risk	1/53 (1.89%)	3/57 (5.26%)	0/20 (0.00%)	0/6 (0.00%)	3/15 (20.00%)
Libido decreased † [1]					
# participants affected / at risk	0/53 (0.00%)	0/57 (0.00%)	1/20 (5.00%)	0/6 (0.00%)	0/15 (0.00%)
Renal and urinary disorders					

Dysuria † 1					
# participants affected / at risk	**0/53 (0.00%)**	**2/57 (3.51%)**	**0/20 (0.00%)**	**1/6 (16.67%)**	**0/15 (0.00%)**
Glycosuria † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Haematuria † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**1/6 (16.67%)**	**0/15 (0.00%)**
Micturition urgency † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Pollakiuria † 1					
# participants affected / at risk	**1/53 (1.89%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**1/6 (16.67%)**	**0/15 (0.00%)**
Proteinuria † 1					
# participants affected / at risk	**2/53 (3.77%)**	**1/57 (1.75%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Reproductive system and breast disorders					
Benign prostatic hyperplasia † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Respiratory, thoracic and mediastinal disorders					
Cough † 1					
# participants affected / at risk	**1/53 (1.89%)**	**2/57 (3.51%)**	**1/20 (5.00%)**	**1/6 (16.67%)**	**1/15 (6.67%)**
Dysphonia † 1					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Dyspnoea † 1					
# participants affected / at risk	**5/53 (9.43%)**	**3/57 (5.26%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**2/15 (13.33%)**
Hypoxia † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**

Nasal dryness † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Painful respiration † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Pleural effusion † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Reflux laryngitis † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Rhinitis allergic † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Rhinorrhoea † [1]					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Sinus congestion † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Throat tightness † [1]					
# participants affected / at risk	**1/53 (1.89%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Skin and subcutaneous tissue disorders					
Alopecia † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Dry skin † [1]					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Eczema † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Exfoliative rash † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**

Hyperhidrosis † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**3/57 (5.26%)**	**1/20 (5.00%)**	**1/6 (16.67%)**	**1/15 (6.67%)**
Night sweats † [1]					
# participants affected / at risk	**3/53 (5.66%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Palmar-plantar erythrodysaesthesia syndrome † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Rash † [1]					
# participants affected / at risk	**4/53 (7.55%)**	**1/57 (1.75%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**2/15 (13.33%)**
Skin exfoliation † [1]					
# participants affected / at risk	**1/53 (1.89%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Skin hyperpigmentation † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Skin lesion † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Skin ulcer † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Social circumstances					
Alcohol use † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Vascular disorders					
Axillary vein thrombosis † [1]					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Flushing † [1]					
# participants affected / at risk	**5/53 (9.43%)**	**4/57 (7.02%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**2/15 (13.33%)**
Hypertension † [1]					

# participants affected / at risk	**3/53 (5.66%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Hypotension † 1					
# participants affected / at risk	**1/53 (1.89%)**	**1/57 (1.75%)**	**2/20 (10.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Lymphoedema † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Orthostatic hypotension † 1					
# participants affected / at risk	**0/53 (0.00%)**	**1/57 (1.75%)**	**0/20 (0.00%)**	**0/6 (0.00%)**	**1/15 (6.67%)**
Subclavian vein thrombosis † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**
Thrombophlebitis superficial † 1					
# participants affected / at risk	**0/53 (0.00%)**	**0/57 (0.00%)**	**1/20 (5.00%)**	**0/6 (0.00%)**	**0/15 (0.00%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

☑ **Restriction Description:** Principal Investigators are NOT employed by the organization sponsoring the study. Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed. The terms and conditions of Novartis' agreements with its investigators may vary. However, Novartis does not prohibit any investigator from publishing. Any publications from a single-site are postponed until the publication of pooled data (i.e.,data from all sites) in clinical trial.

Results Point of Contact:

Name/Title: Study Director
Organization: Novartis Pharmaceuticals
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No publications provided

Responsible Party:	Novartis (Novartis Pharmaceuticals)
ClinicalTrials.gov Identifier:	NCT00690430 History of Changes
Other Study ID Numbers:	**CSOM230C2303** 2007-000739-25 (EudraCT Number)
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Results First Received:	April 5, 2013
Last Updated:	June 25, 2013
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Austria: Agency for Health and Food Safety
Belgium: Federal Agency for Medicines and Health Products, FAMHP
Brazil: Ministry of Health
European Union: European Medicines Agency
Canada: Health Canada
France: Ministry of Health
Germany: Ministry of Health
Israel: Ministry of Health
Italy: Ministry of Health
Netherlands: Independent Ethics Committee
Norway: The National Committees for Research Ethics
Poland: Ministry of Health
Spain: Ministry of Health
Sweden: Institutional Review Board
United Kingdom: Research Ethics Committee