Clinical trial results:
A Phase II, Open-label, Multicentre, Randomised Study of the Pharmacokinetics, Pharmacodynamics, Efficacy, and Safety of CAM2029 in Two Patient Groups with Acromegaly and Neuroendocrine Tumours (NET) Previously Treated with Sandostatin® LAR®

Summary

EudraCT number	2013-000533-12
Trial protocol	DE IT
Global end of trial date	16 February 2016

Results information

Result version number	v1 (current)
This version publication date	02 March 2017
First version publication date	02 March 2017

Trial information

Trial identification

Sponsor protocol code	HS-12-455

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02299089
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CAMURUS AB
Sponsor organisation address	Ideon Science Park, Sölvegatan 41, Sweden, SE 223 70 Lund
Public contact	Clinical Programme Management, Camurus AB, +46 462865730, info@camurus.com
Scientific contact	Clinical Programme Management, Camurus AB, +46 462865730, info@camurus.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 February 2016
Global end of trial reached?	Yes
Global end of trial date	16 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to characterise the pharmacokinetic (PK) profile of octreotide after each injection of CAM2029 (during Period 1) as compared with baseline PK Sandostatin long acting release (LAR) (during Period 0) in patients with acromegaly and NETs.

Protection of trial subjects:

The study was conducted according to the ethical principles of the Declaration of Helsinki. Informed consent was obtained from each patient in writing before any study-specific procedure was performed. The study was described by a nurse/study coordinator/the Investigator, who answered any questions, and written information was also provided. Final informed consent was retrieved by the physician, either investigator or co-investigator.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 January 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Italy: 3
Worldwide total number of subjects	12
EEA total number of subjects	12

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	6

From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study had planned to enroll 24 patients, however, only 12 patients (7 with acromegaly and 5 with neuroendocrine tumors [NETs]) were enrolled in this study.

Pre-assignment

Screening details:

Screening took place during the 14-day screening period from Day -42 to Day -29.

Period 1

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

Blinding implementation details:

This was an open label trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	Acromegaly

Arm description:

Twenty-eight days after the last injection of Sandostatin LAR (i.e. on Day 0), patients were randomized into the CAM2029 treatment phase (i.e. Period 1) and received their first subcutaneous thigh injection of 20 mg or 10 mg CAM2029 on Day 0. Patients randomized to receive 20 mg of CAM2029 were administered three upper thigh subcutaneous injections CAM2029 20 mg q4w on Days 0, 28 and 56; whereas patients randomized to receive 10 mg of CAM2029 were administered six upper thigh injections CAM2029 10 mg q2w on Days 0, 14, 28, 42, 56 and 70.

Arm type	Experimental
Investigational medicinal product name	CAM2029
Investigational medicinal product code	
Other name	Octreotide hydrochloride FluidCrystal injection depot
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients were randomized to receive either 10 mg or 20 mg of CAM2029. Patients randomized to 20 mg of CAM2029 were administered three upper anterior thigh SC injections of CAM2029 20 mg q4w on Days 0, 28, and 56 and patients randomized to 10 mg of CAM2029 were administered six upper anterior thigh SC injections of CAM2029 10 mg q2w on Days 0, 14, 28, 42, 56, and 70.

Arm title	NETs

Arm description:

Twenty-eight days after the last injection of Sandostatin LAR (i.e. on Day 0), patients were randomized into the CAM2029 treatment phase (i.e. Period 1) and received their first subcutaneous thigh injection of 20 mg or 10 mg CAM2029 on Day 0. Patients randomized to receive 20 mg of CAM2029 were administered three upper thigh subcutaneous injections of CAM2029 20 mg q4w on Days 0, 28 and 56; whereas patients randomized to receive 10 mg of CAM2029 were administered six upper thigh injections CAM2029 10 mg q2w on Days 0, 14, 28, 42, 56 and 70.

Arm type	Experimental
Investigational medicinal product name	CAM2029
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Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients were randomized to receive either 10 mg or 20 mg of CAM2029. Patients randomized to 20 mg of CAM2029 were administered three upper anterior thigh SC injections of CAM2029 20 mg q4w on Days 0, 28, and 56 and patients randomized to 10 mg of CAM2029 were administered six upper anterior thigh SC injections of CAM2029 10 mg q2w on Days 0, 14, 28, 42, 56, and 70.

Number of subjects in period 1	Acromegaly	NETs
Started	7	5
Completed	7	5

Baseline characteristics

Reporting groups	
Reporting group title	Acromegaly
Reporting group description:	
Twenty-eight days after the last injection of Sandostatin LAR (i.e. on Day 0), patients were randomized into the CAM2029 treatment phase (i.e. Period 1) and received their first subcutaneous thigh injection of 20 mg or 10 mg CAM2029 on Day 0. Patients randomized to receive 20 mg of CAM2029 were administered three upper thigh subcutaneous injections CAM2029 20 mg q4w on Days 0, 28 and 56; whereas patients randomized to receive 10 mg of CAM2029 were administered six upper thigh injections CAM2029 10 mg q2w on Days 0, 14, 28, 42, 56 and 70.	
Reporting group title	NETs
Reporting group description:	
Twenty-eight days after the last injection of Sandostatin LAR (i.e. on Day 0), patients were randomized into the CAM2029 treatment phase (i.e. Period 1) and received their first subcutaneous thigh injection of 20 mg or 10 mg CAM2029 on Day 0. Patients randomized to receive 20 mg of CAM2029 were administered three upper thigh subcutaneous injections of CAM2029 20 mg q4w on Days 0, 28 and 56; whereas patients randomized to receive 10 mg of CAM2029 were administered six upper thigh injections CAM2029 10 mg q2w on Days 0, 14, 28, 42, 56 and 70.	

Reporting group values	Acromegaly	NETs	Total
Number of subjects	7	5	12
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	3	6
From 65-84 years	4	2	6
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	61	63.6	
standard deviation	± 9.45	± 4.39	-
Gender categorical Units: Subjects			
Female	3	0	3
Male	4	5	9

End points

End points reporting groups

Reporting group title	Acromegaly

Reporting group description:

Twenty-eight days after the last injection of Sandostatin LAR (i.e. on Day 0), patients were randomized into the CAM2029 treatment phase (i.e. Period 1) and received their first subcutaneous thigh injection of 20 mg or 10 mg CAM2029 on Day 0. Patients randomized to receive 20 mg of CAM2029 were administered three upper thigh subcutaneous injections CAM2029 20 mg q4w on Days 0, 28 and 56; whereas patients randomized to receive 10 mg of CAM2029 were administered six upper thigh injections CAM2029 10 mg q2w on Days 0, 14, 28, 42, 56 and 70.

Reporting group title	NETs

Reporting group description:

Twenty-eight days after the last injection of Sandostatin LAR (i.e. on Day 0), patients were randomized into the CAM2029 treatment phase (i.e. Period 1) and received their first subcutaneous thigh injection of 20 mg or 10 mg CAM2029 on Day 0. Patients randomized to receive 20 mg of CAM2029 were administered three upper thigh subcutaneous injections of CAM2029 20 mg q4w on Days 0, 28 and 56; whereas patients randomized to receive 10 mg of CAM2029 were administered six upper thigh injections CAM2029 10 mg q2w on Days 0, 14, 28, 42, 56 and 70.

Subject analysis set title	Sandostatin LAR 10 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This analysis group contains patients who received Sandostatin LAR 10 mg prior to the first CAM2029 injection. PK analysis set consisted of all patients who had received the study drug as scheduled.

Subject analysis set title	Sandostatin LAR 20 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This analysis group contains patients who received Sandostatin LAR 20 mg prior to the first CAM2029 injection. PK analysis set consisted of all patients who had received the study drug as scheduled.

Subject analysis set title	Sandostatin LAR 30 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This analysis group contains patients who received Sandostatin LAR 30 mg prior to the first CAM2029 injection. PK analysis set consisted of all patients who had received the study drug as scheduled.

Subject analysis set title	CAM2029 10 mg q2w (Acromegaly)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Randomized patients received 6 upper anterior thigh SC injections of CAM2029 10 mg q2w. PK analysis set consisted of all patients who had received the study drug as scheduled.

Subject analysis set title	CAM2029 10 mg q2w (NETs)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Randomized patients received 6 upper anterior thigh SC injections of CAM2029 10 mg q2w. PK analysis set consisted of all patients who had received the study drug as scheduled.

Subject analysis set title	CAM2029 20 mg q4w (Acromegaly)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Randomized patients received 3 upper anterior thigh SC injections of CAM2029 20 mg q4w. PK analysis set consisted of all patients who had received the study drug as scheduled.

Subject analysis set title	CAM2029 20 mg q4w (NETs)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Randomized patients received 3 upper anterior thigh SC injections of CAM2029 20 mg q4w. PK analysis set consisted of all patients who had received the study drug as scheduled.

Primary: AUC from 0 to 28 days over the final dosing intervals for Sandostatin LAR and CAM2029 study periods (AUC0-28d) in patients with acromegaly

End point title	AUC from 0 to 28 days over the final dosing intervals for Sandostatin LAR and CAM2029 study periods (AUC0-28d) in patients with acromegaly[1]

End point description:

The PK endpoints included the octreotide plasma concentration curve versus time and PK parameters for Sandostatin LAR and CAM2029 in patients with acromegaly. Serial blood samples were collected from Day -28 to Day 84.

End point type	Primary

End point timeframe:

Sandostatin LAR 10 mg and 30 mg on Day -28 (Period 0) and CAM2029 10 mg q2w and 20 mg q4w on Day 0 and Day 56 (Period 1).

Notes:

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

End point values	Sandostatin LAR 10 mg	Sandostatin LAR 30 mg	CAM2029 10 mg q2w (Acromegaly)	CAM2029 20 mg q4w (Acromegaly)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	4	3	2
Units: day*ng/mL				
geometric mean (geometric coefficient of variation)				
Day -28 (n = 1, 4, 0, 0)	6.23 (± 0)	21.8 (± 58.7)	0 (± 0)	0 (± 0)
Day 0 (n = 0, 0, 3, 2)	0 (± 0)	0 (± 0)	87.1 (± 49.1)	72.2 (± 9.3)
Day 56 (n = 0, 0, 2, 2)	0 (± 0)	0 (± 0)	84.4 (± 82.1)	77.2 (± 26.2)

Statistical analyses

No statistical analyses for this end point

Primary: AUC from 0 to 28 days over the final dosing intervals for Sandostatin LAR and CAM2029 study periods (AUC0-28d) in patients with NETs

End point title	AUC from 0 to 28 days over the final dosing intervals for Sandostatin LAR and CAM2029 study periods (AUC0-28d) in patients with NETs[2]

End point description:

The PK endpoints included the octreotide plasma concentration curve versus time and PK parameters for Sandostatin LAR and CAM2029 in patients with NETs. Serial blood samples were collected from Day -28 to Day 84.

End point type	Primary

End point timeframe:

Sandostatin LAR 20 mg and 30 mg on Day -28 (Period 0) and CAM2029 10 mg q2w and 20 mg q4w on Day 0 and Day 56 (Period 1).

Notes:

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

End point values	Sandostatin LAR 20 mg	Sandostatin LAR 30 mg	CAM2029 10 mg q2w (NETs)	CAM2029 20 mg q4w (NETs)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	4	1	4
Units: day*ng/mL				
geometric mean (geometric coefficient of variation)				
Day -28 (n = 1, 4, 0, 0)	27.8 (± 0)	36.5 (± 50.5)	0 (± 0)	0 (± 0)
Day 0 (n = 0, 0, 1, 3)	0 (± 0)	0 (± 0)	72.9 (± 0)	132 (± 26.9)
Day 56 (n = 0, 0, 1, 4)	0 (± 0)	0 (± 0)	83.3 (± 0)	131 (± 27.6)

Statistical analyses

No statistical analyses for this end point

Primary: Concentration levels assessed prior to next injection for the final (Sandostatin LAR, CAM2029 q4w) or penultimate (CAM2029 q2w only) dosing interval (Ctrough) in patients with acromegaly

End point title	Concentration levels assessed prior to next injection for the final (Sandostatin LAR, CAM2029 q4w) or penultimate (CAM2029 q2w only) dosing interval (Ctrough) in patients with acromegaly[3]

End point description:

The PK endpoints included the octreotide plasma concentration curve versus time and PK parameters for Sandostatin LAR and CAM2029 in patients with acromegaly. Serial bood samples were collected from Day -28 to Day 84.

End point type	Primary

End point timeframe:

Sandostatin LAR 10 mg and 30 mg on Day -28 (Period 0) and CAM2029 10 mg q2w and 20 mg q4w on Day 0 and Day 56 (Period 1).

Notes:

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

End point values	Sandostatin LAR 10 mg	Sandostatin LAR 30 mg	CAM2029 10 mg q2w (Acromegaly)	CAM2029 20 mg q4w (Acromegaly)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	4	3	2
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day -28 (n = 1, 4, 0, 0)	0.225 (± 0)	1.07 (± 63)	0 (± 0)	0 (± 0)
Day 0 (n = 0, 0, 3, 2)	0 (± 0)	0 (± 0)	1.28 (± 31)	0.322 (± 127.3)
Day 56 (n = 0, 0, 2, 2)	0 (± 0)	0 (± 0)	1.01 (± 23.6)	0.979 (± 38.2)

Statistical analyses

No statistical analyses for this end point

Primary: Concentration levels assessed prior to next injection for the final (Sandostatin LAR, CAM2029 q4w) or penultimate (CAM2029 q2w only) dosing interval (Ctrough) in patients with NETs

End point title	Concentration levels assessed prior to next injection for the final (Sandostatin LAR, CAM2029 q4w) or penultimate (CAM2029 q2w only) dosing interval (Ctrough) in patients with NETs[4]

End point description:

The PK endpoints included the octreotide plasma concentration curve versus time and PK parameters for Sandostatin LAR and CAM2029 in patients with NETs. Serial blood samples were collected from Day -28 to Day 84.

End point type	Primary

End point timeframe:

Sandostatin LAR 20 mg and 30 mg on Day -28 (Period 0) and CAM2029 10 mg q2w and 20 mg q4w on Day 0 and Day 56 (Period 1).

Notes:

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

End point values	Sandostatin LAR 20 mg	Sandostatin LAR 30 mg	CAM2029 10 mg q2w (NETs)	CAM2029 20 mg q4w (NETs)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	4	1	4
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day -28 (n = 1, 3, 0, 0)	0.901 (± 0)	1.19 (± 46.9)	0 (± 0)	0 (± 0)
Day 0 (n = 0, 0, 1, 4)	0 (± 0)	0 (± 0)	1.8 (± 0)	1.7 (± 40.5)
Day 56 (n = 0, 0, 1, 4)	0 (± 0)	0 (± 0)	1.27 (± 0)	1.45 (± 90)

Statistical analyses

No statistical analyses for this end point

Primary: Maximum observed plasma concentration over the final (Sandostatin LAR, CAM2029 q4w) or penultimate (CAM2029 q2w only) dosing interval (Cmax) for patients with acromegaly

End point title	Maximum observed plasma concentration over the final (Sandostatin LAR, CAM2029 q4w) or penultimate (CAM2029 q2w only) dosing interval (Cmax) for patients with acromegaly[5]

End point description:

The PK endpoints included the octreotide plasma concentration curve versus time and PK parameters for Sandostatin LAR and CAM2029 in patients with acromegaly. Serial blood samples were collected from Day -28 to Day 84.

End point type	Primary

End point timeframe:

Sandostatin LAR 10 mg and 30 mg on Day -28 (Period 0) and CAM2029 10 mg q2w and 20 mg q4w on Day 0 and Day 56 (Period 1).

Notes:

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

End point values	Sandostatin LAR 10 mg	Sandostatin LAR 30 mg	CAM2029 10 mg q2w (Acromegaly)	CAM2029 20 mg q4w (Acromegaly)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	4	3	2
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day -28 (n = 1, 4, 0, 0)	0.349 (± 0)	1.25 (± 70)	0 (± 0)	0 (± 0)
Day 0 (n = 0, 0, 3, 2)	0 (± 0)	0 (± 0)	9.21 (± 65.4)	13 (± 33.8)
Day 56 (n = 0, 0, 2, 2)	0 (± 0)	0 (± 0)	7.83 (± 169.1)	11.1 (± 23.4)

Statistical analyses

No statistical analyses for this end point

Primary: Maximum observed plasma concentration over the final (Sandostatin LAR, CAM2029 q4w) or penultimate (CAM2029 q2w only) dosing interval (Cmax) for patients with NETs

End point title	Maximum observed plasma concentration over the final (Sandostatin LAR, CAM2029 q4w) or penultimate (CAM2029 q2w only) dosing interval (Cmax) for patients with NETs[6]

End point description:

The PK endpoints included the octreotide plasma concentration curve versus time and PK parameters for Sandostatin LAR and CAM2029 in patients with NETs. Serial blood samples were collected from Day -28 to Day 84.

End point type	Primary

End point timeframe:

Sandostatin LAR 20 mg and 30 mg on Day -28 (Period 0) and CAM2029 10 mg q2w and 20 mg q4w on Day 0 and Day 56 (Period 1).

Notes:

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

End point values	Sandostatin LAR 20 mg	Sandostatin LAR 30 mg	CAM2029 10 mg q2w (NETs)	CAM2029 20 mg q4w (NETs)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	4	1	4
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day -28 (n = 1, 4, 0, 0)	1.68 (± 0)	2.11 (± 69)	0 (± 0)	0 (± 0)
Day 0 (n = 0, 0, 1, 3)	0 (± 0)	0 (± 0)	6.33 (± 0)	15 (± 52.4)
Day 56 (n = 0, 0, 1, 4)	0 (± 0)	0 (± 0)	5.61 (± 0)	15.2 (± 30)

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with acromegaly whose Insulin-like growth factor-1 (IGF-1) levels are above and within normal limits on Day 84

End point title	Proportion of patients with acromegaly whose Insulin-like growth factor-1 (IGF-1) levels are above and within normal limits on Day 84

End point description:

The proportion of patients with IGF-1 levels within or above normal on Day 84 were summarized by treatment.

End point type	Secondary

End point timeframe:

Day 84 (Period 1).

End point values	CAM2029 10 mg q2w (Acromegaly)	CAM2029 20 mg q4w (Acromegaly)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3	2		
Units: Participants				
Within normal limits	2	1		
Above upper limit of normal (ULN)	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with acromegaly with growth hormone (GH) levels <2.5 µg/L on Day 84

End point title	Proportion of patients with acromegaly with growth hormone (GH) levels <2.5 µg/L on Day 84

End point description:

The proportion of patients with normalization of GH (adjusted for age and gender) <2.5 µg/L, at baseline and on Day 84 were summarized by treatments.

End point type	Secondary

End point timeframe:

Day 84 (Period 1).

End point values	CAM2029 10 mg q2w (Acromegaly)	CAM2029 20 mg q4w (Acromegaly)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3	2		
Units: Participants				
GH levels below 2.5 ug/L	2	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from the date of signing of informed consent to the final follow up visit.

Adverse event reporting additional description:

In case of early termination (before Day 84), the patients were monitored for safety for 28 days after the last CAM2029 treatment cycle and underwent assessments and procedures at the end of the Post-treatment Phase (Day 111).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Acromegaly

Reporting group description:

Twenty-eight days after the last injection of Sandostatin LAR (i.e. on Day 0), patients were randomized into the CAM2029 treatment phase (i.e. Period 1) and received their first subcutaneous thigh injection of 20 mg or 10 mg CAM2029 on Day 0. Patients randomized to receive 20 mg of CAM2029 were administered three upper thigh subcutaneous injections CAM2029 20 mg q4w on Days 0, 28 and 56; whereas patients randomized to receive 10 mg of CAM2029 were administered six upper thigh injections CAM2029 10 mg q2w on Days 0, 14, 28, 42, 56 and 70.

Reporting group title	NETs

Reporting group description:

Twenty-eight days after the last injection of Sandostatin LAR (i.e. on Day 0), patients were randomized into the CAM2029 treatment phase (i.e. Period 1) and received their first subcutaneous thigh injection of 20 mg or 10 mg CAM2029 on Day 0. Patients randomized to receive 20 mg of CAM2029 were administered three upper thigh subcutaneous injections of CAM2029 20 mg q4w on Days 0, 28 and 56; whereas patients randomized to receive 10 mg of CAM2029 were administered six upper thigh injections CAM2029 10 mg q2w on Days 0, 14, 28, 42, 56 and 70.

Serious adverse events	Acromegaly	NETs	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Anastomotic ulcer hemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Acromegaly	NETs	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)	3 / 5 (60.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
General physical health deterioration			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Injection site pain			
subjects affected / exposed	2 / 7 (28.57%)	1 / 5 (20.00%)	
occurrences (all)	6	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Throat irritation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Mood altered			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Investigations			

Insulin - like growth factor increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	0 / 7 (0.00%)	2 / 5 (40.00%)	
occurrences (all)	0	2	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Eyelid disorder			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 7 (28.57%)	1 / 5 (20.00%)	
occurrences (all)	2	1	
Diverticulum intestinal			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Food poisoning			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Haematochezia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Hiatus hernia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	

Large intestine polyp			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Proctitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	1 / 7 (14.29%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Osteoarthritis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Diabetes mellitus			
subjects affected / exposed	1 / 7 (14.29%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Hyperglycaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 June 2014	Amendment 1 was implemented based on request from Swedish Health Authority primarily: 1. Updated the name of the Medical Monitor. 2. Clarified the exclusion criteria for each patient population to exclude patients with angina or a history of myocardial infarction within 6 months prior to starting treatment. 3. Clarified that patients were to restart their pre-study regimen with Sandostatin LAR on Day 84 (Period 2). 4. Clarified the Schedule of Events Table that safety laboratory test samples would only be taken on dosing days for each patient population.
25 July 2014	Amendment 2 was implemented based on request from the French Independent Ethics Committee: 1. Added assessments for pre-dose fasting plasma glucose on all days when PK sampling was performed and provided instruction for the management of elevated fasting plasma glucose. 2. Added procedures and specifications to manage hepatic safety by monitoring clinical laboratory values. 3. Added an HbA1c test to occur on Day 56.
29 August 2014	Amendment 3 primarily implemented the following modifications: 1. Specified urgent safety measures as the trigger for early termination on a study level. 2. Added patient discontinuation criteria.
23 September 2014	Amendment 4 was a substantial global amendment to implement the following modifications, including country-specific (previous) amendments: 1. Authorized the use of Longastatina LAR for patients in Italy. Longastatina LAR is the same drug as Sandostatin LAR and is manufactured by the same company, but is commercialized as Longastatina LAR in Italy. 2. Updated the name of the Medical Monitor. 3. Changed the injection site from buttock to upper thigh. 4. Specified urgent safety measures as the trigger for early termination on a study level. 5. Clarified the exclusion criteria for each patient population to exclude patients with angina or a history of myocardial infarction within 6 months prior to screening. 6. Updated exclusion criteria regarding previous surgeries to include the 2-month period before screening rather than randomization. 7. Updated exclusion criteria regarding previous alcohol abuse to include the 12-month period before screening rather than randomization. 8. Added exclusion criteria regarding prior medications. 9. Clarified that patients would restart their pre-study regimen with Sandostatin LAR on Day 84 (Period 2). 10. Added patient discontinuation criteria based on safety criteria. 11. Added procedures and specifications to manage hepatic safety by monitoring clinical laboratory values. 12. Added an HbA1c test to occur on Day 56. 13. Added assessments for pre-dose fasting plasma glucose on all days when PK sampling performed and provided instruction for the management of elevated fasting plasma glucose. 14. Allowed historical abdominal ultrasound of the gallbladder for study use, if was performed within 2 months prior to screening. 15. Clarified the Schedule of Events Tables that safety laboratory test samples would only be taken on dosing days for each patient population.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported