Clinical trial results:
Anamorelin HCl in the Treatment of Non-Small Cell Lung Cancer – Cachexia (NSCLC-C): A Randomized, Double-Blind, Placebo-Controlled, Multicenter, Phase 3 Study to Evaluate the Safety and Efficacy of Anamorelin HCl in Patients with NSCLC-C

Summary

EudraCT number	2010-023648-34
Trial protocol	BE NL ES DE CZ IT SI HU PL
Global end of trial date	22 October 2014

Results information

Result version number	v1
This version publication date	15 September 2016
First version publication date	15 September 2016

Trial information

Trial identification

Sponsor protocol code	HT-ANAM-301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Other : ROMANA 1

Notes:

Sponsors

Sponsor organisation name	Helsinn Therapeutics (US), Inc.
Sponsor organisation address	170 Wood Avenue South, 5th Floor, Iselin, NJ, United States, 08830
Public contact	Richard K. Bourne, Ph.D., Helsinn Therapeutics (US), Inc., +1 732-603-2852, richard.bourne@helsinn.com
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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	04 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 January 2014
Global end of trial reached?	Yes
Global end of trial date	22 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To evaluate the effect of Anamorelin HCl on lean body mass (LBM) as measured by dual energy X-ray absorptiometry (DXA)
2. To evaluate the effect of Anamorelin HCl on muscle strength as measured by handgrip strength (HGS)

Protection of trial subjects:

The study was designed and monitored in accordance with Sponsor procedures, which comply with the ethical principles of Good Clinical Practice (GCP) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 June 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Russian Federation: 12
Country: Number of subjects enrolled	Serbia: 13
Country: Number of subjects enrolled	Ukraine: 199
Country: Number of subjects enrolled	Belarus: 24
Country: Number of subjects enrolled	United States: 37
Country: Number of subjects enrolled	Canada: 15
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Poland: 74
Country: Number of subjects enrolled	Slovenia: 9
Country: Number of subjects enrolled	Spain: 16
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	Czech Republic: 27
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Italy: 14

Worldwide total number of subjects	484
EEA total number of subjects	184

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)	320
From 65 to 84 years	164
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Approximately 477 patients with advanced NSCLC-C (defined as unresectable Stage III and Stage IV and a weight loss of ≥ 5% body weight within 6 months prior to screening or a screening body mass index [BMI] < 20 kg/m2) were to be randomized 2:1 to anamorelin HCl 100 mg or placebo.

Pre-assignment

Screening details:

Central randomization stratified patients by geographic region, by chemotherapy and/or radiation therapy status and by weight loss over prior 6 months.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo tablets.

Arm title	Anamorelin HCl

Arm description:

Active drug

Arm type	Experimental
Investigational medicinal product name	Anamorelin HCl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Anamorelin HCl; 100 mg tablets; oral administration QD for 12 weeks, at least 1 hour before the first meal of the day.

Number of subjects in period 1	Placebo	Anamorelin HCl
Started	161	323
Completed	121	231
Not completed	40	92
Unrelated AE	3	12
Lost to follow-up	-	1
Death	20	38
Other	7	8
Study drug-related AE	-	1
Withdrawal by patient	10	32

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description: Placebo	
Reporting group title	Anamorelin HCl
Reporting group description: Active drug	

Reporting group values	Placebo	Anamorelin HCl	Total
Number of subjects	161	323	484
Age categorical Units: Subjects			
≤ 65 years	105	215	320
> 65 years	56	108	164
Gender categorical Units: Subjects			
Female	40	76	116
Male	121	247	368
Race Units: Subjects			
White	159	319	478
Black or African American	0	1	1
Asian	0	1	1
Missing	2	2	4
Geographic region Units: Subjects			
North America	17	35	52
West Europe	62	122	184
East Europe + Russia	82	166	248
Australia	0	0	0

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo	
Reporting group title	Anamorelin HCl
Reporting group description:	
Active drug	
Subject analysis set title	ITT Population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The ITT Population included all randomized patients.	
Subject analysis set title	MITT Population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The MITT Population included all randomized patients who received any study drug and for whom at least 1 post-baseline co-primary efficacy variable (LBM or HGS) observation was obtained.	

Primary: Change in Lean Body Mass

End point title	Change in Lean Body Mass
End point description:	
Change in Lean Body Mass (LBM) from baseline over 12 weeks for the ITT Population. Change from baseline over 12 weeks was defined as the average of the change from baseline at Week 6 and the change from baseline at Week 12.	
End point type	Primary
End point timeframe:	
Change in Lean Body Mass from Baseline Over 12 Weeks	

End point values	Placebo	Anamorelin HCl		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	316		
Units: kg				
median (confidence interval 95%)	-0.47 (-1 to 0.21)	0.99 (0.61 to 1.36)		

Statistical analyses

Statistical analysis title	LBM statistical analysis
Comparison groups	Placebo v Anamorelin HCl

Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon rank sum test

Primary: Change in Handgrip Strength

End point title	Change in Handgrip Strength

End point description:

Change in Handgrip Strength (HGS) of the non-dominant hand from baseline over 12 weeks for the ITT Population. Change from baseline over 12 weeks was defined as the average of the change from baseline at Week 6 and the change from baseline at Week 12.

End point type	Primary

End point timeframe:

Change in Handgrip Strength of the Non-Dominant Hand from Baseline Over 12 Weeks

End point values	Placebo	Anamorelin HCl		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	316		
Units: kg				
median (confidence interval 95%)	-1.58 (-2.99 to -1.14)	-1.1 (-1.69 to -0.4)		

Statistical analyses

Statistical analysis title	HGS statistical analysis
Comparison groups	Placebo v Anamorelin HCl
Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1475
Method	Wilcoxon rank sum test

Secondary: Change in FAACT A/CS Domain Score

End point title	Change in FAACT A/CS Domain Score

End point description:

Change in the Functional Assessment of Anorexia/Cachexia Treatment (FAACT) 12-item Additional Concerns Subscale (A/CS) domain score from baseline overall (i.e., over 12 weeks) for the MITT Population.

End point type	Secondary

End point timeframe:

Change in FAACT A/CS Domain Score from Baseline Over 12 Weeks

End point values	Placebo	Anamorelin HCl		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	282		
Units: score				
least squares mean (standard error)	1.92 (± 0.805)	4.12 (± 0.752)		

Statistical analyses

Statistical analysis title	FAACT A/CS statistical analysis
Comparison groups	Placebo v Anamorelin HCl
Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	Mixed models analysis

Secondary: Change in FACIT-F Fatigue Domain Score

End point title	Change in FACIT-F Fatigue Domain Score

End point description:

Change in the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) domain score from baseline overall (i.e., over 12 weeks) for the MITT Population.

End point type	Secondary

End point timeframe:

Change in FACIT-F Fatigue Domain Score from Baseline Over 12 Weeks

End point values	Placebo	Anamorelin HCl		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	140	280		
Units: score				
least squares mean (standard error)	-1.19 (± 0.933)	0.26 (± 0.886)		

Statistical analyses

Statistical analysis title	FACIT-F statistical analysis
Comparison groups	Placebo v Anamorelin HCl

Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0544
Method	Mixed models analysis

Secondary: Change in Body Weight

End point title	Change in Body Weight

End point description:

Change in body weight (BW) from baseline overall (i.e., over 12 weeks) for the MITT Population.

End point type	Secondary

End point timeframe:

Change in Body Weight from Baseline Over 12 Weeks

End point values	Placebo	Anamorelin HCl		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	283		
Units: kg				
least squares mean (standard error)	0.14 (± 0.363)	2.2 (± 0.326)		

Statistical analyses

Statistical analysis title	BW statistical analysis
Comparison groups	Placebo v Anamorelin HCl
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events that occurred during the clinical trial, commenced with the first dose of study drug through the 28 day post-treatment follow-up visit.

Adverse event reporting additional description:

Adverse events that occurred following the signature of the informed consent, but prior to the first dose of study drug were not reported as adverse events in this trial. The adverse event reporting period also ended if the patient began an alternative therapy within 28 days of the last administration of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14

Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Anamorelin HCl
Reporting group description: -	
Reporting group title	Total: Placebo and Anamorelin HCl

Reporting group description:

TEAEs were defined as AEs with an onset date on or after the first dose date of the extension trial study drug and up to and including 7 days post-last dose date of the extension trial study drug.

Serious adverse events	Placebo	Anamorelin HCl	Total: Placebo and Anamorelin HCl
Total subjects affected by serious adverse events			
subjects affected / exposed	48 / 161 (29.81%)	82 / 320 (25.63%)	130 / 481 (27.03%)
number of deaths (all causes)	30	59	89
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	12 / 161 (7.45%)	24 / 320 (7.50%)	36 / 481 (7.48%)
occurrences causally related to treatment / all	0 / 12	0 / 24	0 / 36
deaths causally related to treatment / all	0 / 12	0 / 24	0 / 36
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iliac artery occlusion			

subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inferior vena caval occlusion			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 161 (0.62%)	2 / 320 (0.63%)	3 / 481 (0.62%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 3
General physical health deterioration			
subjects affected / exposed	1 / 161 (0.62%)	3 / 320 (0.94%)	4 / 481 (0.83%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 2
Pain			
subjects affected / exposed	1 / 161 (0.62%)	0 / 320 (0.00%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 161 (0.62%)	1 / 320 (0.31%)	2 / 481 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	1 / 161 (0.62%)	1 / 320 (0.31%)	2 / 481 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

Chronic obstructive pulmonary disease			
subjects affected / exposed	3 / 161 (1.86%)	4 / 320 (1.25%)	7 / 481 (1.46%)
occurrences causally related to treatment / all	0 / 4	0 / 5	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 161 (0.00%)	3 / 320 (0.94%)	3 / 481 (0.62%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Pulmonary haemorrhage			
subjects affected / exposed	1 / 161 (0.62%)	3 / 320 (0.94%)	4 / 481 (0.83%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 3
Dyspnoea			
subjects affected / exposed	2 / 161 (1.24%)	0 / 320 (0.00%)	2 / 481 (0.42%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	2 / 161 (1.24%)	0 / 320 (0.00%)	2 / 481 (0.42%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Bronchopulmonary hemorrhage			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Haemoptysis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 320 (0.00%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Epistaxis			
subjects affected / exposed	0 / 161 (0.00%)	2 / 320 (0.63%)	2 / 481 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			

subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 161 (0.62%)	2 / 320 (0.63%)	3 / 481 (0.62%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 320 (0.00%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	2 / 161 (1.24%)	0 / 320 (0.00%)	2 / 481 (0.42%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Myocardial infarction			
subjects affected / exposed	1 / 161 (0.62%)	0 / 320 (0.00%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Atrial flutter			

subjects affected / exposed	1 / 161 (0.62%)	0 / 320 (0.00%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	1 / 161 (0.62%)	0 / 320 (0.00%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Atrial fibrillation			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 161 (1.86%)	5 / 320 (1.56%)	8 / 481 (1.66%)
occurrences causally related to treatment / all	0 / 3	0 / 6	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	3 / 161 (1.86%)	0 / 320 (0.00%)	3 / 481 (0.62%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			

subjects affected / exposed	1 / 161 (0.62%)	2 / 320 (0.63%)	3 / 481 (0.62%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 161 (0.62%)	3 / 320 (0.94%)	4 / 481 (0.83%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	3 / 161 (1.86%)	1 / 320 (0.31%)	4 / 481 (0.83%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Idiopathic thrombocytopenic purpura			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 161 (0.62%)	1 / 320 (0.31%)	2 / 481 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	1 / 161 (0.62%)	0 / 320 (0.00%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal ulcer			

subjects affected / exposed	1 / 161 (0.62%)	1 / 320 (0.31%)	2 / 481 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 161 (0.62%)	1 / 320 (0.31%)	2 / 481 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 161 (0.62%)	0 / 320 (0.00%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 161 (0.00%)	2 / 320 (0.63%)	2 / 481 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			

subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	1 / 161 (0.62%)	0 / 320 (0.00%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 320 (0.00%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary tract obstruction			
subjects affected / exposed	1 / 161 (0.62%)	0 / 320 (0.00%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 161 (0.62%)	0 / 320 (0.00%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 161 (0.62%)	1 / 320 (0.31%)	2 / 481 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bone pain			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	4 / 161 (2.48%)	4 / 320 (1.25%)	8 / 481 (1.66%)
occurrences causally related to treatment / all	0 / 5	0 / 4	0 / 9
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 2
Cellulitis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 320 (0.00%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 161 (0.62%)	1 / 320 (0.31%)	2 / 481 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 161 (0.62%)	0 / 320 (0.00%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 320 (0.00%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			

subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobar pneumonia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 161 (0.00%)	2 / 320 (0.63%)	2 / 481 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 2
Oral candidiasis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis acute			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis C			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 161 (0.00%)	3 / 320 (0.94%)	3 / 481 (0.62%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			

subjects affected / exposed	2 / 161 (1.24%)	0 / 320 (0.00%)	2 / 481 (0.42%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	1 / 161 (0.62%)	1 / 320 (0.31%)	2 / 481 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 320 (0.31%)	1 / 481 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 161 (0.00%)	2 / 320 (0.63%)	2 / 481 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	Anamorelin HCl	Total: Placebo and Anamorelin HCl
Total subjects affected by non-serious adverse events			
subjects affected / exposed	84 / 161 (52.17%)	182 / 320 (56.88%)	266 / 481 (55.30%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	14 / 161 (8.70%)	50 / 320 (15.63%)	64 / 481 (13.31%)
occurrences (all)	20	78	98
Aspartate aminotransferase increased			
subjects affected / exposed	15 / 161 (9.32%)	37 / 320 (11.56%)	52 / 481 (10.81%)
occurrences (all)	21	52	73
Blood alkaline phosphatase increased			

subjects affected / exposed	10 / 161 (6.21%)	34 / 320 (10.63%)	44 / 481 (9.15%)
occurrences (all)	14	40	54
Platelet count decreased			
subjects affected / exposed	10 / 161 (6.21%)	14 / 320 (4.38%)	24 / 481 (4.99%)
occurrences (all)	16	30	46
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	66 / 161 (40.99%)	119 / 320 (37.19%)	185 / 481 (38.46%)
occurrences (all)	114	179	293
Leukopenia			
subjects affected / exposed	10 / 161 (6.21%)	16 / 320 (5.00%)	26 / 481 (5.41%)
occurrences (all)	10	17	27
Neutropenia			
subjects affected / exposed	22 / 161 (13.66%)	28 / 320 (8.75%)	50 / 481 (10.40%)
occurrences (all)	34	34	68
Thrombocytopenia			
subjects affected / exposed	23 / 161 (14.29%)	29 / 320 (9.06%)	52 / 481 (10.81%)
occurrences (all)	34	42	76
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	9 / 161 (5.59%)	19 / 320 (5.94%)	28 / 481 (5.82%)
occurrences (all)	10	23	33
Fatigue			
subjects affected / exposed	13 / 161 (8.07%)	25 / 320 (7.81%)	38 / 481 (7.90%)
occurrences (all)	15	28	43
Pyrexia			
subjects affected / exposed	1 / 161 (0.62%)	15 / 320 (4.69%)	16 / 481 (3.33%)
occurrences (all)	1	16	17
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 161 (5.59%)	17 / 320 (5.31%)	26 / 481 (5.41%)
occurrences (all)	9	21	30
Nausea			
subjects affected / exposed	15 / 161 (9.32%)	29 / 320 (9.06%)	44 / 481 (9.15%)
occurrences (all)	21	44	65
Vomiting			

subjects affected / exposed	8 / 161 (4.97%)	25 / 320 (7.81%)	33 / 481 (6.86%)
occurrences (all)	8	27	35
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 161 (4.97%)	14 / 320 (4.38%)	22 / 481 (4.57%)
occurrences (all)	9	14	23
Dyspnoea			
subjects affected / exposed	11 / 161 (6.83%)	19 / 320 (5.94%)	30 / 481 (6.24%)
occurrences (all)	13	24	37
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 161 (4.97%)	13 / 320 (4.06%)	22 / 481 (4.57%)
occurrences (all)	8	15	23
Hyperglycaemia			
subjects affected / exposed	10 / 161 (6.21%)	35 / 320 (10.94%)	45 / 481 (9.36%)
occurrences (all)	11	41	52

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 March 2012	Protocol amendment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported