Clinical trial results:
Anamorelin HCl in the Treatment of Non-Small Cell Lung Cancer – Cachexia (NSCLC-C): An Extension Study

Summary

EudraCT number	2010-023650-36
Trial protocol	HU BE NL GB ES CZ PL DE IT SI
Global end of trial date	22 April 2014

Results information

Result version number	v2 (current)
This version publication date	06 November 2016
First version publication date	30 June 2016
Version creation reason	• Changes to summary attachments Added the State to the sponsor's address.

Trial information

Trial identification

Sponsor protocol code	HT-ANAM-303

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01395914
WHO universal trial number (UTN)	-
Other trial identifiers	Other: ROMANA 3

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
Scientific contact	Richard K. Bourne, Ph.D., Helsinn Therapeutics (US), Inc., +1 732-603-2852, richard.bourne@helsinn.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	04 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 April 2014
Global end of trial reached?	Yes
Global end of trial date	22 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of Anamorelin HCl

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	14 November 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 167
Country: Number of subjects enrolled	Slovenia: 1
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Czech Republic: 14
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Hungary: 55
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	United States: 20
Country: Number of subjects enrolled	Belarus: 14
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Serbia: 6
Country: Number of subjects enrolled	Ukraine: 97
Country: Number of subjects enrolled	Russian Federation: 100
Country: Number of subjects enrolled	Australia: 10
Worldwide total number of subjects	513
EEA total number of subjects	256

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)	356
From 65 to 84 years	157
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients who completed dosing in either of the original trials of anamorelin HCl in the treatment of NSCLC-C (HT-ANAM-301 or HT-ANAM-302) were able to enroll in this study and continue to receive the study drug to which they were assigned, either anamorelin HCl 100 mg or placebo QD for an additional 12 weeks.

Pre-assignment

Screening details:

The primary purpose of this extension study was to permit patients who completed dosing in the original 12-week trials to have the option of continuing to receive randomized study drug for an additional 12 weeks, to further evaluate the safety and tolerability of anamorelin HCl.

Period 1

Period 1 title	Extension Study (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	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.

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

Number of subjects in period 1	Anamorelin HCl	Placebo
Started	345	168
Completed	273	131
Not completed	72	37
Lost to follow-up	6	2
Unrelated to study drug AE	6	1
Study drug-related AE	1	-
Death	23	17
Other	9	3
Withdrawal by patient	27	14

Baseline characteristics

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

Reporting group values	Anamorelin HCl	Placebo	Total
Number of subjects	345	168	513
Age categorical Units: Subjects			
≤ 65 years	236	120	356
> 65 years	109	48	157
Gender categorical Units: Subjects			
Female	83	43	126
Male	262	125	387
Race Units: Subjects			
White	344	166	510
Asian	0	1	1
Native Hawaiian or Other Pacific Islander	1	0	1
Missing	0	1	1
Geographic region Units: Subjects			
North America	19	5	24
West Europe	135	72	207
East Europe + Russia	184	88	272
Australia	7	3	10

End points

End points reporting groups

Reporting group title	Anamorelin HCl
Reporting group description: Active drug	
Reporting group title	Placebo
Reporting group description: Placebo	
Subject analysis set title	ITT Population
Subject analysis set type	Intention-to-treat
Subject analysis set description: The Intent-to-Treat (ITT) Population includes all enrolled patients of the extension trial.	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description: The Safety Population includes all patients who received any extension trial study drug.	

Primary: To evaluate the safety and tolerability of anamorelin HCl

End point title	To evaluate the safety and tolerability of anamorelin HCl[1]
End point description:	
End point type	Primary
End point timeframe: Over the 12-week treatment period	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The primary purpose of this extension study was to permit patients who completed dosing in the original 12-week trials to have the option of continuing to receiving study drug for an additional 12 weeks to further evaluate the safety and tolerability of anamorelin HCl. Therefore, no formal statistical hypothesis testing or sample size calculation was conducted.

End point values	Anamorelin HCl	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	93		
Units: Percent	52	56		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Body Weight

End point title	Change in Body Weight
End point description:	
End point type	Secondary
End point timeframe: Change in body weight from baseline of the original trial and baseline of the extension trial to Weeks 4,	

8, and 12.

End point values	Anamorelin HCl	Placebo	ITT Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	320	158	513	
Units: kg				
least squares mean (standard error)	3.06 (± 0.631)	0.92 (± 0.697)	2.13 (± 0.451)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Handgrip Strength of the Non-Dominant Hand

End point title	Change in Handgrip Strength of the Non-Dominant Hand

End point description:

End point type	Secondary

End point timeframe:

Change and percent change in HGS of the non-dominant hand from baseline of the original trial and baseline of the extension trial to Weeks 8 and 12.

End point values	Anamorelin HCl	Placebo	ITT Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	287	141	513	
Units: kg				
least squares mean (standard error)	-0.83 (± 0.929)	-0.55 (± 1.036)	-0.28 (± 0.646)	

Statistical analyses

No statistical analyses for this end point

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	21 / 167 (12.57%)	44 / 343 (12.83%)	65 / 510 (12.75%)
number of deaths (all causes)	22	35	57
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer metastatic			
subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm progression			
subjects affected / exposed	7 / 167 (4.19%)	16 / 343 (4.66%)	23 / 510 (4.51%)
occurrences causally related to treatment / all	0 / 7	0 / 16	0 / 23
deaths causally related to treatment / all	0 / 7	0 / 16	0 / 23
Tumour haemorrhage			

subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Injury, poisoning and procedural complications			
Splenic rupture			
subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Tracheo-oesophageal fistula			
subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
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			
Angina unstable			
subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	1 / 167 (0.60%)	0 / 343 (0.00%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	1 / 167 (0.60%)	0 / 343 (0.00%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			

subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
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	1 / 167 (0.60%)	3 / 343 (0.87%)	4 / 510 (0.78%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	1 / 167 (0.60%)	1 / 343 (0.29%)	2 / 510 (0.39%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	2 / 167 (1.20%)	1 / 343 (0.29%)	3 / 510 (0.59%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 167 (0.60%)	1 / 343 (0.29%)	2 / 510 (0.39%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	3 / 167 (1.80%)	1 / 343 (0.29%)	4 / 510 (0.78%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 3	0 / 1	0 / 4
Oedema peripheral			
subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Multi-organ failure			
subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Sudden death			
subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Gastrointestinal disorders			
Duodenal ulcer			
subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	1 / 167 (0.60%)	1 / 343 (0.29%)	2 / 510 (0.39%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 2
Oesophagitis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
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 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
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			
Acute respiratory failure			
subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 167 (0.60%)	2 / 343 (0.58%)	3 / 510 (0.59%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 167 (0.60%)	0 / 343 (0.00%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Respiratory failure			
subjects affected / exposed	1 / 167 (0.60%)	2 / 343 (0.58%)	3 / 510 (0.59%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 3
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
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			
Lower respiratory tract infection			
subjects affected / exposed	0 / 167 (0.00%)	1 / 343 (0.29%)	1 / 510 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 167 (0.00%)	4 / 343 (1.17%)	4 / 510 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1

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	72 / 167 (43.11%)	135 / 343 (39.36%)	207 / 510 (40.59%)
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	25 / 167 (14.97%)	45 / 343 (13.12%)	70 / 510 (13.73%)
occurrences (all)	37	56	93
Neutropenia			
subjects affected / exposed	8 / 167 (4.79%)	18 / 343 (5.25%)	26 / 510 (5.10%)
occurrences (all)	8	21	29
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	14 / 167 (8.38%)	19 / 343 (5.54%)	33 / 510 (6.47%)
occurrences (all)	14	20	34
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 167 (5.99%)	12 / 343 (3.50%)	22 / 510 (4.31%)
occurrences (all)	10	13	23

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