# 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 | 2010-023649-31 |
| Trial protocol | HU GB PL |
| Global end of trial date | 10 October 2014 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 28 October 2016 |
| First version publication date | 28 October 2016 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | HT-ANAM-302 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01387282 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Other: ROMANA 2 |

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 | 31 October 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 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 | 14 July 2011 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| 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 | Poland: 203 |
| Country: Number of subjects enrolled | United Kingdom: 1 |
| Country: Number of subjects enrolled | Hungary: 108 |
| Country: Number of subjects enrolled | Australia: 22 |
| Country: Number of subjects enrolled | Israel: 13 |
| Country: Number of subjects enrolled | Russian Federation: 133 |
| Country: Number of subjects enrolled | United States: 15 |
| Worldwide total number of subjects | 495 |
| EEA total number of subjects | 312 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 | 0 |

| wk | |
|---|---|
| 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) | 317 |
| From 65 to 84 years | 178 |
| 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 | 165 | 330 |
| Completed | 118 | 233 |
| Not completed | 47 | 97 |
| Unrelated AE | 4 | 6 |
| Lost to follow-up | 1 | 4 |
| Death | 16 | 47 |
| Other | 1 | 5 |
| Study drug-related AE | 2 | 2 |
| Withdrawal by patient | 23 | 33 |

## 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 | 165 | 330 | 495 |
| Age categorical<br>Units: Subjects | | | |
| ≤ 65 years | 108 | 209 | 317 |
| > 65 years | 57 | 121 | 178 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 43 | 90 | 133 |
| Male | 122 | 240 | 362 |
| Race<br>Units: Subjects | | | |
| White | 162 | 326 | 488 |
| Black or African American | 1 | 2 | 3 |
| Asian | 1 | 0 | 1 |
| Native Hawaiian or Other Pacific Islander | 0 | 1 | 1 |
| Other | 1 | 1 | 2 |
| Geographic region<br>Units: Subjects | | | |
| North America | 5 | 10 | 15 |
| West Europe | 75 | 142 | 217 |
| East Europe + Russia | 77 | 164 | 241 |
| Australia | 8 | 14 | 22 |

## 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 | 157 | 321 | | |
| Units: kg | | | | |
| median (confidence interval 95%) | -0.98 (-1.49 to -0.41) | 0.65 (0.38 to 0.91) | | |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | LBM statistical analysis |
| Comparison groups | Placebo v Anamorelin HCl |

| | |
|---|---|
| Number of subjects included in analysis | 478 |
| 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 | 157 | 321 | | |
| Units: kg | | | | |
| median (confidence interval 95%) | -0.95 (-1.56 to 0.04) | -1.49 (-2.06 to -0.58) | | |

### Statistical analyses

| **Statistical analysis title** | HGS statistical analysis |
|---|---|
| Comparison groups | Placebo v Anamorelin HCl |
| Number of subjects included in analysis | 478 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.648 |
| Method | Wilcoxon rank sum test |

## Secondary: Change in A/CS Domain Score from Baseline

| | |
|---|---|
| End point title | Change in A/CS Domain Score from Baseline |

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 | 136 | 268 | | |
| Units: score | | | | |
| least squares mean (standard error) | 1.34 (± 1.032) | 3.48 (± 0.944) | | |

**Statistical analyses**

| Statistical analysis title | FAACT A/CS statistical analysis |
|---|---|
| Comparison groups | Placebo v Anamorelin HCl |
| Number of subjects included in analysis | 404 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0016 |
| 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 | 136 | 268 | | |
| Units: score | | | | |
| least squares mean (standard error) | 1.23 (± 1.293) | 1.37 (± 1.169) | | |

**Statistical analyses**

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

| | |
|---|---|
| Number of subjects included in analysis | 404 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8637 |
| 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 | 136 | 268 | | |
| Units: kg | | | | |
| least squares mean (standard error) | -0.57 (± 0.438) | 0.95 (± 0.386) | | |

### Statistical analyses

| **Statistical analysis title** | BW statistical analysis |
|---|---|
| Comparison groups | Placebo v Anamorelin HCl |
| Number of subjects included in analysis | 404 |
| 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 | 27 / 161 (16.77%) | 73 / 330 (22.12%) | 100 / 491 (20.37%) |
| number of deaths (all causes) | 21 | 48 | 69 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Neoplasm progression | | | |
| subjects affected / exposed | 10 / 161 (6.21%) | 25 / 330 (7.58%) | 35 / 491 (7.13%) |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 25 | 0 / 35 |
| deaths causally related to treatment / all | 0 / 10 | 0 / 25 | 0 / 35 |
| Gastric cancer | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Epiglottic carcinoma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Vascular disorders | | | |
| Circulatory collapse | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 330 (0.00%) | 1 / 491 (0.20%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 330 (0.00%) | 1 / 491 (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 |
| Extremity necrosis | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| General disorders and administration site conditions | | | |
| Death | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 3 / 330 (0.91%) | 3 / 491 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 3 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 3 / 330 (0.91%) | 3 / 491 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 1 / 330 (0.30%) | 2 / 491 (0.41%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 4 / 330 (1.21%) | 4 / 491 (0.81%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary haemorrhage | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 5 / 330 (1.52%) | 5 / 491 (1.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 5 |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 330 (0.00%) | 1 / 491 (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 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 2 / 330 (0.61%) | 2 / 491 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Completed suicide | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |

| | | | |
|---|---|---|---|
| Investigations | | | |
| Blood creatine increased | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Blood glucose increased | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (0.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Head injury | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Fall | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 1 / 330 (0.30%) | 2 / 491 (0.41%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial tachycardia | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Tachycardia paroxysmal | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Nervous system disorders | | | |
| Convulsion | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 1 / 330 (0.30%) | 2 / 491 (0.41%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cerebrovasculary insufficiency | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 161 (1.86%) | 3 / 330 (0.91%) | 6 / 491 (1.22%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 2 / 330 (0.61%) | 3 / 491 (0.61%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 2 / 161 (1.24%) | 2 / 330 (0.61%) | 4 / 491 (0.81%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Pancytopenia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 161 (0.00%) | 2 / 330 (0.61%) | 2 / 491 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Agranulocytosis | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 / 161 (0.00%) | 2 / 330 (0.61%) | 2 / 491 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 330 (0.00%) | 1 / 491 (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 |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 330 (0.00%) | 1 / 491 (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 |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 6 / 330 (1.82%) | 6 / 491 (1.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 6 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |

| | | | |
|---|---|---|---|
| Sepsis | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 330 (0.00%) | 1 / 491 (0.20%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Tuberculosis | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 330 (0.00%) | 1 / 491 (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 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 330 (0.00%) | 1 / 491 (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 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 330 (0.00%) | 1 / 491 (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 |
| Infective exacerbation of chronic obstructive airways disease | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 330 (0.00%) | 1 / 491 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Dehydration | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 1 / 330 (0.30%) | 2 / 491 (0.41%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Electrolyte imbalance | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (0.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (0.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 330 (0.30%) | 1 / 491 (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 |

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 / 161 (44.72%) | 156 / 330 (47.27%) | 228 / 491 (46.44%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Neoplasm progression | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 2 / 330 (0.61%) | 2 / 491 (0.41%) |
| occurrences (all) | 0 | 2 | 2 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 21 / 161 (13.04%) | 48 / 330 (14.55%) | 69 / 491 (14.05%) |
| occurrences (all) | 28 | 61 | 89 |
| Leukopenia | | | |
| subjects affected / exposed | 6 / 161 (3.73%) | 25 / 330 (7.58%) | 31 / 491 (6.31%) |
| occurrences (all) | 7 | 29 | 36 |
| Neutropenia | | | |
| subjects affected / exposed | 10 / 161 (6.21%) | 31 / 330 (9.39%) | 41 / 491 (8.35%) |
| occurrences (all) | 14 | 48 | 62 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 16 / 161 (9.94%) | 29 / 330 (8.79%) | 45 / 491 (9.16%) |
| occurrences (all) | 19 | 30 | 49 |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 13 / 161 (8.07%) | 19 / 330 (5.76%) | 32 / 491 (6.52%) |
| occurrences (all) | 13 | 20 | 33 |
| Vomiting | | | |
| subjects affected / exposed | 9 / 161 (5.59%) | 9 / 330 (2.73%) | 18 / 491 (3.67%) |
| occurrences (all) | 12 | 11 | 23 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 7 / 161 (4.35%) | 13 / 330 (3.94%) | 20 / 491 (4.07%) |
| occurrences (all) | 8 | 15 | 23 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 14 / 161 (8.70%) | 29 / 330 (8.79%) | 43 / 491 (8.76%) |
| occurrences (all) | 15 | 35 | 50 |

| | | | |
|---|---|---|---|
| Metabolism and nutrition disorders<br>Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all) | 3 / 161 (1.86%)<br>3 | 23 / 330 (6.97%)<br>32 | 26 / 491 (5.30%)<br>35 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 11 April 2012 | Protocol amendment. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported