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

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Based on the data available, Anamorelin HCl produces an increase in total body weight and Lean Body Mass in patients with advanced cancer, and specifically in patients with NSCLC, in addition to increasing muscle strength and improving quality of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Appetite and general nutritional disorders
Study type	Interventional

Summary

ID

NL-OMON37977

Source
ToetsingOnline

Brief title
Helsinn HT-ANAM-301 study (ROMANA 1)

Condition

- Appetite and general nutritional disorders
- Miscellaneous and site unspecified neoplasms benign

Synonym
cachexia, wasting syndroom

Research involving
Human

Sponsors and support

Primary sponsor: Helsinn Therapeutics (U.S.), Inc
Source(s) of monetary or material Support: Helsinn Therapeutics

Intervention

Keyword: Anamorelin HCL, Cachexia, Non-Small Cell Lung Cancer

Outcome measures

Primary outcome

To evaluate the effect of Anamorelin HCl on lean body mass as measured by dual

energy X-ray absorptiometry (DXA)

To evaluate the effect of Anamorelin HCl on muscle strength as measured by

handgrip strength

Secondary outcome

To evaluate the effect of Anamorelin HCl on body weight

To evaluate the effect of Anamorelin HCl on quality of life as assessed using

the FAACT (Functional Assessment of Anorexia/Cachexia Treatment) and the

FACIT-F (Functional Assessment of Chronic Illness Therapy - Fatigue)

To evaluate the effect of Anamorelin HCl on overall survival

To evaluate the safety and tolerability of Anamorelin HCl

To evaluate the effect of Anamorelin HCl on quality of life as assessed using

the

Hunger Assessment Scale (see Appendix IV)

Study description

Background summary

Unexpected and rapid weight loss is universally recognized as a sign of disease. The importance of weight loss as both a symptom of cancer and contributor to morbidity and mortality from the disease has been recognized for many years. Up to 80% of terminally ill patients with cancer develop cachexia, which is often the direct cause of death. Despite the significant importance of cancer cachexia, treatments are lacking. The drugs most commonly employed on an off-label basis are the appetite stimulants megestrol acetate and dronabinol, however, the majority of their induced weight gain is fat, not LEAN BODY MASS. Anamorelin HCl, by virtue of its ghrelin agonist activity and growth hormone (GH) releasing effects, serves a dual role in the reversal of cancer induced anorexia and cachexia. Anamorelin HCl is an orally active ghrelin mimetic and GH secretagogue. Growth hormone and GH secretagogues have a broad array of beneficial actions on various body systems, characterized by anabolic effects on Lean Body Mass and bone. The ghrelin mimetic, MK-7677, increases body weight and reverses the negative nitrogen balance induced by starvation in healthy volunteers; these effects are independent of its orexigenic effects. Acute administration of ghrelin to cancer patients exhibiting anorexia and weight loss increases appetite and food intake.
In Phase II clinical studies conducted by Helsinn Therapeutics, Anamorelin HCl was administered to patients with cancer-induced cachexia, and demonstrated an increase in Lean Body Mass, handgrip strength (HGS), and directional benefit in patient-reported outcomes. The non-peptidic small molecule Anamorelin HCl offers the promise of an orally available drug.
Weight loss with cachexia is a common presenting sign in NSCL-C. Overall the patients with weight loss had a significantly lower response rate, shorter progression free survival, and shorter overall survival than those not reporting weight loss.

Study objective

Based on the data available, Anamorelin HCl produces an increase in total body weight and Lean Body Mass in patients with advanced cancer, and specifically in patients with NSCLC, in addition to increasing muscle strength and improving quality of life measures. Therefore, the 100 mg daily dosing and study duration for 12 weeks was selected based on both the safety and efficacy data obtained in previous Anamorelin HCl clinical trials, and a low survival rate in

NSCLC patients. The primary purpose of this trial is to further evaluate the impact of Anamorelin HCl on Lean Body Mass as measured by DXA and on muscle strength as measured by Hand Grip Strength in patients with advanced NSCLC-C.

Study design

This study is a randomized, double-blind, parallel-group, placebo-controlled study to assess the safety and efficacy of Anamorelin HCl in NSCLC-C patients. Eligible patients will be randomized (2:1) to Anamorelin HCl 100 mg or placebo taken once daily (QD) for a total of 12 weeks. Patients will be instructed to take the study drug at least 1 hour before their first meal of the day. Central randomization will stratify patients by geographic region (North America vs. rest of world), by chemotherapy and/or radiation therapy status, and by weight loss over prior 6 months . Patients who complete the 12 week treatment period will have the option of continuing in a separate double-blind extension study (HT-ANAM-303) in which patients will continue to be administered Anamorelin HCl 100 mg QD or placebo QD for an additional 12 weeks. This extension study will be submitted as a separate protocol.

Intervention

Investigational is Anamorelin HCl; 100 mg tablets; oral administration QD for 12 weeks, at least 1 hour before the first meal of the day. Subjects will have their blood drawn at 5 visits, will receive total body Dexa scans at 3 visits. Subjects will receive one CT-scan (or MRI) if a recent scan isn*t available at the start of the trial.

Study burden and risks

The study consists of a period of 18 weeks with 1) a screening period of 2 weeks at most, 2) a dubbel blind treatment period of 12 weeks and 3) a follow-up period of 4 weeks. There will be 7 visits in total and after this the patient will be tracked to register survival.
Blood will be drawn at almost all visits. There will be 4 physical examinations, 3 ECGs and urine will be collected twice. Also 3 Dxa scans and if needed 1 MRI or CT-scan will be done. The Hand Grip Strenght will be measured 3 times.
Anamorelin HCl has been studied in approximately 156 healthy volunteers and in approximately 254 patients with cancer. Side effects that were reported frequently (in more than 10% of patients) with the use of the study drug are the following: swelling of the hands or feet, diarrhea, nausea, constipation, weakness, fever, and increased blood sugar. Infrequent side effects (occurring in fewer than 10% of patients) include: decreases in blood pressure following the first dose and increases in liver function tests. The studies conducted so far are not large enough to determine if there is an effect (either improvement or worsening) of Anamorelin HCl on either overall survival or tumor growth. As

such the effect of the study drug on survival is not yet known.

Contacts

Public
Helsinn Therapeutics (U.S.), Inc

1140 US Highway 22 Suite 101
Bridgewater, New Jersey 08807
US
Scientific
Helsinn Therapeutics (U.S.), Inc

1140 US Highway 22 Suite 101
Bridgewater, New Jersey 08807
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Females and males at least 18 years of age
• Documented histologic or cytologic diagnosis of AJCC Stage III or IV NSCLC. Stage III patients must have unresectable disease.
• With regard to chemotherapy and/or radiation therapy:
o Patients may be receiving maintenance chemotherapy.
o Patients planning to initiate a new chemotherapy and/or radiation therapy regimen may do so only within ±14 days of randomization.
o Patients may have completed a chemotherapy and/or radiation therapy and/or have no plan to initiate a new regimen within 12 weeks from

randomization. At least 14 days must elapse from the completion of the chemotherapy and/or radiation therapy prior to randomization.
• Involuntary weight loss of *5% body weight within 6 months prior to screening or a screening BMI <20 kg/m2. Weights may have been measured or obtained and documented by patient history.
• Body mass index *30 kg/m2
• ECOG performance status *2 (Appendix I)
• Estimated life expectancy of >4 months at the time of screening
• Adequate hepatic function, defined as aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels *5 * upper limit of normal (ULN)
• Adequate renal function, defined as creatinine *2 * ULN, or calculated creatinine clearance *30 ml/minute
• The patient is able to understand and comply with the procedures for the Hand Grip Strenght evaluation
• If the patient is a woman of childbearing potential or a fertile man, he/she must agree to use an effective form of contraception during the study and for 30 days following the last dose of study medication (an effective form of contraception is abstinence, a hormonal contraceptive, or a double-barrier method)
• Must be willing and able to give signed informed consent and, in the opinion of the Investigator, to comply with the protocol tests and procedures.

Exclusion criteria

• Other forms of lung cancer (eg, small cell, mesothelioma)
• Women who are pregnant or breast-feeding
• Known HIV, hepatitis (B & C), or active tuberculosis
• Patients who are currently actively receiving chemotherapy and/or radiation therapy for disease treatment. Patients must not be planning to initiate chemotherapy and/or radiation therapy in the middle of the 12-week treatment period at the time of randomization.
• Had major surgery within 4 weeks prior to randomization. Patients must be well recovered from acute effects of surgery prior to screening. Patients should not have plans to undergo major surgical procedures during the treatment period.
• Currently taking prescription medications intended to increase appetite or treat weight loss;
• Patients unable to readily swallow oral tablets. Patients with severe gastrointestinal disease or intractable or frequent vomiting are excluded
• Has an active, uncontrolled infection
• Has uncontrolled diabetes mellitus
• Has untreated clinically relevant hypothyroidism
• Has known or symptomatic brain metastases
• Patients receiving strong CYP3A4 inhibitors within 14 days of randomization
• Patients receiving tube feedings or parenteral nutrition (either total or partial). Patients must have discontinued these treatments for at least 6 weeks prior to Day 1, and throughout the study duration
• Other clinical diagnosis, ongoing or intercurrent illness that in the Investigator*s opinion would prevent the patient*s participation

• Has had previous exposure to Anamorelin HCl
• Patients actively receiving a concurrent investigational agent

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-08-2011
Enrollment:	80
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Anamorelin HCL
Generic name:	nvt

Ethics review

Approved WMO

Date:	20-06-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	21-10-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-01-2012
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	27-01-2012
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	16-03-2012
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	28-03-2012
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	12-04-2012
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	01-08-2012
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	22-08-2012
Application type:	Amendment

Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	17-09-2012
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	12-10-2012
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	15-10-2012
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	21-03-2013
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	25-04-2013
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	19-08-2013
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	23-08-2013
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2010-023648-34-NL
Other	IND 066855
CCMO	NL36802.068.11

Study results

Date completed: 14-05-2014

Actual enrolment: 2

Summary results
Trial is onging in other countries