A Phase 1, Double-blind, Randomized, Placebo-controlled, Single Ascending Dose Study To Evaluate The Safety, Tolerability, And Pharmacokinetics Of Paltusotine In Healthy Subjects

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON51860

Source
ToetsingOnline

Brief title
Paltusotine single ascending dose safety and PK study.

Condition

- Other condition
- Endocrine disorders congenital
- Endocrine and glandular disorders NEC

Synonym
acromegaly, extreme growth and carcinoid syndrome

Health condition

Pituitary Gland disorder (acromegaly)

Research involving
Human

Sponsors and support

Primary sponsor: Crinetics Pharmaceuticals, Inc.
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Paltusotine, Pharmacokinetics, SAD

Outcome measures

Primary outcome

To evaluate the safety and tolerability of single doses of paltusotine starting

at 80 mg up to a maximum of 240 mg

Secondary outcome

To evaluate the PK of single doses of paltusotine

Study description

Background summary

Paltusotine is administered orally and acts on a receptor called the somatostatin receptor subtype 2. This receptor type is a target for a number of currently approved injectable drugs to treat conditions like acromegaly and neuroendocrine tumors. Acromegaly is a hormonal disorder resulting from the production of too much growth hormone. Too much growth hormone causes bones to increase in size, including the hands, feet and face. Paltusotine is an investigational drug that inhibits growth hormone release and could be a potential candidate for the treatment of acromegaly.

Paltusotine, like other substances that act on the somatostatin receptor, is also expected to be a potential candidate for the treatment of neuroendocrine tumors. Neuroendocrine tumors are caused by tumors usually found in the liver or the gut. Sometimes, these tumors can secrete substances such as serotonin and other vasoactive substances. Symptoms most commonly include cutaneous

flushing, and recurrent watery diarrhea and cramping.

Study objective

In this study we will investigate how safe specific doses of the compound paltusotine are and how well these are tolerated when they are used by healthy participants.

We also investigate how much of the compound is broken down and absorbed in the bloodstream of the body (this is called pharmacokinetics).

Participants will receive paltusotine or placebo. A placebo is a compound without any active ingredient. Please note that when the term *study compound* is used in this document, we mean paltusotine, placebo, or both.

Paltusotine has been used by humans in a research setting before. In addition, it has been extensively tested in the laboratory and on animals. Paltusotine will be tested at various dose levels in this study.

For this study we are looking for up to 27 healthy males and females. The participants will be divided into 3 different groups (9 participants per group). You will participate in 1 of these groups.

Study design

Screening -> Day -28 up to Day -3

In-house stay -> Day -2 to Day 3

Visit -> Day 5

Follow-up visit -> Day 8

Subjects will be given paltusotine or placebo as an oral solution of 40 milliliters (mL), 80 mL or less, or 120 mL or less. After administration of the study compound, the vial will be rinsed twice with 50 mL of water, which they will also be required to drink. Thereafter they are also required to drink an additional amount of 100 mL, 60 mL or more, or 20 mL or more of water so that the total ingested volume will be 240 mL in total (eg, 40 mL study compound+(2x50 mL water)+100 mL water=240 mL, approximately 1 cup). They will be required to drink the total 240 mL within 2 minutes. To mask the taste of both oral solutions, paltusotine or placebo, peppermint strips will be used before and after solution intake.

Whether they will receive paltusotine or placebo will be determined by chance and they will not have a choice as to whether they receive paltusotine or

placebo. Per group, 6 participants will receive paltusotine and 3 participants will receive placebo. Neither the subject, nor the investigators know if paltusotine or placebo will be administered; we call this a double-blinded study. However, if it is important for their health, for example in case of a serious side effect, this information can be looked up during the study.

For safety reasons, initially 2 participants will receive the study compound in each group. One participant will receive paltusotine, and 1 will receive placebo. After administration, the safety and tolerability of the study compound in these 2 participants will be closely monitored. If there are no concerns about the safety and tolerability within 24 hours after administration, then the remaining 7 participants (5 will receive paltusotine and 2 will receive placebo) in the same group will receive the study compound.

Intervention

Group | Treatment | How often

1 | paltusotine 80 mg (oral solution of 40 mL) or placebo | once daily on Day 1
2 | paltusotine 160 mg (oral solution of 80 mL) or lower* or placebo | once daily on Day 1
3 | paltusotine 240 mg (oral solution of 120 mL) or lower* or placebo | once daily on Day 1
* In case the dose level will be lower than planned, subjects will be informed verbally.

The dose for the next group will only be increased if the lower dose of the previous group was found to be well tolerated and if necessary in case of no objection by the Medical Research Ethics Committee. The study will be discontinued or the dose will be decreased if, in the opinion of the investigators, unacceptable side effects appear.

Study burden and risks

Blood draw
Drawing blood may be painful or cause some bruising. The use of the indwelling cannula (a tube in a vein in the arm) can sometimes lead to inflammation, swelling, hardening of the vein, blood clotting, and bleeding in the environment (bruising) of the puncture site. In some individuals, a blood draw can sometimes cause pallor, nausea, seating, low heart rate, or drop in blood pressure with dizziness or fainting.

In total, we will take about 87 milliliters (mL) of blood from screening to follow-up. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken at once each time. If the investigator thinks it is necessary for the safety of a participant, extra

samples might be taken for possible additional testing. If this happens, the total amount of blood drawn may be more than the amount indicated above.

Heart tracing
To make a heart tracing, electrodes (small, plastic patches) will be placed on arms, chest, and legs. To monitor your heart activity, electrodes (small, plastic patches) will be placed on the chest and abdomen. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Fasting
If they have to fast for a prolonged time during the study, this may lead to symptoms such as dizziness, headache, stomach upset, or fainting.

Coronavirus test
Samples for the coronavirus test will be taken from the back of the nose and throat using swabs. Taking the samples only takes a few seconds, but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of the throat may cause them to gag. When the sample is taken from the back of the nose, they may experience a stinging sensation and the eyes may become watery.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Sex: male or female.
2. Age: 18 to 55 years, inclusive, date of signing informed consent.
3. Body mass index (BMI): 18.0 to 30.0 kg/m2, inclusive, date of signing informed consent.
4. Body weight: >=62.5 kg for Group 3 only.
5. Status: healthy subjects.
6. At screening, female subjects may be of childbearing potential but not pregnant or lactating, or they may be of nonchildbearing potential (either surgically sterilized or physiologically incapable of becoming pregnant, or at least 1 year postmenopausal [amenorrhea duration of 12 consecutive months]); nonpregnancy will be confirmed for all female subjects by a negative serum pregnancy test conducted at screening, admission to the clinical research center, and at the follow-up visit,
7. Female subjects of childbearing potential who have a fertile male sexual partner must agree to use adequate contraception from at least 12 weeks prior to administration of the study drug until 90 days after the follow up visit. Adequate contraception is defined as using hormonal contraceptives or an intrauterine device combined with at least 1 of the following forms of contraception: a diaphragm, a cervical cap, or a condom. Total abstinence from heterosexual intercourse, in accordance with the lifestyle of the subject, is also acceptable.
8. Male subjects, if not surgically sterilized, must agree to use adequate contraception and not donate sperm from admission to the clinical research center until 90 days after the follow-up visit. Adequate contraception for the male subject (and his female partner, if she is of childbearing potential) is defined as using hormonal contraceptives or an intrauterine device combined with at least 1 of the following forms of contraception: a diaphragm, a cervical cap, or a condom. Total abstinence, in accordance with the lifestyle of the subject, is also acceptable.
9. All prescribed medication must have been stopped at least 30 days prior to admission to the clinical research center. An exception is made for hormonal contraceptives, which may be used throughout the study. Another exception is made for SARS-CoV-2 vaccines, which are allowed up to 2 weeks prior to admission to the clinical research center.
10. All over-the-counter medication, vitamin preparations and other food supplements, or herbal medications (eg, St. John*s wort) must have been stopped at least 30 days prior to admission to the clinical research center. An exception is made for paracetamol, which is allowed up to admission to the

clinical research center.

Further criteria apply, see protocol.

Exclusion criteria

1. Employee of PRA or the Sponsor.
2. History of relevant drug and/or food allergies.
3. Smoking more than 5 cigarettes, 1 cigar, or 1 pipe daily; the use of tobacco products in the 48 hours (2 days) prior to admission to the clinical research center is not allowed.
4. History of alcohol abuse or drug addiction (including soft drugs like cannabis products) in the last year.
5. Positive drug and alcohol screen (opiates, methadone, cocaine, amphetamines [including ecstasy], cannabinoids, barbiturates, benzodiazepines, tricyclic antidepressants, and alcohol) at screening and admission to the clinical research center.
6. Average intake of more than 21 units of alcohol per week (1 unit of alcohol equals approximately 250 mL of beer, 100 mL of wine, or 35 mL of spirits).
7. Positive screen for hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV) antibodies, or human immunodeficiency virus (HIV) 1 and 2 antibodies. Subjects with previous hepatitis C infection that is now cured may be eligible.
8. Participation in a drug study within 30 days prior to drug administration in the current study. Participation in 4 or more other drug studies in the 12 months prior to drug administration in the current study.
9. Participation in any previous clinical study with paltusotine.
10. History of hypersensitivity reactions to any excipients in the study drug.

Further criteria apply, see protocol.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-01-2022
Enrollment:	27
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Paltusotine
Generic name:	N/A

Ethics review

Approved WMO Date:	13-12-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-01-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2021-005883-22-NL
CCMO	NL79847.056.21

Study results

Results posted: 01-02-2023

First publication
13-12-2022