An open-label, non-randomized, fixed-sequence crossover study to investigate the effects of the proton pump inhibitor esomeprazole on the pharmacokinetics of elinzanetant (BAY 3427080) as well as assessment of the absolute bioavailability of elinzanetant using a single intravenous microtracer dose of [13C5]BAY 3427080 in male and female healthy participants.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Menopause related conditions
Study type	Interventional

Summary

ID

NL-OMON50454

Source
ToetsingOnline

Brief title
Esomeprazole interaction and AB study for elinzanetant (BAY 3427080)

Condition

- Menopause related conditions

Synonym
hot flashes, Postmenopausal symptoms

Research involving
Human

Sponsors and support

Primary sponsor: Bayer AG
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Elinzanetant, Esomeprazole, Pharmacokinetics

Outcome measures

Primary outcome

To investigate the effect of multiple doses of esomeprazole on the PK of

elinzanetant

Secondary outcome

To investigate the safety and tolerability of elinzanetant

To determine the absolute bioavailability of elinzanetant after single oral

administration of elinzanetant together with an IV microtracer dose of

[13C5]BAY3427080

Study description

Background summary

Elinzanetant is a new compound that may potentially be used for the treatment

of postmenopausal vasomotor symptoms (VMS; hot flashes and night sweats). During the menopause, the amount of estrogen in the blood decreases. Research shows that this affects the brain center that regulates body temperature. Elinzanetant blocks a chemical in the brain (neurokinin 1 and 3) that is involved in the regulation of the body temperature. This could lead to effective treatment of VMS in postmenopausal women.

Study objective

Elinzanetant is an investigational compound. It is not approved for sale. That means it can only be used in studies like this one. Elinzanetant has been extensively tested in the laboratory. It has also been already administered to approximately 300 healthy males and females in 10 clinical trials.

In this study we investigate the influence of the acidity in the gastro intestinal tract on how quick and to what extent elinzanetant is processed by the body (this is called pharmacokinetics). We will also investigate how safe the compound is and how well it is tolerated when it is used by healthy participants alone and in combination with esomeprazole.

Esomeprazole been used by patients for over 20 years for the treatment of reflux and peptic ulcers. In this study, the acidity in the gastro intestinal tract will be changed (made less acidic) with esomeprazole to see if this affects how elinzanetant is processed by the body.

The processing of elinzanetant administered as capsules will also be compared to the processing of elinzanetant administered as intravenous (iv; in the vein) infusion. The iv infusion of elinzanetant is a very low dose. The elinzanetant in the infusion is also made heavier by adding a carbon-13 atom to it. Carbon-13 is called an isotope and is not radioactive. This makes it possible to compare the amount of elinzanetant which is administered via the infusion with the amount administered as capsules and how both are processed by the body.

Study design

The study will take a maximum of 10 weeks from the screening until the follow-up visit.

For the study it is necessary that the volunteer stays in the research center for 21 days (20 nights).

The volunteer will be given elinzanetant as oral capsules with 240 milliliters (mL) of water and as an intravenous infusion. Esomeprazole will be given as oral tablets with 240 mL of water.

During the first hour after administration of the study compound on Day 1 and Day 13 the volunteer is not be allowed to lie down (except when instructed to do so by one of the investigators), as this may influence the uptake of the study compound.

On Day 13, the dose of esomeprazole is given very early: around 6 o*clock in the morning.

Intervention

Day | Treatment | Route | Timing | How often
1 | Elinzanetant 120 mg (2x60 mg soft gelatin capsules) | oral | Morning | once
| [13C5]Elinzanetant 100 µg in 10 mL over 30 minutes | intravenous infusion | 1 hour after oral administration | once
9-13 | Esomeprazole 40 mg (1 tablet) | oral | Morning | once daily
13 | Elinzanetant 120 mg (2x60 mg soft gelatin capsules) | oral | 3 hours after esomeprazole | once

Study burden and risks

Possible side effects:
The study compound may cause side effects
Elinzanetant has already been studied in approximately 510 persons, approximately 300 healthy persons and 210 patients with troublesome-postmenopausal VMS (hot flashes and night sweats) and other conditions. The following side effects are very often observed (in 1 in 10 people or more):
- Somnolence
- Fatigue
- Dizziness
- Constipation

The study compound may also have (serious) side effects that are still unknown. In addition to unknown side effects, there is a (small) chance that an allergic reaction will occur. This can be caused by the study compound or other ingredients that are used to prepare the formulation.

Esomeprazole may also cause side effects. The most important ones are:
- Headache
- Abdominal pain
- Diarrhea
- Nausea

Possible Discomforts:
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 not take more than 500 milliliters (mL) of blood from the volunteer. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken 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 the volunteer his arms, chest and legs. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Coronavirus test
Samples for the coronavirus test will be taken from the back of the volunteer his 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 volunteer his throat may cause him to gag. When the sample is taken from the back of the volunteer his nose, he may experience a stinging sensation and his eyes may become watery.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Participant must be 18 to 65 years of age inclusive, at the time of signing the informed consent.
2. Participants who are overtly healthy as determined by medical evaluation including medical history, physical examination, laboratory tests, and cardiac monitoring.
3. Body weight of at least 50 kg and body mass index (BMI) within the range of 18.0 to 30.0 kg/m^2 (inclusive).
4. Male and female
Contraceptive use by men or women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies.
- Male participants: Male participants of reproductive potential must agree to use a condom (with or without spermicide) when sexually active. This applies for the time period between the signing of the
informed consent form (ICF) until 5 days after the last dose of study intervention. Female partners of childbearing potential of male participants do not need to follow special precautions.
- Female participants: Women of childbearing potential will have to use highly effective non-hormonal contraception when having sexual intercourse with a male partner from signing the ICF until 5 days after last dose of the study drug.
-- Women of non-childbearing potential are not required to use contraception. Non-childbearing potential is defined as
- Postmenopausal state confirmed by follicle stimulating hormone (FSH) level >33.4 U/L, or above reference range from the local laboratory, or
- Surgically sterilized by bilateral tubal ligation, bilateral oophorectomy with or without hysterectomy, or hysterectomy documented by medical report verification.

Exclusion criteria

1. Any clinically relevant abnormal findings in medical history and physical examination which in the opinion of the investigators, may put the participant

at risk because of his/her participation in the trial or provide difficulties in interpreting the trial data.
2. History or evidence of any clinically relevant cardiovascular, gastrointestinal, endocrine, hematologic, hepatic, immunologic, metabolic, urologic, pulmonary, neurologic, dermatologic, psychiatric, renal and/or other clinically relevant disease, as judged by the investigator.
3. Pre-existing diseases for which it can be assumed that the absorption, distribution, metabolism, elimination and effects of the study intervention will not be normal.
4. Any medical disorder, condition or history of such that would impair the participant's ability to participate or complete this study in the opinion of the investigator.
5. Known hypersensitivity to the study interventions (active substances, or excipients of the preparations).
6. Known severe allergies e.g., allergies to more than 3 allergens, allergies affecting the lower respiratory tract - allergic asthma, allergies requiring therapy with corticosteroids, urticaria or significant nonallergic drug reactions.
7. Relevant diseases within the last 4 weeks prior to the first study intervention administration.
8. Febrile illness within 4 weeks before first study intervention administration.
9. Contraindications for the use of esomeprazole, especially known hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency
10. Use of drugs which may affect absorption (e.g. loperamide, metoclopramide) within 1 week before first study drug administration.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-09-2021

Enrollment:	14
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N/A
Generic name:	Elinzanetant
Product type:	Medicine
Brand name:	Nexium
Generic name:	Esomeprazole
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	07-09-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-09-2021
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	EUCTR2021-002032-24-NL
CCMO	NL78829.056.21

Study results

First publication
21-07-2022