A Randomized, Drug-Drug Interaction Study to Assess the Safety and Pharmacokinetics of VNRX7145 and Ceftibuten (VNRX5024) in Healthy Adult Volunteers

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In this study we will investigate how safe the new compound VNRX-7145 and the combination of 2 study compounds, the new compound VNRX7145 and the approved compound ceftibuten, are and how well they are tolerated when they are used by healthy...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON51149

Source
ToetsingOnline

Brief title
DDI on safety of PK of VNRX-7145 and Ceftibuten (VNRX-5024)

Condition

- Bacterial infectious disorders

Synonym
Serious infections

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Ceftibuten, DDI, VNRX-7145

Outcome measures

Primary outcome

Part 1

To evaluate the PK of VNRX 7145, its active metabolite VNRX5236 and ceftibuten when a single dose of VNRX 7145 is co-administered with ceftibuten compared to single doses of VNRX-7145 or ceftibuten administered alone.

Part 2

To evaluate the safety of repeated doses of 500 mg VNRX-7145 administered q8h for 10 days in healthy adult volunteers.

Part 3

To evaluate the safety of multiple doses (10 days) of orally administered VNRX 7145 at 2 dose levels when co-administered with ceftibuten.

Secondary outcome

Part 1

To evaluate the safety of a single dose of VNRX-7145 co-administered with ceftibuten compared to VNRX 7145 or ceftibuten administered alone.

Part 2

To evaluate the PK of VNRX-7145 and its active metabolite VNRX-5236 with repeated doses (q8h for 10 days) of 500 mg VNRX-7145 in healthy adult volunteers.

Part 3

To evaluate the PK of VNRX-7145, its active metabolite VNRX-5236, and ceftibuten following multiple doses (10 days) of orally administered VNRX-7145 at 2 dose levels when co-administered with ceftibuten.

Study description

Background summary

The resistance of bacteria against antibiotics is an increasing problem in the treatment of bacterial infections. A group of antibiotics, β-lactam antibiotics, is less effective because bacteria develop an enzyme (β-lactamase) that breaks down a central part of this group of antibiotics. VNRX-7145 is a new compound that may potentially be used to improve the treatment of serious bacterial infections. In the body, VNRX-7145 is converted to the active β-lactamase inhibitor VNRX-5236.

Ceftibuten is an approved β-lactam antibiotic that is used to treat serious bacterial infections (including inflammation in the lung, trachea, throat, sinuses, middle ear, and bladder). The Sponsor is developing VNRX7145 to be used in combination with ceftibuten.

Study objective

In this study we will investigate how safe the new compound VNRX-7145 and the combination of 2 study compounds, the new compound VNRX7145 and the approved compound ceftibuten, are and how well they are tolerated when they are used by healthy participants.

We also investigate how quickly and to what extent VNRX-7145 and/or ceftibuten are absorbed, transported, and eliminated from the body. In addition in part 2, we look at the antibiotic effect of VNRX-7145 and ceftibuten in urine and blood.

In part 1 we compare the effects of ceftibuten and VNRX-7145 alone with the combination of ceftibuten and VNRX-7145.
In part 2 and 3 we compare the effects of ceftibuten in combination with VNRX-7145 or placebo.
Ceftibuten is already being used in the treatment of serious bacterial infections at a dose of 400 mg per day. The dose used in this study (in part 2 and 3) is higher (3 times 400 mg per day), but has been used by humans before.

VNRX-7145 has been used by humans before. In addition, it has been extensively tested in the laboratory and on animals. In this study, VNRX-7145 will be tested at 2 dose levels. The combination of VNRX-7145 and ceftibuten has not been given to humans before.

Study design

The study will take a maximum of 7 weeks from the screening until the follow-up visit. For the study it is necessary that subjects stay in the research center for 1 period of 13 days (12 nights).

Part 1

Screening > Day -28 up to Day 2 prior to the first study drug administration
Arrival > Day -1
In-house stay > Day -1 up to Day 12
Departure > Day 12
Follow-up > Day 16 (±2 days)

Study compound administration on Day 1, Day 5 and Day 9. Subjects will be given VNRX-7145 and ceftibuten, as oral capsules with 240 milliliters (mL) of (tap)

water. They will receive VNRX-7145 (Treatment 1A), ceftibuten (Treatment 1B), and VNRX-7145 and ceftibuten (Treatment 1C). The sequence in which they will receive the treatments will be decided by chance. One of the investigators will inspect your hands and mouth after the study compound intake. This it to check if you have taken the study compound.

Part 2 and 3

Screening > Day -28 up to Day 2 prior to the first study drug administration
Arrival > Day -1
In-house stay > Day -1 up to Day 12
Departure > Day 12
Follow-up > Day 17 (±2 days)

Part 2
Subjects will receive the following treatment 3 times daily (every 8 hours): 500 mg VNRX-7145 or placebo (Treatment 2). Which treatment they receive will be determined by chance. Nine (9) participants will receive VNRX-7145 and 3 participants will receive placebo.

Part 3
Study compound administration on Day 1 to Day 10. Subjects will be given VNRX-7145 or placebo and ceftibuten, as oral capsules with 240 milliliters (mL) of (tap) water. They will receive one of the following treatments 3 times daily (every 8 hours): 400 mg ceftibuten with 300 mg VNRX-7145 (Treatment 3A), 400 mg ceftibuten with 500 mg VNRX-7145 (Treatment 3B), or ceftibuten placebo with VNRX-7145 placebo (Treatment 3C) . Which treatment they receive will be determined by chance. Ten (10) participants will receive Treatment 3A, 10 participants will receive Treatment 3B, and 4 participants will receive Treatment 3C. One of the investigators will inspect your hands and mouth after the study compound intake. This it to check if you have taken the study compound.

Part 3 will only proceed after Part 2 is completed and the study compound was well tolerated.

Intervention

Part 1

Treatment name | Treatment | How often
Treatment 1A | VNRX-7145 500 mg | once
Treatment 1B | Ceftibuten 400 mg | once
Treatment 1C | VNRX-7145 500 mg and Ceftibuten 400 mg | once

Part 2 and 3

Treatment name | Day | Treatment | How often
Treatment 2 | 1 to 9 | VNRX-7145 500 mg or VNRX-7145 Placebo | 3 times daily
Treatment 2 | 10 | VNRX-7145 500 mg or VNRX-7145 Placebo | once
Treatment 3A | 1 to 9 | VNRX-7145 300mg + Ceftibuten 400 mg | 3 times daily
Treatment 3A | 10 | VNRX-7145 300mg + Ceftibuten 400 mg | once
Treatment 3B | 1 to 9 | VNRX-7145 500mg + Ceftibuten 400 mg | 3 times daily
Treatment 3B | 10 | VNRX-7145 500mg + Ceftibuten 400 mg | once
Treatment 3C | 1 to 9 | VNRX-7145 Placebo + Ceftibuten Placebo | 3 times daily
Treatment 3C | 10 | VNRX-7145 Placebo + Ceftibuten Placebo | once

Study burden and risks

Blood draw
Drawing blood may be painful or cause some bruising. The use of the indwelling cannula 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, sweating, low heart rate, or drop in blood pressure with dizziness or fainting.

In total, we will take about 500 mL of blood in part 1, 200 mL of blood in part 2 and 450 mL of blood in part 3. These amounts 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 will be more than the amount indicated above.

Heart tracing
To make a heart tracing, electrodes will be placed on 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 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 subject 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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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Willing to participate in the study, give written informed consent, and comply with the study restrictions including lifestyle restriction outlined in Section 6.4 of the protocol.
2. Healthy male and female .subjects between 18 and 55 years of age (inclusive).
3. Body mass index (BMI): >=18.5 kg/m2 and <=32.0 kg/m2, at Screening.
4. Normal blood pressure at Screening and Day -1, defined as a systolic value greater than or equal to 90 mm Hg and less than or equal to 140 mm Hg and a diastolic value less than 90 mm Hg. Values outside the range for inclusion may be retested once if there is a clinical rationale for the out-of-range value.
5. Urine dipstick results for protein are negative or trace at Screening and Day -1.

Exclusion criteria

1. Employee or family members of the clinical research organization (CRO), CRC, or the Sponsor.
2. Female who is pregnant, lactating, or planning to attempt to become pregnant during this study or within 90 days after dosing of study drug.

3. Male with a female partner who is pregnant or lactating or planning to become pregnant within 90 days after the last dose of study drug administration.
4. Subject is participating in any other clinical study that involves the administration of an investigational product at the time of screening or during the course of the study or has received treatment with an investigational product in the 30 days before Screening (90 days for an injectable biological agent). See Protocol Section 7.6 Concomitant Treatment for more details.
5. Subject has a congenital or acquired immunodeficiency syndrome.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-05-2021
Enrollment:	54
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Isocef
Generic name:	Ceftibuten

Ethics review

Approved WMO

Date:	18-02-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-05-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-07-2021
Application type:	Amendment
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	EUCTR2021-001566-37-NL
CCMO	NL77461.056.21