A single-center, open-label study to investigate the mass balance, excretion pathways, and metabolites after a single oral dose of 500 mg, 3.7 MBq, [14C]BTZ-043 in healthy male volunteers

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Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON50849

Source
ToetsingOnline

Brief title
Mass balance, excretion pathways, and metabolites of 14C-labeled BTZ-043

Condition

- Other condition

Synonym
Tuberculosis

Health condition

Tuberculosis

Research involving
Human

Sponsors and support

Primary sponsor: University Hospital LMU Klinikum
Source(s) of monetary or material Support: Academia

Intervention

Keyword: [14C]BTZ-043, Healthy volunteers, Tuberculosis

Outcome measures

Primary outcome

- To determine the rates and routes of excretion of [14C]BTZ-043-related radioactivity, including mass balance of total drug-related radioactivity in urine and feces (and vomit, if applicable), following the oral administration of a single 500 mg dose of [14C]BTZ-043 in healthy male volunteers.

- To determine the PK of total radioactivity in whole blood and in plasma.

- To characterize the plasma PK of BTZ-043 and main metabolites by liquid chromatography-mass spectrometry (LC-MS), if applicable.

- To characterize the urine concentrations of BTZ-043 and main metabolites by LC-MS, if applicable.

Secondary outcome

- To assess the safety and tolerability of a single 500 mg oral dose of BTZ-043 administered to healthy male volunteers.

Study description

Background summary

BTZ-043 is a new compound that may potentially be used for the treatment of tuberculosis. Tuberculosis is the most deadly infectious disease in the world that generally affects the lungs and is usually caused by the Mycobacterium tuberculosis bacteria. New compounds are urgently needed to combat multidrug-resistant Mycobacterium tuberculosis (which is not responding to some compounds anymore), which remains a serious public-health challenge.

Study objective

In this study we will investigate how quickly and to what extent BTZ-043 is absorbed, transported, metabolized, and eliminated from the body (this is called pharmacokinetics). BTZ-043 is radioactively labelled with carbon-14 (14C). In this way BTZ-043 can be traced in blood, urine, and feces.

We will also investigate how safe the new compound BTZ-043 is and how well it is tolerated when it is used by healthy participants.

Study design

The study will take a maximum of 8 weeks from the screening until the follow-up visit.
For the study it is necessary that the volunteer stays in the research center for one period of at least 6 days (5 nights). If necessary, this period can be prolonged to a maximum of 9 days (8 nights).
The volunteer can leave after the 24-hour collection interval on Day 12 and Day 16. There is a follow-up visit on Day 31.

The volunteer will receive a single dose of 500 mg 14C-labeled radioactive BTZ-043.

Intervention

The volunteer will receive a single dose of 500 mg 14C-labeled radioactive BTZ-043.

The volunteer will be given BTZ-043 as a cloudy drink (suspension) of 100 milliliters (mL). After administration of the study compound, the vial will be rinsed twice with 70 mL of water, which the volunteer is also be required to drink. Thereafter the volunteer is also required to drink an additional amount of 140 mL (tap) water.

The volunteer may be given a standardized or a high-fat breakfast after an overnight fast (no eating or drinking) of at least 10 hours. Thereafter, the volunteer will be given the study compound. The volunteer may also receive the study compound without receiving a breakfast. Fasting continues for another 4 hours after dosing. Water is allowed during fasting, except from 1 hour prior to dosing until 1 hour after dosing.

During the first 4 hours after administration of the study compound the volunteer is not be allowed to lie down (with the exception of medical procedures that require lying down), as this may influence the uptake of the study compound.

Study burden and risks

Possible side effects:
The study compound may cause side effects.

BTZ-043 has already been studied in 24 healthy persons and 24 patients with tuberculosis. The following side effects are often observed (in 1 in 10 people or more):
• Dizziness
• Headache
• Hypertension (high blood pressure)
• Nausea
• Hyperhidrosis (increased sweating)
• Abdominal pain

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.

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, sweating, low heart rate, or drop in blood pressure with dizziness or fainting.

In total, we will take about 450 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 will be more than the amount indicated above.

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

Meals
The volunteer may receive a high-fast breakfast before the administration of the study compound. The high-fat breakfast is a big breakfast containing eg, 2 fried eggs, fried potatoes and bacon or brie (see Appendix C for the full composition). The volunteer must consume the whole breakfast within 20 minutes. It can be difficult to consume the entire breakfast, particularly for light eaters.

Fasting
If the volunteer has 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 volunters 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 volunteers throat may cause him to gag. When the sample is taken from the back of the volunteers nose, he may experience a stinging sensation and his 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. Sex : male
2. Age : 18 years to 55 years, inclusive, at screening.
3. Body mass index (BMI) : 18.0 to 29.0 kg/m2, inclusive, at screening.
4. Weight : 55 to 90 kg, inclusive, at screening.
5. Status : healthy subjects.
6. 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.
7. All prescribed medication must have been stopped at least 30 days prior to admission to the clinical research center.
8. All over-the-counter medications, vitamin preparations (especially vitamin C), other food supplements, and herbal medications (eg, St. John*s wort) must have been stopped at least 14 days prior to admission to the clinical research center. An exception is made for paracetamol, which is allowed up to 48 hours prior to study drug administration.
9. No vaccination within 14 days prior to study drug administration.
10. Ability and willingness to abstain from alcohol from 48 hours (2 days) prior to screening and admission to the clinical research center.
11. Ability and willingness to abstain from methylxanthine-containing beverages or food (coffee, tea, cola, chocolate, and energy drinks), grapefruit (juice), corn (whole corn kernels and popcorn), cruciferous vegetables, and bitter oranges from 48 hours (2 days) prior to admission to the clinical research center.
12. Good physical and mental health on the basis of medical history, physical examination, clinical laboratory, ECG, and vital signs, as judged by the Investigator.
13. Willing and able to sign the ICF.

Exclusion criteria

1. Participation in another study with a radiation burden of >0.1 mSv and <=1 mSv in the period of 1 year prior to screening; a radiation burden of >1.1 mSv and <=2 mSv in the period of 2 years prior to screening; a radiation burden of >2.1 mSv and <=3 mSv in the period of 3 years prior to screening, etc.
2. Exposure to radiation for diagnostic reasons (except dental X-rays and plain X-rays of thorax and bony skeleton [excluding spinal column]), or during work within 1 year prior to drug administration.
3. Irregular defecation pattern (less than once per day on average).
4. Employee of PRA, Nuvisan, or the Sponsor.
5. History of relevant drug and/or food allergies.
6. Using tobacco products within 60 days prior to drug administration.
7. History of alcohol abuse or drug addiction (including soft drugs like cannabis products).
8. Positive drug and alcohol screen (opiates, methadone, cocaine, amphetamines [including ecstasy], cannabinoids, barbiturates, benzodiazepines, gamma-hydroxybutyric acid, tricyclic antidepressants, and alcohol) at screening or admission to the clinical research center.
9. Average intake of more than 24 grams of alcohol per day.
10. Positive screen for hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV) antibodies, or HIV 1 and 2 antibodies.
11. Participation in a drug study within 30 days prior to drug administration in the current study. Participation in more than 4 drug studies in the 12 months prior to drug administration in the current study.
12. Donation or loss of more than 450 mL of blood within 60 days prior to drug administration. Donation or loss of more than 1.5 liters of blood in the 10 months prior to drug administration in the current study.
13. Significant and/or acute illness within 5 days prior to drug administration that may impact safety assessments, in the opinion of the Investigator.
14. Unwillingness to consume the Food and Drug Administration (FDA)-recommended high-fat breakfast.
15. Unsuitable veins for infusion or blood sampling.
16. Positive nasopharyngeal PCR test for SARS-CoV-2 on Day -1.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	27-09-2021
Enrollment:	4
Type:	Actual

Ethics review

Approved WMO Date:	14-07-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	12-08-2021
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	EUCTR2021-000449-42-NL
ClinicalTrials.gov	NCT04874948
CCMO	NL77661.056.21

Study results

Date completed: 09-11-2021

Results posted: 08-11-2022

First publication
25-10-2022