AN OPEN-LABEL, SINGLE-DOSE, SINGLE-PERIOD STUDY DESIGNED TO ASSESS THE MASS BALANCE RECOVERY, METABOLITE PROFILE AND METABOLITE IDENTIFICATION OF [14C]-OLOROFIM ADMINISTERED VIA THE ORAL ROUTE TO HEALTHY MALE SUBJECTS.

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

Summary

ID

NL-OMON48360

Source
ToetsingOnline

Brief title
[14C]-Olorofim

Condition

- Fungal infectious disorders

Synonym
Serious fungal infections

Research involving
Human

Sponsors and support

Primary sponsor: F2G Biotech GmBH
Source(s) of monetary or material Support: Farmaceutische Industrie.

Intervention

Keyword: Olorofim, Serious fungal infections

Outcome measures

Primary outcome

• To assess the mass balance recovery after a single oral dose of

[14C]-olorofim (Cohort A only)

• To provide plasma, urine, bile and faecal samples for metabolite profiling

and structural identification

Secondary outcome

• To determine the routes and rates of elimination of [14C]-olorofim

• To identify the chemical structure of each metabolite accounting for more

than 10% (by AUC) of circulating total radioactivity

• To further explore the oral pharmacokinetics (PK) of [14C]-olorofim

• To evaluate the extent of distribution of total radioactivity into blood

cells (Cohort A only)

• To evaluate the biliary elimination of olorofim-related material (Cohorts B1

and B2 only)

• To provide additional safety and tolerability information for olorofim.

Study description

Background summary

Olorofim is a new compound that may eventually be used for the treatment of serious fungal infections. Fungal infections are especially dangerous for patients with an immune system that is not working properly, like cancer patients, patients in the intensive care unit and transplantation patients.
With an improperly working immune system a fungus could invade the blood stream which can be fatal.
The currently available treatments have limitations, such as causing significant adverse reactions, they interact with other medications, and some strains of fungus have become resistant to some antifungal drugs (meaning the drugs do not work anymore).
Olorofim has a new mechanism of action compared to the available antifungal treatments. Olorofim inhibits a substance (enzyme) that is involved in cell multiplication. In this way olorofim prevents the growth and spread of the fungus in the body.

Study objective

The purpose of this study is to investigate how quickly and to what extent olorofim is absorbed and eliminated from the body. Olorofim will be labelled with 14 Carbon (14C) and is thus radioactive. In this way olorofim can be traced in blood, urine and stool and bile.

The bile will be collected via a nasoduodenal tube.

It will also be investigated how safe the new compound olorofim is and how well it is tolerated when it is administered to healthy volunteers. Olorofim has been administered to humans before.

Study design

The volunteer is given 120 mg of [14 C] olorofim as a drink of approximately 30 milliliters (mL). After the administration of the test substance, the bottle will be rinsed a few times with water, which you should also drink. A total of 240 ml of the test substance / water should be drunk.

During the first 2 hours after administration of the test substance, the volunteer should not lie down (except when indicated by one of the researchers), as this may influence the uptake of the test substance.

Part A:
The study will consist of 1 group with 6 volunteers.

The actual study will consist of 1 period during which they will stay in the research center for up to 16 days (15 nights). If necessary, they will return to the research center for one or two 24-hour collection of urine and feces on Day 21 and Day 28. For these collection intervals, they are expected in the research center at 11.00 hour in the morning of Day 21 and Day 28, and they can leave after the 24-hour collection interval (Day 22 and/or Day 29).

Day 1 is the day of administration of the study compound. The volunteers are expected at the research center at 14:00 h in the afternoon prior to the day of administration of the study compound. They will leave the research center on Day 15 of the study (unless radioactivity levels permits to leave earlier).

Part B:
The study will consist of 2 groups (Group B1 and Group B2) with a total of 6 volunteers (with at least 2 volunteers in a group). One can participate in one of the groups. The actual study consists of 1 period during which the volunteers will stay in the research center for 6 days (5 nights).

Day 1 is the day of administration of the study compound. They are expected at the research center at 14:00 h in the afternoon prior to the day of administration of the study compound. They will leave the research center on Day 5 of the study.

On Day 1, approximately 2 hours before administration of the study compound, a nasoduodenal tube will be inserted through the nose into the duodenum . A nasoduodenal tube is a slim flexible tube that under local anesthesia, is inserted via the nose, through the esophagus (gullet) and stomach, placed with its tip in the duodenum (first part of the intestines) to take samples of the liquid (bile) in the duodenum. The tube will be inserted once and will remain in place for up to 8 hours (for Group B1) or 14 hours (Group B2).

Intervention

Not applicable.

Study burden and risks

Drawing blood and/or insertion of the indwelling cannula (tube in an arm vein) may be painful or cause some bruising.

In total, we will take maximally resp. 450 milliliters (mL) or 300 milliliters (mL) of blood. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time.

To make a heart tracing, electrodes (small, plastic patches) will be pasted at specific locations on the arms, chest and legs. Prolonged use of these

electrodes can cause skin irritation (rash and itching).

During a period of 6 hours (Group B1) or 12 hours (Group B2) after administration of the study compound on Day 1 they will have samples of the fluid (bile) in the duodenum collected via the nasoduodenal tube.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

healthy males
18 - 55 years
50 - 100 kilograms
BM) 18 - 30 kilograms/meter2

non smokers

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study.

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):	08-08-2019
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO Date:	27-06-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-07-2019

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	EUCTR2018-004561-13-NL
CCMO	NL70439.056.19