A single-center, open-label study to evaluate the absorption, distribution, metabolism and excretion (ADME) and pharmacokinetics of LOU064 following a single dose of [14C]LOU064 administered orally or intravenouslyl in healthy male and female subjects at steady-state.

Published: 24-07-2019
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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON49324

Source
ToetsingOnline

Brief title
ADME of LOU064 following a single dose of [14C]LOU064

Condition

- Autoimmune disorders

Synonym
autoimmune and chronic inflammatory diseases

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Farmaceutische Industrie.

Intervention

Keyword: ADME, autoimmune diseases, LOU064

Outcome measures

Primary outcome

To determine the rates and routes of excretion of [14C]LOU064-related radioactivity, including mass balance of total drug-related radioactivity in urine and feces.

To determine the pharmacokinetics (PK) of total radioactivity in blood and plasma of [14C]LOU064.

To characterize the blood PK of LOU064 and known key metabolites, if applicable.

Secondary outcome

To assess the safety and tolerability of multiple oral doses of 100 mg of LOU064 administered to healthy male/female subjects.

Study description

Background summary

LOU064 is a new compound that may eventually be used for the treatment of autoimmune and chronic inflammatory diseases. LOU064 inhibits the enzyme Bruton*s tyrosine kinase which is present in immune cells and is essential for signaling through various receptors. The effect of LOU064 on Bruton*s tyrosine kinase is believed to be an attractive way to treat various autoimmune and chronic inflammatory diseases, including rheumatoid arthritis, multiple sclerosis, atopic dermatitis and asthma.

Study objective

The purpose of this study is to investigate how quickly and to what extent LOU064 is absorbed, broken down, and eliminated from the body. LOU064 will be labeled with 14 carbon (14C) and is thus radioactive. In this way LOU064 can be traced in blood, urine, and feces. LOU064 has been administered to humans before. It has also been previously tested in the laboratory and on animals.

It will also be investigated how safe the new compound LOU064 is and how well it is tolerated when it is administered to healthy volunteers.

Furthermore, the effect of the genetic information on the body*s response to LOU064 will be investigated. This part of the study is optional.

Part 2A and 2B:
In Part 1, 5 volunteers received LOU064 as oral capsules twice a day. The morning administration of Day 2 was with radioactive [14C]LOU064 (as a drink). The results of Part 1 did not show clearly how LOU064 was absorbed and excreted by the body. Therefore, in this Part 2, [14C]LOU064 will be administered as an intravenous injection (solution of the compound administered directly into a blood vessel). One volunteer will receive a capsule of LOU064 twice a day for 5 days, with radiolabeled [14C]LOU064 as an intravenous injection on Day 2 (Part 2A). The second volunteer will receive LOU064, twice daily, as a capsule for 9 days, with radiolabeled [14C]LOU064 as an intravenous injection on Day 6 (Part 2B).
It will also be investigated how safe the new compound LOU064 is and how well it is tolerated when it is administered to healthy volunteers.
Furthermore, the effect of your genetic information on the body*s response to LOU064 will be investigated. This part of the study is optional.

Study design

The participation from screening until the follow-up visit will last up to 9 weeks.

The volunteer will receive 9 doses of 100 milligram (mg) of non-radiolabeled LOU064 as 2 oral capsules (containing 50 mg of non-radiolabeled LOU064 each) with 240 milliliters (mL) of (tap) water. One of the investigators will inspect

the hands and mouth after each study treatment intake, to check whether the volunteers have actually taken the study treatment. They will furthermore receive 1 dose of 100 mg of 14C-labeled LOU064 as an oral solution of 20 mL. After this they will receive a glass with 240 mL water, that they will also have to drink. The [14C]LOU064 dose contains 0.074 MBq (2 µCi) radioactivity. After administration of [14C]LOU064, the vial will be rinsed with water, which they will also be required to drink. All subjects will receive the same study treatment.

The study will consist of 1 period during which the volunteer will stay in the research center for 12 days (11 nights).

Day 1 is the day of the first administration of the study treatment. They are expected at the research center at 14:00 h in the afternoon prior to the day of the first administration of the study treatment, so on Day -1. They will leave the research center on Day 11 of the study. The volunteer will also have to take into account the 4 additional 24-hour visits for the collection of urine. feces and blood.

For the additional 24-hour visits, they are expected at the research center at 11:00 h in the morning of Days 15, 19, 23 and/or 27. They will leave the research center on Days 16, 20, 24 and/or 28, respectively.

During the stay, the urine and feces will be collected and blood will be sampled each day to measure the amount of radioactivity. Depending on the test results of the amount of radioactivity left in the blood, urine and/or feces, 24-hour visits can be cancelled.

Part 2A and 2B:
The participation from screening until the follow-up visit will last about 9 weeks (Part 2A) or 10 weeks (Part 2B).
The volunteer will receive 100 milligram (mg) of non-radiolabeled LOU064 twice daily for 5 days or 9 days. Each non-radiolabeled dose of LOU064 will be administered as 2 oral capsules (containing 50 mg of non-radiolabeled LOU064 each) with 240 milliliters (mL) of water. One of the investigators will inspect the hands and mouth after each study treatment intake, to check whether they have actually taken the study treatment. On Day 2 or Day 6, 1 hour after the capsules with LOU064, you will receive intravenous injection of 2 mL with 0.1 mg radio-labeled [14C]LOU064. The [14C]LOU064 dose contains 0.074 MBq (2 µCi) of radioactivity.

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 up to 500 mL of blood from the volunteer.

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).

This study involves using radioactive markers. The additional amount of radiation the volunteers will be exposed to in this study is 3.2 µSv

Contacts

Public
Novartis

Lichtstrasse 35
Basel CH-4056
CH
Scientific
Novartis

Lichtstrasse 35
Basel CH-4056
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

healthy male or female of non-childbearing potential.
18 - 55 years of age.
BMI 18.0 - 30.0 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):	29-08-2019
Enrollment:	7
Type:	Actual

Ethics review

Approved WMO

Date:	24-07-2019
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-08-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-09-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-11-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-11-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-11-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-12-2020
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	EUCTR2019-001047-52-NL
CCMO	NL70801.056.19