A single-center, randomized, double-blind, placebo-controlled, single ascending dose study to investigate the pharmacokinetics, pharmacodynamic effects, safety and tolerability of single doses of RO5459072 in healthy volunteers.

Published: 05-11-2014
Last updated: 21-04-2024

The purpose of the study is to investigate to what extent RO5459072 is safe and well tolerated. It will also be investigated how quickly and to what extent RO5459072 is absorbed, distributed to and removed from the body (this is called...

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

Summary

ID

NL-OMON41854

Source
ToetsingOnline

Brief title
RO5459072 Single Ascending Dose Study

Condition

- Autoimmune disorders

Synonym
Lupus

Research involving
Human

Sponsors and support

Primary sponsor: F. Hoffmann-La Roche Ltd.
Source(s) of monetary or material Support: Farmaceutische Industrie.

Intervention

Keyword: Lupus Nephritis, RO5459072

Outcome measures

Primary outcome

Primary: To investigate the safety and tolerability of RO5459072 in healthy volunteers.

Secondary outcome

Secondary:

* To investigate the effects of RO5459072 on pharmacodynamic measures of cathepsin S activity.

* To characterize the relationship between RO5459072 exposure and pharmacodynamic measures of cathepsin S activity.

* To characterize the single dose pharmacokinetics of RO5459072 and assess dose proportionality.

* To explore the influence of genotype on the pharmacokinetic and pharmacodynamic effects of RO5459072.

* To collect samples for exploratory metabolite profiling.

Study description

Background summary

RO5459072 is a new investigational compound that may eventually be used for the treatment of autoimmune diseases such as lupus nephritis. Lupus is a disease of the immune system where the defense mechanisms can damage any part of the body (skin, joints, and/or organs inside the
body). Lupus nephritis is a damage of the kidneys due to this disease.
RO5459072 is a compound that inhibits the protein cathepsin S. This protein naturally occurs in the body and plays an important role in the immune system. In autoimmune diseases like Lupus, cathepsin S may be
overactive. This is the first time that this compound will be given to humans.

Study objective

The purpose of the study is to investigate to what extent RO5459072 is safe and well tolerated. It will also be investigated how quickly and to what extent RO5459072 is absorbed, distributed to and removed from the body (this is called pharmacokinetics). In addition, the effect of the compound on cathepsin S activity and on other proteins in the blood will be investigated (this is called pharmacodynamics). Furthermore, how metabolites (degradation products) of RO5459072 are removed from the body and the effect of food on the compound*s tolerability and pharmacokinetics may be investigated.

Study design

Before the study the volunteer will undergo a pre-study screening during which they will be subjected to a number of medical examinations. Similar examinations will be performed after the study at the post-study screening.

The actual study will consist of 4 periods during which the volunteers will stay in the clinical research center for 5 days (4 nights) (Period 1) or 4 days (3 nights) (Periods 2-4). The time interval between the different periods that they will participate in will be at least 4 weeks.

The volunteers will be admitted to the clinical research center on Day -2 (Period 1) and on Day -1 (Periods 2-4) and will leave the clinical research center on Day 3 of each period. Day 1 of each period is the day of administration of study medication. The volunteers will be required not to have consumed any food or drinks during the 4 hours prior to arrival in the clinical research center (with the exception of water).
The post-study screening will take place 7-14 days after the last time you have been administered study medication.
The participation to the entire study, from pre-study screening until the post-study screening, will be approximately 22 weeks.

On Day 1 of each period the volunteers will receive a single dose of RO5459072

or placebo with 240 milliliters of tap water. For the higher dose levels an additional 240 mL of tap water will be permitted (since the number of capsules to take will be higher). In most cases they will receive the medication after an overnight fast (no food or drinks with the exception of water) of at least 8 hours. However, it is possible that the volunteers will receive the study drug once after a standard high fat breakfast that they will have to finish completely.
It will be determined during the study whether this will be the case and in which period.

For all groups it is applicable that on Day 1 of each period fasting will continue until 4 hours after study drug administration. Then the volunteers will receive a lunch. During fasting before and after intake of the study medication, they are allowed to drink water with the exception of the first 2 hours after study drug administration. One of the investigators will inspect the volunteers hands and mouth after study medication intake.

Intervention

This study will be performed in 16 healthy volunteers, divided over 2 groups, which will participate in an alternating design. Volunteers in Group A will participate in the 1st, 3rd, 5th and 7th periods and volunteers in Group B will participate in the 2nd, 4th, 6th, and 8th periods.
Each group will contain 8 participants. The volunteers can participate in one group only.

Study burden and risks

All potential drugs cause adverse events; the extent to which this occurs differs. As RO5459072 will be administered to humans for the first time in this study, adverse effects of RO5459072 in humans have not been reported to date. RO5459072 has been studied in animals at high dose levels and administered repeatedly for up to 13 weeks. In these studies in rats and monkeys, adverse findings were observed only in animals receiving very high doses. At these dose levels, the animals were exposed to RO5459072 blood levels that were more than 250 times higher than the concentrations that are thought to be needed for the medication to be effective. The animal findings at these high doses included changes in the kidney, the heart and in the liver. In the animals with no adverse events, the blood levels of RO5459072 were still at least 66 times higher than the blood concentration expected to have clinical effects. From this data it is not anticipated to see significant changes in humans at the dose levels that will be given in this study; however your health will be closely monitored throughout the study.
In a preliminary rat study , there was some evidence that RO5459072 at high dose levels may cause birth defects. However, this was observed at dose levels

that were much higher than those that will be used in humans. In rabbits, no birth defects were observed. This study will exclude
women who could become pregnant. Overall, data from animal studies do not indicate particular safety risks associated with
RO5459072 treatment.

Contacts

Public
F. Hoffmann-La Roche Ltd.

Grenzachterstrasse 124
Basel 4070
CH
Scientific
F. Hoffmann-La Roche Ltd.

Grenzachterstrasse 124
Basel 4070
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy subjects
18 and 60 years of age, inclusive
BMI 18 - 30 kilogram/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
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-12-2014
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	RO5459072
Generic name:	RO5459072

Ethics review

Approved WMO Date:	05-11-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-11-2014
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	EUCTR2014-003538-23-NL
CCMO	NL51238.056.14