A SINGLE-CENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, ASCENDING DOSE STUDY TO INVESTIGATE THE PHARMACOKINETICS, PHARMACODYNAMIC EFFECTS, SAFETY AND TOLERABILITY OF REPEATED DOSING OF RO5459072 IN HEALTHY SUBJECTS

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

Summary

ID

NL-OMON42481

Source
ToetsingOnline

Brief title
RO5459072 MAD 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

To investigate the effects of RO5459072 on pharmacodynamic measures of

cathepsin S activity and immune function.

Secondary outcome

* To investigate the safety and tolerability of repeated dosing with RO5459072.

* To characterize the steady state pharmacokinetics of RO5459072 and assess

time dependency.

* To characterize the relationship between RO5459072 exposure and

pharmacodynamic parameters

* To explore the influence of intrinsic factors and alternative dosing regimens

on the pharmacokinetics 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 and Sjögren*s

syndrome. Lupus nephritis and Sjögren*s syndrome are diseases 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. Sjögren*s syndrome is a damage of the saliva and tear glands due to this disease, leading to dry mouth and dry eyes. RO5459072 is a compound that inhibits the enzyme cathepsin S. This enzyme naturally occurs in the body and plays an important role in the immune system. In the latter autoimmune diseases, cathepsin S may be overactive. RO5459072 is not registered as a drug but has been given to humans before.

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, it will be investigated how degradation products (metabolites) of RO5459072 are removed from the body. Furthermore, the effect of the compound on cathepsin S activity, white blood cells and on other proteins in the blood will be investigated (this is called pharmacodynamics).
The subject will also undergo a delayed-type hypersensitivity (DTH) test twice to investigate your immune response.

Study design

The actual study will consist of one period during which you will stay in the clinical research center in Groningen for 12 days (11 nights).

During the study the subject will receive RO5459072 or placebo with 240 milliliters of tap water. In Groups B, C and D, an additional 240 mL of tap water may be permitted (since the number of capsules to take may be higher). On Days 1 and 9 the subject will be dosed within 30 minutes after the start of breakfast. Lunch will be served approximately 4 hours after dosing, followed by an optional snack at approximately 7 hours after dosing and dinner approximately 10 hours after dosing. In between meals the subjects are allowed to drink water, except for 1 hour before and 1 hour after study drug administration. On Day 1 the subject will follow same meal schedule as on Days 1 and 9. On all other days, meals (including breakfast, lunch, an optional snack and dinner) may be served at convenience.

Intervention

This study will be performed in maximally 36 healthy volunteers, divided over up to 4 groups (Groups A, B, C and D). Each group will contain 9 volunteers. The subjects can participate in one group only.

Study burden and risks

All potential drugs cause adverse events; the extent to which this occurs differs. Single dose administration of RO5459072 has been studied previously in 17 healthy male and female volunteers. The most frequently observed adverse effects were: frequency micturition increased, feeling heaviness lower limbs, loose stools, bloating, inflammation of the hair follicles (folliculitis), headache, nervousness, dizziness, pain lower back, and sleepiness. Most of the adverse events reported were mild in intensity, and judged as not related to the study compound by the Principal Investigator in charge of the study conduct.

The injections under the skin of the subject's arm during the skin test are slightly painful and may cause a raised, thickened local area of skin and redness. As a result of the skin test, there is a very small chance that the subjects will have a severe hypersensitivity reaction or that the subjects will develop a small scar on the injection spots.

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 male and female subjects
18 to 60 years old, iinclusive
BMI between 18.0 and 30.0 kg/m^2

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):	10-08-2015
Enrollment:	36
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	18-06-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-06-2015
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	EUCTR2015-001838-15-NL
CCMO	NL53871.056.15