A two-part, phase 1, randomized, single blind, placebo-controlled, single centre study to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of LAS191954 following oral administration of single and multiple ascending doses in healthy male volunteers

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

Summary

ID

NL-OMON42989

Source
ToetsingOnline

Brief title
LAS191954 SAD/MAD study

Condition

- Other condition

Synonym
autoimmune and blistering disease, dermatological

Health condition

pemphigus vulgaris (auto-immune intradermal blistering disease)

Research involving
Human

Sponsors and support

Primary sponsor: Almirall
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: bullous autoimmune disease, LAS191954, Pemphigus Vulgaris

Outcome measures

Primary outcome

- To evaluate safety and tolerability of LAS191954 administered orally as a

single dose and as multiple doses in healthy male volunteers.

- To evaluate the pharmacokinetics of LAS191954 administered orally as a single

dose and as multiple doses in healthy male volunteers.

- To evaluate the pharmacodynamic effects of LAS191954 administered orally as a

single dose and as multiple doses in healthy male volunteers.

Secondary outcome

-

Study description

Background summary

LAS191954 is a new investigational compound that may eventually be used for the

treatment of pemphigus vulgaris, a dermatological, autoimmune and blistering disease. In an autoimmune disease the immune system recognizes the body*s own cells as foreign. This may result in the formation of antibodies against one*s own tissues. The enzyme (protein) phosphoinositide 3 kinase (PI3K) plays an important role in the activation of immune cells. This enzyme (PI3K) can be inhibited by LAS191954, which may result in an improvement of the disease.

Study objective

The purpose of both parts is to investigate how safe LAS191954 is and how well LAS191954 is tolerated. Also will be investigated how quickly and to what extent LAS191954 is absorbed into, distributed in, and eliminated from the body (this is called pharmacokinetics). In addition, the effect of LAS191954 on certain blood markers will be investigated (this is called pharmacodynamics).

Study design

Part 1:
The study will consist of 3 periods. During Period 1 the will stay in the clinical research center in Groningen for 4 days (3 nights): from the afternoon of Day -2 (2 days before administration of the study compound) to the morning of Day 2. During Periods 2 and 3 the volunteer will stay in the clinical research center in Groningen for 3 days (2 nights): from the afternoon of Day -1 (1 day before administration of the study compound) to the morning of Day 2. You will receive the next treatment approximately 28 after the previous treatment.

During the study the volunteer will receive LAS191954 or placebo as oral capsules with 240 milliliters of tap water. The study compound will be given under fasted conditions. This means that the volunteer is not allowed to eat for at least 4 hours before administration of the study compound. During fasting the volunteer is allowed to drink water with the exception of 0.5 hour prior to until 2 hours after administration of the study compound. Fasting will continue until 2 hours after administration of the study compound. Then he will be asked to swallow a glucose solution.

Part 2:
The study will consist of 1 period during which the volunteer will stay in the clinical research center in Groningen for 10 days (9 nights): from the afternoon of Day -2 (2 days before administration of the study compound) to the morning of Day 8.

The study will consist of 1 period during which you will receive LAS191954 or placebo twice daily for 6 days (Days 1-6) with a single dose of LAS191954 or placebo in the morning of Day 7. LAS191954 and placebo will be given in the form of oral capsules.

Intervention

Part 1:
The study will consist of 3 periods during which the volunteer will receive LAS191954 or placebo once per period. LAS191954 and placebo will be given as oral capsules.

Part 2:
The study will consist of 1 period during which you will receive LAS191954 or placebo twice daily for 6 days (Days 1-6) with a single dose of LAS191954 or placebo in the morning of Day 7. LAS191954 and placebo will be given in the form of oral capsules.

Study burden and risks

All potential drugs cause adverse events; the extent to which this occurs differs. As LAS191954 will be administered to man for the first time in this study, adverse effects of LAS191954 in man have not been reported to date.

In animal studies with LAS191954 and in studies with study compounds with the same mechanism of action, the following adverse effects were observed: hyperglycemia (increased blood glucose level), hypertriglyceridemia (increased fat level in blood), decrease in white blood cells, increase in blood pressure, liver toxicity (increase in liver enzymes), pneumonitis, diarrhea, abdominal pain, nausea, fever, cough, chills, intestinal perforation, skin inflammation, rash and allergic reactions.

In animal studies with LAS191954 the male reproductive system was affected after 4 weeks of treatment with LAS191954. Results of animal studies with LAS191954 with a treatment duration of 2 weeks, allow to investigate the study compound in repeated administration to humans up to 14 days. Nevertheless, since a potential effect on men fertility cannot be ruled out, the fertility of volunteers in the current study will be monitored by measuring some fertility markers (inhibin B, follicle stimulating hormone and testosterone).

Procedures: pain, minor bleeding, bruising, possible infection

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

- willing to participate in this study
- healthy Caucasian male
- age between 18 and 45 years of age, inclusive
- BMI between 18.5 and 29.9 kilograms/meter2
- do not smoke and did not smoke during at least 6 months prior to the pre-study screening. Able to abstain from smoking from admission to the clinical research center and during stay in the clinical research center
- at the pre-study screening state of health must satisfy the study entry requirements

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:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-05-2016
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO Date:	18-04-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-04-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-09-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	16-09-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-10-2016
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	EUCTR2015-001068-20-NL
CCMO	NL57303.056.16