A Randomized, Placebo-Controlled, Double-blind, Multiple Dose, Phase 1 Study to Evaluate the Safety, Tolerability, and Pharmacokinetics Following Intravenous Administration of SRK-001 in Healthy Participants.

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

Summary

ID

NL-OMON52159

Source
ToetsingOnline

Brief title
Multiple Dose Study on Safety, Tolerability, and PK of SRK-001

Condition

- Autoimmune disorders

Synonym
SLE, systemic lupus erythematosus

Research involving
Human

Sponsors and support

Primary sponsor: Sarkana Pharma, Inc.
Source(s) of monetary or material Support: pharmaceutical industry

Intervention

Keyword: Multiple dose, Pharmacokinetics, Safety, SRK-001

Outcome measures

Primary outcome

TEAEs and SAEs.

Secondary outcome

• AUC0-tau at steady state

• Half-life (t1/2)

• Concentrations at end of infusion (Cmax) and

end of dosing interval (Ctrough)

Study description

Background summary

SRK-001 is a compound being investigated for the potential treatment of systemic lupus erythematosus (SLE). SLE is an autoimmune disease where the immune system turns against its own cells. Cells are the building blocks of our body. The immune system is supposed to protect the body against pathogens, such as bacteria and viruses. This is done with antibodies. Antibodies clear up the pathogens, but in SLE, antibodies turn against their own cells. This can cause inflammation anywhere in the body. This is often affecting the skin, joints, kidneys, lungs, and brain. SRK-001 aims to neutralize a specific protein (IL 21) that plays an important role in SLE. Neutralizing IL-21 might decrease the response of the immune system.

Study objective

In this study, SRK-001 is being investigated to see how safe it is and how well it is tolerated when it is administered to healthy participants.

We will also investigate how quickly and to what extent SRK-001 is absorbed, distributed, and eliminated from the body (this is called pharmacokinetics). In addition, we will look at the effect of SRK-001 on the levels of the protein IL 21 in your blood.

We will compare the effects of SRK-001 with the effects of a placebo. A placebo is a compound without any active ingredient. Please note that when the term *study compound* is used in this document, we mean SRK-001, placebo, or both.

SRK-001 (previously known as LY3200327) has been investigated in humans before (see trial number NCT02595736 on clinicaltrials.gov). In addition, it has been extensively tested in the laboratory and in animals

Study design

Group 1, 1a and 3:

For the research it is necessary that the volunteer stays in the research center for 4 periods. The first stay lasts 5 days (4 nights), the second stay lasts 2 days (1 night), the third stay also lasts 2 days (1 night) and the fourth stay lasts 5 days (4 nights). In addition, the volunteer will return to the research center for 6 visits, including 2 follow-ups at the end of the study.

Below is an overview of the days on which the volunteer will visit the research center and spend the night there.

Inspection: Day -28 to Day -2
Stay: from Day -1 to Day 4 + Day 14 to Day 15* + Day 28 to Day 29 + Day 42 to Day 46
* This is a short visit for Group 1 on Day 15 and an overnight stay for Groups 1a and 3.
Visits: Day 8 + Day 50 + Day 57 + Day 71
Follow-up visits: Day 113 + Day 155

Day 1 is the first day of study drug administration. The volunteer is expected at the study center on the day before the day of first administration of the study drug (i.e. on Day -1). The volunteer will remain at the research center until all Day 4 examinations are completed.

On Day 14, Day 28 and Day 42, the volunteer will remain at the study center until the studies are completed on Day 15, Day 29 and Day 46, respectively.

For visits, including the 2 follow-ups (Days 8, 50, 57, 71, 113 and 155), the

volunteer will remain until the examinations are completed.

Group 2:

For the research it is necessary that the volunteer stays in the research center for 2 periods. The first stay lasts 5 days (4 nights) and the second stay also lasts 5 days (4 nights). In addition, the volunteer returns to the research center for 7 visits, including 2 follow-ups at the end of the study.

Below is an overview of the days on which the volunteer will visit the research center and spend the night there.

Inspection: Day -28 to Day -2
Stay: from Day -1 to Day 4 + Day 28 to Day 32
Visits: Day 8 + Day 15 + Day 36 + Day 43 + Day 57
Follow-up visits: Day 99 + Day 141

Day 1 is the first day of study drug administration. The volunteer is expected at the study center the day before the day of the first administration of the study drug (i.e. on Day -1). The volunteer will remain at the research center until all Day 4 examinations are completed.

The second study drug administration will occur on Day 28, the first day of the second study center stay. The volunteer will remain in the research center until all examinations are completed on Day 32.

In addition, the volunteer will return to the research center for 7 visits, including 2 follow-up checks (Days 8, 15, 36, 43, 57, 99 and 141).

Intervention

The volunteer will receive the study drugs as an intravenous infusion (solution of the drug administered directly into a blood vessel). Each infusion takes approximately 30 minutes.

Whether the volunteer receives SRK-001 or placebo is determined by chance. A maximum of 8 participants per group receive SRK-001 and 2 participants receive placebo. Neither the volunteer nor the investigators know whether the volunteer is receiving SRK-001 or placebo; We call this a double-blind study. If it is important for health, for example in the case of a serious side effect, this can be looked up.

Groups 1, 1a and 3: The volunteer receives 300 milligrams (mg), 600 mg SRK-001 or placebo, depending on which group the volunteer is in. This dose is given 4 times, once every 2 weeks. The doses are given on Days 1, 15, 29 and 43.

Group 2: The volunteer receives 600 milligrams (mg) of SRK-001 or placebo. This dose is given twice, once every 4 weeks. The dose is given on Days 1 and 29.

Study burden and risks

The study compound may cause side effects.

SRK-001 has been investigated in 50 healthy participants (28 males and 22 females), aged between 21 and 59 years in a previous clinical trial. Single doses of SRK-001 were administered in a vein (intravenously, IV) or under the skin (subcutaneously, SC) at doses up to 600 mg. SRK-001 was found to be well tolerated. Of the 38 participants who received SRK-001 (the others received placebo), there were 4 side effects that were considered to be related to the administration of the study compound, all of mild severity and transient (go away within a short period of time):
- 1 participant who received a 300 mg IV dose of SRK-001 reported blurred vision
- 1 participant who received a 600 mg IV dose of SRK-001 reported dry eyes
- 1 participant who received a 300 mg IV dose of SRK-001 reported drowsiness
- 1 participant who received a 600 mg SC dose of SRK-001 reported fever

In the first group of the current study of 8 participants, one of the participants reported blurred vision after the first dose. It is not known if this participant received 300 mg SRK-001 or placebo. The blurred vision was completely resolved within 48 hours without the need of treatment.

Possible risks related to administration of SRK-001 include:
- Hypersensitivity reactions and reactions at the spot where SRK-001 is administered. The volunteer will be observed for at least 1 hour after the end of each dosing, to monitor if you develop any of these side effects.
- Formation of antibodies against SRK-001 that may result in other side effects or may limit how well SRK 001 works. We will collect blood samples to monitor this.

Given the number of participants is few that have received SRK-001, the observation in monkeys of periorbital edema (swelling around the eyes) and eye related disorders may be relevant. These effects occurred shortly after infusion, were transient, and the frequency and severity were dependent on the infused amount of SRK-001.

The study compound may also have (serious) side effects that are still unknown. In addition to unknown side effects, there is a (small) chance that an allergic reaction will occur. This can be caused by the study compound or other ingredients that are used to prepare the formulation.

If during the study more information becomes available regarding side effects that may be related to the study compound, the responsible doctor will inform the volunteer about this.

Blood draw
Drawing blood may be painful or cause some bruising. In some individuals, a blood draw can sometimes cause pallor, nausea, seating, low heart rate, or drop in blood pressure with dizziness or fainting.

In total, we will take about 170 milliliters (mL) of blood from the volunteer. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time. If the investigator thinks it is necessary for the safety of a participant, extra samples might be taken for possible additional testing. If this happens, the total amount of blood drawn may be more than the amount indicated above.

Heart tracing
To make a heart tracing, electrodes (small, plastic patches) will be placed on the arms, chest, and legs. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Coronavirus test
Samples for the coronavirus test will be taken from the back of the nose and throat using swabs (the same way as is done at the GGD). Taking the samples only takes a few seconds, but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of the throat may cause you to gag. When the sample is taken from the back of the nose, the volunteer may experience a stinging sensation and the eyes may become watery.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Participant must be 18 to 65 years of age at the time of signing the informed consent.
2. Participants who have clinical chemistry laboratory values within acceptable range for the population, as per investigator judgment
3. Body mass index of 18 to 32 kg/m2, inclusive
4. Healthy male participants
a. Nonvasectomized male participants must agree to abstain from sexual intercourse or use a condom as well as 1 additional highly effective method of contraception (<1% failure rate) or effective method of contraception with all sexual partners of
childbearing potential during the study and for 90 days following the last dose of study intervention.
b. Must agree not to donate sperm from start of dosing until 90 days beyond the last dose of study intervention.
c. No restrictions are required for a vasectomized male provided his vasectomy has been performed and confirmed to be effective by a semen sample lacking sperm at least 3 months or more prior to screening. A male who has been vasectomized or <3 months prior to screening must follow the same restrictions as a nonvasectomized male.
5. Healthy female participants of childbearing potential who have a fertile male sexual partner must be willing and able to practice effective contraception from screening to 90 days after the last dose of study intervention. Sexually active participants must use a combination of 2 of the following methods of contraception, including at least 1 so-called 'barrier' method:
a. hormonal contraceptives (oral, transdermal patches, vaginal, or injectable)
b. intrauterine device with or without hormones
c. condom, diaphragm, or cervical cap ('barrier' method)
d. sexual abstinence, and
e. vasectomized partner.
Contraceptive requirements do not apply for participants who are exclusively in a same-sex relationship.

Further criteria apply, see protocol.

Exclusion criteria

1. Have any concomitant disorder that, in the opinion of the investigator, would preclude participation in the study.
2. For at least 30 days prior to randomization, participants must have no symptoms and/or signs of confirmed or suspected infection (including COVID-19) and must have completed any appropriate anti-infective treatment.
3. Have human immunodeficiency virus (HIV) infection.
4. Have a current infection with hepatitis B virus (HBV) (that is, positive for hepatitis B surface antigen and/or polymerase chain reaction positive for HBV DNA.
5. Have a current infection with hepatitis C virus (HCV) (that is, positive for HCV RNA).

Further criteria apply, see protocol.

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:	Completed
Start date (anticipated):	23-11-2021
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	22-09-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-11-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-04-2022
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	EUCTR2021-003991-15-NL
CCMO	NL79005.056.21

Study results

Date completed: 05-09-2022

Results posted: 18-07-2023

Summary results
Trial ended prematurely

First publication
11-07-2023