A DOUBLE-BLIND, PLACEBO-CONTROLLED DOSE ESCALATION STUDY OF THE SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF A SUBCUTANEOUS DOSE OF SHK-186 IN HEALTHY SUBJECTS

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The purpose of the study is to investigate to what extent ShK-186 is tolerated. How quickly and to what extent ShK-186 is absorbed and eliminated from the body (this is called pharmacokinetics) will be investigated.

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

Summary

ID

NL-OMON36904

Source
ToetsingOnline

Brief title
ShK-186 SAD study

Condition

- Autoimmune disorders

Synonym
Disorder in which the body makes antibodies against body□s own proteins

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Autoimmune diseases, ShK-186

Outcome measures

Primary outcome

Pharmacokinetics: plasma drug concentrations, pharmacokinetic parameters

Safety: adverse events, vital signs, ECG-parameters, laboratory parameters,

physical examination

Secondary outcome

n/a

Study description

Background summary

ShK-186 is a new investigational compound that may eventually be used for the treatment of several autoimmune diseases. In an autoimmune disease the immune system recognizes the body*s own cells and/or substances as foreign. This may result in the formation of antibodies against one*s own tissues. ShK-186 can possibly inhibit this autoimmune response.
ShK-186 is not registered as a drug. This is the first time that this compound is being given to humans.

Study objective

The purpose of the study is to investigate to what extent ShK-186 is tolerated.
How quickly and to what extent ShK-186 is absorbed and eliminated from the body (this is called pharmacokinetics) will be investigated.

Study design

This is a single-center, double-blind, placebo-controlled study with 7 planned successive escalating cohorts, each containing approximately 8 subjects. Each group of 8 subjects will be split. The first two subjects will be dosed on the same day (one ShK 186 and one placebo). After dosing, the safety and tolerability of ShK-186 in these subjects will be closely monitored for 24 hours. If there are no concerns about the safety and tolerability, then the remaining 6 subjects will be dosed at least two days (48 hours) after the first two subjects.

Procedures and assessments:
Screening and follow-up: medical history, vital signs (temperature, respiratory rate, and supine blood pressure and pulse), 12-lead electrocardiogram (ECG), clinical laboratory (clinical chemistry, haematology, and urinalysis), pregnancy test (females only) and immunogenicity; at eligibility screening: informed consent, demographics, weight, height, Body Mass Index (BMI), hepatitis B surface antigen (HBsAg), anti-hepatitis C virus (HCV), and anti-human immunodeficiency virus (HIV)1/2, and drug screen; to be repeated upon submission: weight, medical history (interim medical history only), 12-lead ECG, vital signs (temperature, respiratory rate, and supine blood pressure and pulse), clinical laboratory (clinical chemistry, haematology, and urinalysis), drug screen, and pregnancy test (females only)

Observation period: one period in the clinic from one day prior until 2 days after drug administration, followed by 3 ambulant visits

Blood sampling:
for pharmacokinetics of ShK-186 concentrations in plasma: pre-dose, 1 and 5 min, 0.25, 0.5, 1, 2, 4, 8, 12, 24, and 72 h post-dose, and otherwise at each visit
for immunogenicity: on Day 15

Safety assessments: adverse events and concomitant medications: throughout the study; vital signs: pre-dose, at multiple timepoints post-dose, and otherwise daily at each visit; clinical laboratory (including clinical chemistry, haematology, and urinalysis): pre-dose, 2 and 8 h post-dose, and on Day 2, 4, 8and 15; 12-lead ECG: pre-dose, 5 min post-dose, and on Day 2 and 8

Intervention

Group 1: one 5 mcg SC injection of ShK-186 or placebo on Day 1, after an overnight fast
Group 2: one 15 mcg SC injection of ShK-186 or placebo on Day 1, after an overnight fast
Group 3: one 30 mcg SC injection of ShK-186 or placebo on Day 1, after an overnight fast
Group 4: one 60 mcg SC injection of ShK-186 or placebo on Day 1, after an overnight fast

Group 5: one 120 mcg SC injection of ShK-186 or placebo on Day 1, after an overnight fast
Group 6: one 240 mcg SC injection of ShK-186 or placebo on Day 1, after an overnight fast
Group 7: one 480 mcg SC injection of ShK-186 or placebo on Day 1, after an overnight fast

Study burden and risks

Registration of adverse effects: During the entire investigation all adverse effects will be documented.
Blood draw, indwelling canula: During this study less than 500 ml of blood will be drawn. It is anticipated that an indwelling cannula will be inserted for blood draws on Day 1 and 2. The blood draws on the other days will be drawn by direct puncture of the vein.
Heart trace (ECG*s): ECG*s will be made regularly.

As ShK-186 will be administered to humans for the first time in this study, the adverse effects in man are not known. Since ShK-186 is a protein administered by injection, there is a possibility for an allergic reaction.
ShK-186 has been studied in animals. Based on effects seen in animal studies, there is a risk of temporary sensation of tingling, burning, pricking, or numbness of the skin and nausea or vomiting. These effects may occur shortly after drug administration and demonstrate a prolonged duration. However, these adverse effects were generally seen at doses higher than what will be administered during this study.

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
- 18-45 yrs, inclusive
- BMI: 18.0-30.0 kg/m2, inclusive and weigh > 50 kg
- the volunteers did not smoke during at least 30 days prior to the screening

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):	27-08-2012
Enrollment:	56
Type:	Anticipated

Ethics review

Approved WMO Date:	04-07-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-07-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-12-2012
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	EUCTR2012-002200-41-NL
CCMO	NL41242.056.12