A Single and Multiple Ascending Dose, Placebo-Controlled, Double-Blind, Phase 1 Study of KY1005 in Healthy Volunteers

Published: 10-04-2017
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Primary objective:To evaluate the safety and tolerability of KY1005.Secondary objectives:To evaluate the pharmacokinetics (PK) of KY1005 following single and repeat doses.Exploratory objectives:- To evaluate the immunogenicity of KY1005;- To assess...

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

Summary

ID

NL-OMON45487

Source
ToetsingOnline

Brief title
A Study of KY1005 in Healthy Volunteers

Condition

- Autoimmune disorders

Synonym
N/A

Research involving
Human

Sponsors and support

Primary sponsor: Kymab Limited
Source(s) of monetary or material Support: Kymab Limited

Intervention

Keyword: KY1005, Pharmacokinetics, Safety and Tolerability

Outcome measures

Primary outcome

The safety and tolerability of KY1005 will be evaluated by

measurement/recording of:

- Adverse events (AEs);

- Vital signs;

- Laboratory safety tests;

- ECGs;

- Changes in physical examination;

- Changes in anti-viral antibody levels and viral deoxyribonucleic acid (DNA);

- Changes in acute cytokine levels (selected cohorts).

Secondary outcome

- Serum concentrations of KY1005;

- Serum anti-KY1005 antibody titres;

- Serum anti-Immucothel and anti-TT antibody titers;

- Immunophenotyping (analysis of cell subsets) in whole blood and evaluation of

OX40L and/or OX40 expression on specific cell subsets where evaluable;

- A blood sample taken before the first dose of study drug will be processed

and stored for possible future sequencing for single nucleotide polymorphisms

and/or deletions/duplications;

- Any excess serum samples after planned analyses are complete will be retained

for future evaluation of target related PD markers.

Study description

Background summary

KY1005 is a human anti-OX40 ligand (OX40L) monoclonal antibody that binds OX40L to block interaction with its receptor, OX40. Blockade of the OX40/OX40L co-stimulation pathway represents a scientifically plausible approach to modulating the persistent inflammation caused by autoreactive memory T-cell populations, and may provide a means of inducing immune tolerance to autoantigens (e.g., in autoimmune disease) or alloantigens (e.g., following transplants).

Study objective

Primary objective:
To evaluate the safety and tolerability of KY1005.

Secondary objectives:
To evaluate the pharmacokinetics (PK) of KY1005 following single and repeat doses.

Exploratory objectives:
- To evaluate the immunogenicity of KY1005;
- To assess pharmacodynamics (PD) effects of KY1005 on immunophenotype (cell subsets), OX40L and/or OX40 expression by flow cytometry (where evaluable);
- To evaluate the effect of KY1005 on neo-antigen and recall antigen in vivo and ex vivo immunological responses in healthy volunteers;

Study design

This is a single and multiple ascending dose, placebo-controlled, double-blind, Phase 1 study of KY1005 in eight cohorts of healthy volunteers (Cohorts 1 through 8).

The study will be carried out at one centre and will comprise dose escalation and immunisation challenges to assess effects on immune system of KY1005 in healthy volunteers. In Cohorts 1 to 8, two sentinel healthy volunteers (one KY1005: one placebo) will be deployed in every cohort and the decision to progress with the first dose to the remaining six healthy volunteers will be made by the Principal Investigator (PI or medically qualified designee) if there are no safety concerns 48 hours after the infusion of these sentinel healthy volunteers.

The decision to dose escalate between cohorts will only be made after all available safety information up to study Day 11 from at least six healthy volunteers in the immediately preceding cohort, and all other available cumulative safety information, as well as PK data in the case of Cohorts 4 and 6 have been reviewed by at least the PI (or medically qualified designee) and the sponsor Study Responsible Medical Officer (SRMO) (or medically qualified designee).

Intervention

Investigational Medicinal Products

Cohorts 1 to 3 will receive a single dose;
Cohorts 4 to 8 will receive three doses; an initial loading dose on Day 1 and two maintenance doses of no more than a nominal 50% of the loading dose, administered on Day 29 and Day 57;

Non-Investigational Medicinal Products

The following Non-Investigational Medicinal Products (NIMPs) will be administered to volunteers in Cohorts 4 to 8 of the study:

Tetanus Toxoid: 0.5 mL on day 64;
Immucothel®/Alhydrogel® 2% (European Pharmacopoeia: EP): 0.1 mg/0.9 mg in 0.5 mL on day 64.

Study burden and risks

There is no direct benefit to you from taking part in the study. The results of the study will provide valuable information for future research.
For new drugs, such as KY1005 side effects are not known yet. There may be unexpected side effects. The effects associated a with an immune system inhibitor medication are for instance infections.
For this study, a cannula will be inserted into one of the veins in the arm and blood samples are taken frequently. This may result in a small local haemorrhage which resolves after several days.

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

Subjects must fulfill all of the following criteria for entry into the study.
1. Volunteer to participate in the clinical trial and provide signed informed consent.
2. Cohorts 1 to 8: Male, aged 18 to 45 years.
3. Subjects with a female spouse/partner of childbearing potential must agree to use effective birth control starting at screening and continuing throughout the clinical study period and for a period of up to 6 months after study completion.
4. Cohorts 4 to 8: previous immunisation with tetanus toxoid (TT) but not within 6 months prior to the screening visit as reported by the volunteer.
5. Cohorts 4 to 8: anti-TT immunoglobulin G (IgG) response > 0.1 IU/mL and * 50 IU/mL at screening.

Exclusion criteria

1. Experiencing a clinically significant, chronic or acute infection requiring treatment at screening or prior to first IMP administration.
2. A body weight of * 60.0 kg or * 120.0 kg.
3. A body mass index (BMI) * 18.0 or * 30.0 kg.
4. History of disease of the central nervous system, cardiovascular system, kidney, liver, digestive system, respiratory system or metabolic/endocrine system or suffered from other

disease that in the opinion of the PI (or medically qualified designee) may make participation unsafe for the subject or interfere with trial evaluations or otherwise considered clinically significant.
5. History of immunological abnormality (e.g., immune suppression, severe allergy or anaphylaxis) that in the opinion of the PI (or medically qualified designee) may make participation unsafe for the subject or interfere with trial evaluations or otherwise considered clinically significant.
6. History of malignancy, or known current malignancy.
7. Leukocyte absolute value < 3.50 × 109/L or > 9.50 × 109/L, neutrophil absolute value < 1.8 × 109/L, platelet counts < 100 × 109/L, haemoglobin < 12.0 g/dL.
8. Taken part in other clinical trials within 3 months of screening for this study or > four trials in the year preceding the first IMP administration.
9. Donated or lost more than 500 mL of blood or plasma within 3 months of screening.
10. Cohorts 1 to 8: prescription drug taken within 2 weeks of screening or likely to be taken during the trial.
11. Live immunisation within 3 months of screening or plans to receive such immunisation during the clinical trial or for a period of 6 months after the end of the trial.
12. Taking or likely to take over-the-counter (OTC) medication, including herbal medicines, that in the opinion of the PI (or medically qualified designee) may make participation unsafe for the subject or interfere with trial evaluations.
13. Hepatitis B surface antigen (HbsAg), Hepatitis C antibody (HCV-Ab), or Human Immunodeficiency Virus (HIV) positive.
14. History of or current drug or substance abuse considered significant by the PI (or medically qualified designee) including a positive urine drug screen.
15. Current smoker and/or regular user of other nicotine-containing products (e.g., patches).
16. Average consumption of more than 14 units of alcohol/week.
17. Clinically significant abnormal screening values in clinical (electrocardiogram (ECG), vital signs, physical examination) and laboratory tests in the opinion of the PI (or medically qualified designee).
18. Cannot communicate adequately or cannot commit to full participation in all trial procedures.
19. For Cohorts 4 to 8:
a. Confirmed previous exposure to immunocyanins, such as keyhole limpet haemocyanin (KLH);
b. Known allergy to thiomersal or other components of Tetanus vaccine or Immucothel®;
c. History of schistosomiasis.
20. Any observation that, in the opinion of the PI (or medically qualified designee) makes the subject unsuitable for participation in 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):	29-05-2017
Enrollment:	64
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Immucothel/Alhydrogel 2%
Product type:	Medicine
Brand name:	NA
Generic name:	KY1005
Product type:	Medicine
Brand name:	Tetanus vaccine

Ethics review

Approved WMO Date:	10-04-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-05-2017
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-06-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-06-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-09-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-09-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-11-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-11-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-12-2017
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	EUCTR2016-004839-20-NL
CCMO	NL61388.056.17