A two part, phase 1, randomised, placebo-controlled, single ascending dose study to evaluate the safety, tolerability and pharmacokinetics of GBR 830 in adult healthy volunteers (Part 1) and a randomised, placebo-controlled, pharmacodynamic study to evaluate the effect of single dose of GBR 830 on vaccination response in adult, healthy volunteers (Part 2)

Published: 10-07-2014
Last updated: 21-04-2024

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

Summary

ID

NL-OMON41093

Source
ToetsingOnline

Brief title
GBR 830 SAD and PD study

Condition

- Autoimmune disorders

Synonym
autoimmune disease

Research involving
Human

Sponsors and support

Primary sponsor: Glenmark Pharmaceuticals Limited
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: autoimmune disease, GBR 830

Outcome measures

Primary outcome

Part 1:

To evaluate the safety and tolerability of single ascending doses of GBR 830 in

adult healthy volunteers.

Part 2:

To evaluate the effect of a single dose of GBR 830 in adult, healthy volunteers

on

-T-cell dependent primary (naïve) antibody response to neo-antigen KLH and

-T-cell dependent recall/memory antibody response to Tetanus toxoid (TT)

antigen.

Secondary outcome

Part 1:

To evaluate the PK and immunogenicity of single ascending doses of GBR 830 in adult healthy volunteers.

Part 2:

-To evaluate the effect of single dose of GBR 830 on DTH to intra dermal (i.d) administration of Candida in adult, healthy volunteers.

-To evaluate the safety, tolerability, PK and immunogenicity of single dose of GBR 830 in adult, healthy volunteers.

Study description

Background summary

GBR 830 is a new investigational compound that may eventually be used for the treatment of inflammatory responses in several autoimmune diseases. An autoimmune disease is an illness that occurs when the body tissues are attacked by its own immune system. This occurs for example in rheumatoid arthritis patients.

Antibodies are produced by our own body for host defense against for example bacteria and viruses. However, antibodies can also be prepared in a custom made way by pharmaceutical companies, so that they can be used for medical research and various therapeutic applications. GBR 830 is an antibody designed to specifically recognize, bind and block the function of the OX40 receptor on T cells. A receptor is a protein on the cell surface that can initiate a cell response when a signal molecule binds to the receptor. T cells are a specific type of white blood cells that play an important role in immune responses.

Because GBR 830 is a protein, the body may recognize the drug as foreign. As a result an immune response can occur, for example by making antibodies. The ability of a compound to elicit an immune response is called immunogenicity. The production of antibodies towards the medication leads to reduced efficacy of the medical product. Therefore it will be investigated whether antibodies are produced after administration of GBR 830.

This is the first time that GBR 830 is being given to humans.

Study objective

The purpose of this study is to investigate to what extent GBR 830 is tolerated. It will also be investigated how quickly and to what extent GBR 830 is absorbed and eliminated from the body (this is called pharmacokinetics) and to what extent the body produces antibodies towards GBR 830 (immunogenicity).

In Part 2 of the study it will also be investigated what the effect of GBR 830 is on T cell dependent immune responses (this is called pharmacodynamics).

This study will be performed in 52 healthy male and female volunteers, divided over 5 groups.

Part 1 will be performed in 32 healthy male and female volunteers, divided over 4 groups with 8 volunteers per group.

Part 2 will be performed in 20 healthy male and female volunteers, divided over 2 groups with 10 volunteers per group.

Study design

Part 1:
The actual study will consist of 1 period during which you will stay in the clinical research center in Groningen for 6 days (5 nights). The volunteer will have to come back to the clinical research center in Groningen for 8 additional short visits.

Part 2:
The actual study will consist of 1 period during which you will stay in the clinical research center in Groningen for 4 days (3 nights). The volunteer will have to come back to the clinical research center in Groningen for 7 additional short visits.

Intervention

Part 1:
During the study the volunteer will receive GBR 830 or placebo by an intravenous infusion of 1 hour, approximately 1 hour after completing a light breakfast.

Part 2:
On Day 1 of the study the volunteer will receive GBR 830 or placebo by an intravenous infusion of 1 hour, approximately 1 hour after completing a light breakfast.
On Day 2 the volunteer will receive 1 intramuscular injection with KLH, 1

intramuscular injection with TT, and 1 intradermal injection with Candida.

Study burden and risks

Part 1 and 2:
All potential drugs cause adverse events; the extent to which this occurs differs. As GBR 830 will be administered to humans for the first time in this study and blocking of the OX40 receptor in humans using medication has never been done before, adverse effects of GBR 830 in humans have not been reported to date. However, GBR 830 has been studied in animals. In animals no abnormalities were observed and the study medication was well tolerated. Development of a hypersensitivity reaction to GBR 830 may occur and you may become more susceptible to infections.

Part 2:
Local reactions to an injection with Candida can include redness, swelling, itching, discoloration of the skin and excoriation of the skin around the injection site. These reactions usually subside within a few days the after injection. Sometimes, skin discoloration may persist for several weeks. Progression of the DTH reaction to vesiculation, ulceration and death of tissue are possible.

Adverse effects that may occur after an injection with KLH include redness and swelling at the site of injection. If the volunteer is allergic to KLH an allergic reaction and redness of the skin can occur.

Adverse effects that may occur after an injection with TT include pain, redness and swelling at the site of injection. Other adverse effects that may occur are fever, malaise (feeling of discomfort

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 volunteers
18-55 years, inclusive
BMI: 18.5-32.0 kg/m2, inclusive

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 90 days from the start of the study. In case of donating more than 0.45 liters of blood in the 3 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):	11-09-2014
Enrollment:	52
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Candin
Product type:	Medicine
Brand name:	Immucothel
Product type:	Medicine
Brand name:	Tetanus vaccin

Ethics review

Approved WMO Date:	10-07-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-07-2014
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	EUCTR2014-001870-33-NL
CCMO	NL49946.056.14