A randomized, 2-part, placebo controlled phase 1 study to evaluate safety, tolerability, pharmacokinetics and immunogenicity following single ascending doses (Part 1) and multiple ascending doses (Part 2) of GBR 830 in adult healthy subjects

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

Summary

ID

NL-OMON44196

Source
ToetsingOnline

Brief title
GBR 830 SAD and MAD study

Condition

- Autoimmune disorders

Synonym
autoimmune disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: autoimmune disease, GBR 830

Outcome measures

Primary outcome

- Frequency and severity of treatment-emergent adverse events (TEAEs) and SAEs

for each treatment, based on CTCAE, version 4.03

- Number of DLTs during treatment

Secondary outcome

- Cmax, trough plasma concentration (Ctrough), time at which Cmax is observed

(tmax), AUC to the end of the dosing period (AUC0-tau), AUC from time 0 to

infinity (AUC0-*), and AUC from time 0 unitl the last measurable concentration

(AUC (0-t)), terminal elimination half life (t*), volume of distribution,

clearance, and accumulation ratio (Rac) as applicable

- ADA formation.

Study description

Background summary

GBR 830 is a new investigational compound that may eventually be used for the treatment of 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 patients with rheumatoid arthritis (affecting the

joints), psoriasis (affecting the skin), and Crohn*s disease or ulcerative colitis (affecting the intestines).

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 various therapeutic applications and medical research. GBR 830 is an antibody designed to specifically recognize, bind and block the function of particular receptors on immune cells (e.g. the OX 40 receptor on T cells). A receptor is a protein on the cell surface that can transmit a signal when molecule binds to that receptor. GBR 830 acts on a type of white blood cells (so called T cells) that play an important role in immune responses.

GBR 830 is in development and is not registered as a drug but has been given to humans before.

Study objective

The purpose of the 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). In addition, the effect of GBR 830 on the immune system will be investigated (this is called pharmacodynamics) and the effect of GBR 830 on the body may be explored.

Study design

Part 1:

Before the study the volunteer will undergo a pre-study screening during which the volunteer will be subjected to a number of medical examinations Similar examinations will be performed after the study at the post-study screening.

Day 1 is the day of administration of GBR 830 or placebo. The volunteer is expected at the clinical research center at 11:00 h in the morning prior to the day of administration of study medication (Day -1). The volunteer will be required not to have consumed any food or drinks during 4 hours prior to arrival in the clinical research center (with the exception of water). He/she will stay in the clinical research center in Groningen (location UMCG) for 4 days (3 nights: from Day -1 to Day 3).

The volunteer will return to the clinical research center (location Martini Hospital) for 8 additional short visits: on Day 5, Day 7, Day 8, Day 15, Day 29, Day 43, Day 57 and Day 71 (the post study screening).

The participation to the entire study, from the pre-study screening until the post study screening, will be a maximum of 99 days.

During the study the volunteer will receive a single dose of GBR 830 or placebo as an iv infusion for 1 hour.

Part 2:

Before the study the volunteer will undergo a pre-study screening during which the volunteer will be subjected to a number of medical examinations Similar examinations will be performed after the study at the post-study screening.

Day 1 is the first day of administration of GBR 830 or placebo. The volunteer is expected at the clinical research center at 11:00 h in the morning prior to the day of each administration of the study compound. The volunteer will be required not to have consumed any food or drinks during the 4 hours prior to arrival in the clinical research center (with the exception of water). For each dose, the volunteer will stay in the clinical research center in Groningen (location UCMG) for 3 days (2 nights). Between the 1st and 2nd dose the volunteer will return for two short visits on Day 3 and Day 5 and between the 4th and 5th dose he/she will return for two short visits on Day 24 and Day 26 (location Martini Hospital).

After the volunteer has received all 6 doses, he/she will return to the clinical research center (location Martini Hospital) for 8 additional short visits: on Day 38, Day 40, Day 42, Day 43, Day 50, Day 64, Day 78, and Day 92 (the post study screening).

There will be an option to stay overnight in the clinical research center (location UMCG) from Day 2 to Day 3, from Day 23 to Day 24, and From Day 37 to Day 38. The ambulant visits on Day 3, Day 24 and Day 38 will take place in the clinical research center located at the Martini Hospital.

The participation to the entire study, from the pre-study screening until the post study screening, will be a maximum of 120 days.

During the study the volunteer will receive GBR 830 or placebo as an iv infusion for 1 hour once every week for 6 weeks.

Intervention

Part 1:

Group Day Treatment (mg/kg) How often
1 1 20 mg/kg GBR 830 or placebo Once
2 1 40 mg/kg GBR 830 or placebo Once

Part 2:

Group Day Treatment (mg/kg) How often

3 1, 8, 15, 22, 29 and 36 10 mg/kg GBR 830 or placebo Once every week for 6 weeks
4 1, 8, 15, 22, 29 and 36 20 mg/kg GBR 830 or placebo Once every week for 6 weeks

Study burden and risks

All potential drugs can cause adverse effects; the extent to which this occurs differs. GBR 830 has been studied in animals. In animals no abnormalities were observed and the study medication was well tolerated.

GBR 830 has already been studied in healthy volunteers with dose levels up to 10 mg/kg intravenously. In this previous study that has also been conducted at PRA, GBR 830 was well tolerated at all dose levels without clear adverse effects.

In another study that has recently been completed at PRA, GBR 830 was administered as an iv dose of 600 mg and compared to 75 mg and 600 mg of GBR 830 administered subcutaneously (sc). In this study, GBR 830 was generally well tolerated. However, based on preliminary data there was one adverse event (infusion reaction characterized by acute appearance of hives) that necessitated early discontinuation of the infusion. This adverse event was of mild intensity and resolved swiftly without medical intervention. In addition, a serious adverse event occurred after sc administration of 75 mg GBR 830: neuralgic amyotrophy; this volunteer suffered from acute and severe neck pain. Although the neck pain was transient, it was followed by persistent paralysis of the diaphragm which resulted in shortness of breath when lying flat. This adverse event was of moderate intensity at occurrence and the cause of this rare disorder was not known. As the first symptoms developed two weeks after administration of the drug, a link with the recent administration of GBR 830 could not be definitely ruled out. On the other hand, it could have been a coincidence as well. This serious adverse event is still ongoing but stable.

In another ongoing study, GBR 830 is being tested at a dose of 10 mg/kg in patients with atopic dermatitis (a type of eczema). In this study GBR 830 has been well tolerated so far.

GBR 830 is a so-called *biological*; with respect to the properties of these drugs there is a chance that the volunteers body will develop antibodies against GBR 830. This may induce development of a hypersensitivity or allergic reaction to GBR 830 as described above and the volunteer may become more susceptible to infections. Based on experience with GBR 830 (and other monoclonal antibodies in general), the chance that the volunteer will develop antibodies against the study compound is possible. If antibodies against the new investigational compound are found in the volunteers blood, we expect that with the current knowledge this will have no consequences for his/her health. However, in case the volunteer would develop a condition that could be treated

with GBR 830 in the future, it cannot be predicted whether and how these antibodies may influence the effect of treatment. GBR 830 is being developed for autoimmune diseases like rheumatoid arthritis, ankylosing spondylitis, axial spondyloarthritis, psoriatic arthritis, psoriasis, Crohn*s disease, and ulcerative colitis. If the volunteer would need treatment for one of these diseases, the volunteers doctor will suggest the best possible treatment for him/her. As of today several medications are available or being developed for the treatment of the conditions mentioned.

The volunteer should be aware that the aforementioned adverse events and possibly other, still unknown adverse events, may occur during the 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 volunteers
- 18 - 65 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 3 months before the start of this study. Subjects with a history of donating 1 unit of blood (450 mL) blood in the 3 months prior to IP administration or who intend to donate within 3 months of their last scheduled study visit.

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):	05-07-2017
Enrollment:	32
Type:	Actual

Ethics review

Approved WMO

Date:	22-06-2017

Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-06-2017
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	EUCTR2017-001299-51-NL
CCMO	NL62215.056.17