A PHASE I, SINGLE CENTER, RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED, SINGLE DOSE STUDY IN HEALTHY FEMALE AND ELDERLY VOLUNTEERS AND MULTIPLE ASCENDING DOSE STUDY IN HEALTHY MALE AND FEMALE VOLUNTEERS BETWEEN THE AGES OF 18-80 YEARS TO INVESTIGATE THE SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF GRC 17536

Published: 19-07-2011
Last updated: 28-04-2024

This study is part of a larger program of in total 6 parts. This program was split in two sub programs and each of these sub programs consists of three parts. The current study originally comprised 3 parts and a fourt part is added.The purpose of...

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

Summary

ID

NL-OMON38062

Source
ToetsingOnline

Brief title
SAD and MAD study of GRC 17536 in healthy volunteers

Condition

- Other condition

Synonym
Asthma, COPD

Health condition

Astma, COPD, hoesten, chronische pijn

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Acute or Chronic pain, Asthma, COPD, Cough

Outcome measures

Primary outcome

Pharmacokinetics:

Plasma and urine PK parameters for GRC17536 (Part 1 - 3), concentration of GRC

17356 in Cerebrospinal Fluid (liquor)(Part 4)

Safety :

AEs, haematology, serum biochemistry, urinalysis, 12-lead ECGs, vital signs

(supine and standing systolic and diastolic

blood pressure, pulse rate, respiratory rate, oral body temperature),

continuous cardiac monitoring (Part 2 and 3 in

volunteers *65 yrs), physical examination.

Secondary outcome

n/a

Study description

Background summary

The new compound to be given, GRC 17536, is an investigational compound that may eventually be used for the treatment of acute or chronic pain, asthma or COPD, or excessive cough.
This new compound is not registered as a drug, but has been given to humans before.

The new compound blocks the activity of a protein (called TRPA1) that occurs naturally on nerve cells in the body. This protein works as a *sensor* for stimuli (signals) such as pressure, temperature and irritants (such as air pollution, or tear gas). They allow the body to respond to these stimuli by avoiding or minimising painful movements (e.g., not using a painful arm), or by airway constriction or coughing to limit damage by the inhaled irritant. However, in some cases, the response of the body to the stimulus (i.e., the pain, airway constriction, or cough) may be a bigger problem than the stimulus itself, and we may choose to (completely or partially) suppress the body*s response, e.g., with a drug that blocks TRPA1. The new compound investigated here (GRC 17536) could play a role in such cases, based on its potential to make the nerve cells involved in these responses less susceptible to activation.

Study objective

This study is part of a larger program of in total 6 parts. This program was split in two sub programs and each of these sub programs consists of three parts. The current study originally comprised 3 parts and a fourt part is added.

The purpose of the study is to investigate how safe the compound is and how well the compound is tolerated. The study will also investigate how quickly and to what extent the compound is absorbed and eliminated from the body (this is called pharmacokinetics).

Part 1 of the study will be performed in healthy, young females (aged 18-45 years) and elderly females (aged 46-65 years) and will investigate the properties of the new compound when it is administered in a single dose, such to be compared to single doses given to males studied in a previous study.

Part 2 of the study will be performed in healthy, elderly males and females (65-80 years of age) and will again investigate the properties of the new compound when it is administered in a single dose, such to be compared to the young males and females studied in a previous study and in Part 1 of this study.

Part 3 of the study will be performed in healthy, young (18-45 years of age) and elderly (65-80 years of age) males and females and will investigate the properties of the new compound when it is administered in multiple (repeated), ascending doses. This part consists of four cohorts (3 groups of 4 young and 4 elderly males and 4 elderly females each and one group of 4 young and 4 elderly males and 4 young and 4 elderly females).

Part 4 of the study will be performed in healthy, young (18-45 years of age) male and will investigate the absorption properties of the new compound in Cerebrospinal Fluid (liquor) when it is administered in multiple (repeated), ascending doses. Part 4 is an open label study and consists of 1 group of 6 young healthy males.

Study design

Part 1
The study will consist of 1 period, during which you will stay in the clinical research centre in Groningen for 9 days (8 nights).
You will receive a single dose of 250 mg GRC 17536 or placebo once in the form of a suspension (a cloudy drinking solution). Placebo is a suspension without the active ingredient.

Part 2
The study will consist of 1 period, during which you will stay in the clinical research centre in Groningen for 9 days (8 nights).
You will receive a single dose of 250 mg GRC 17536 or placebo once in the form of a suspension (a cloudy drinking solution). Placebo is a suspension without the active ingredient.

Part 3
The study will consist of 1 period, during which you will stay in the clinical research centre in Groningen for 23 days (22 nights).
The amount of study medication you receive depends on the group you participate in. See below table for the anticipated dose schedule.
For groups L and M: 30 days (29 nights)

Group Dose level / how often
1 30 mg / once daily for 14 days after a meal
2 30 mg / twice daily for 14 days after a meal
3 90 mg / twice daily for 21 days after a meal
4 250 mg / twice daily *for 21 days after a meal

*The final dose will be determined based on the results obtained in Group 1, 2 and 3.

Part 4
The study will consist of 1 period, during which you will stay in the clinical research centre in Groningen for 19 days (18 nights).
During the study, you will receive 250 mg GRC 17536, twice daily for the duration of 14 days.

For all groups:
The screening will include a physical examination including measurement of supine and standing blood pressure and
pulse rate, respiratory rate, body temperature, weight and height, a heart trace (electrocardiogram) recording, and a
number of blood and urine tests. There will also be screened for drugs of abuse, alcohol, Hepatitis B and C, and HIV (=
AIDS test). A pregnancy test will be performed (females only). There will be a two-time follow-up medical examination
when the study is completed. This two-time examination will take place 10 days and 14 days after administration of (the
last) study medication. The first post-study examination will consist of measurements of supine and standing blood
pressure and pulse rate, respiratory rate, and body temperature, a heart trace (electrocardiogram) recording, and a
number of blood and urine tests; the second follow-up examination will consist of a physical examination including
measurements of supine and standing blood pressure and pulse rate, respiratory rate, body temperature and weight, a
heart trace (electrocardiogram) recording, and a number of blood and urine tests.

Intervention

GRC 17536 administered as GRC 17536 potassium granules single or multiple doses in the fed state.

Study burden and risks

In an ongoing study in healthy male volunteers where GRC 17536 was / will be administered in single doses up to 1000 mg the following adverse effects were reported: gastrointestinal tract related symptoms like nausea of short duration reported directly after drug administration, mild abdominal pain, loose stool and flatulence. Other adverse effects which were also considered to be related to the study drug were: feeling weak / fainting (Vasovagal syncope, as response to blood draw or pain) and tiredness.

For the multiple dose part: you should be aware though that taking the study drug for 14 days (for groups L and M: 21 days), concentrations of the study drug and its break-down products (metabolites) in your blood and your organs can be reached that have not been reached in the single dose study mentioned above, depending on which dose group you will be in.

Procedures:
Pain, light bleeding, heamatoma, possibly an infection.
Collection of liquor (Part 4 only): Insertion of the needle, for the collection of liquor, may be painful, similar to drawing blood from the arm by a direct puncture of the vein. Removing the needle is painless. Usually no complications occur during an epidural. Sometimes, during the epidural, a nerve can be hit. Then you will feel an electric pulse or a shooting pain in your leg. This can be painful, but is not harmful. After the epidural, you may experience a headache, nausea or subsequent bleeding of the wound (puncture hole) and there is a small chance of bleeding, infection, or injury to a nerve.

Contacts

Public
Glenmark Pharmaceuticals SA

Glenmark Research Centre, Plot No. A-607, T.T.C. Industrial Area
MIDC, Mahape, Navi Mumbai, India- 400 709
IN
Scientific
Glenmark Pharmaceuticals SA

Glenmark Research Centre, Plot No. A-607, T.T.C. Industrial Area
MIDC, Mahape, Navi Mumbai, India- 400 709
IN

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Part 1: healthy females, 18 - 45 and 46 - 65 years of age, BMI 18.0 - 30.0 kg/m2, no smokers
Part 2: healthy elderly males and females, 65 - 80 years of age, BMI 18.0 - 30.0 kg/m2, no smokers
Part 3: healthy young and elderly males, 18 - 45 and 65 - 80 years of age, and healthy young and elderly females, 18 - 45 years of age and 65 - 80 years of age, BMI 18.0 - 30.0 kg/m2, no smokers
Part 4: healthy males, 18 - 45 years of age, BMI 18.0 - 30.0 kg/m2, no smokers;18 - 80 years of age, male and female, BMI 18.0 - 30.0 kg/m2, no smokers.

Exclusion criteria

Suffering from: hepatitis B, cancer or HIV/AIDS. In case of participation in another drug study within 60 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of have taken part in more than 3 other drug studies (for men) or more than 2 other drug studies (for women) in the 10 months prior to the start of this study, or when having donated more than 1.5 liters of blood (for men) or more than 1.0 liters of blood (for women) in the 10 months prior to 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):	25-08-2011
Enrollment:	74
Type:	Actual

Ethics review

Approved WMO Date:	19-07-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-07-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-10-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-03-2012
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-03-2012
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	EUCTR2011-002978-23-NL
CCMO	NL37538.056.11