A 2-part, randomized, double-blind, placebo-controlled, sequential group, dose-escalation study to assess the safety, tolerability and pharmacokinetics of single and multiple ascending oral doses of GLPG2737 in healthy male sub.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Congenital and hereditary disorders NEC
Study type	Interventional

Summary

ID

NL-OMON42886

Source
ToetsingOnline

Brief title
GLPG2737 SAD and MAD study

Condition

- Congenital and hereditary disorders NEC

Synonym
Cystic fybrosis, Mucoviscidosis

Research involving

Human

Sponsors and support

Primary sponsor: Galapagos SASU
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: cystic fibrosis, GLPG2737

Outcome measures

Primary outcome

- To evaluate the safety and tolerability of single ascending oral doses (SAD)

of GLPG2737 given to healthy male subjects, compared to placebo.

- To evaluate the safety and tolerability of multiple ascending oral doses

(MAD) of GLPG2737 given to healthy male subjects daily for 14 days, compared to

placebo.

Secondary outcome

- To characterize the PK of GLPG2737 and its metabolites (G1125498 and

G1123541) after single and multiple oral administrations.

- To evaluate the potential of interaction with cytochrome P450 (CYP) 3A4 after

repeated dosing with GLPG2737.

Study description

Background summary

GLPG2737 is a new investigational compound that may eventually be used for the treatment of cystic fibrosis (CF). CF is a genetic disorder that causes the body to produce unusually thick mucus. The thick mucus results in malfunction of organs like the lungs, pancreas and liver.

In the human body, the cystic fibrosis transmembrane conductance regulator (CFTR; this is a protein that can be found on the membrane of cells) plays an important role in the transport of salt and water in and out of cells. In CF there are changes (mutations) in the gene (DNA) that is responsible for the production of CFTR and because of these changes, CFTR does not work correctly or it is not produced sufficiently. As a result, the transport of salt and water in and out of cells is disturbed and mucus will become unusually thick. GLPG2737 is thought to improve CFTR functioning by repairing consequences of CFTR mutations.

Study objective

The purpose of the study is to investigate how safe GLPG2737 is and how well GLPG2737 is tolerated. It will also be investigated how quickly and to what extent GLPG2737 is absorbed into, distributed in, and eliminated from the body (this is called pharmacokinetics).

Study design

Part1:
Before the study the volunteer will undergo a screening within 21 days before the day of administration of the study compound (Day 1) during which the volunteer will be subjected to a number of medical examinations (please refer to Chapter 7 of the information booklet). Similar examinations will be performed after the study at the follow-up visit (please refer to Chapter 10 of the information booklet). The volunteer will be required not to have consumed any food or drinks (with the exception of water) during the 4 hours prior to screening visit and the follow-up visit.

The volunteer is expected at the clinical research center on Day -1 at 14:00 h in the afternoon. The volunteer will be required not to have consumed any food or drinks (with the exception of water) during the 4 hours prior to arrival in the clinical research center.

The volunteer will receive GLPG2737 or placebo as an oral suspension in sitting position. The study compound will be given with a syringe (without needle) due to the small volume. After intake of the study compound the volunteer is required to drink 240 milliliters (mL) of water. The study compound will be administered within 30 minutes after the start of breakfast, which the volunteer will need to finish entirely within 20 minutes.

Part 2:
Before the study the volunteer will undergo a screening within 21 days before the day of administration of the study compound (Day 1) during which the volunteer will be subjected to a number of medical examinations (please refer to Chapter 7 of the information booklet). Similar examinations will be

performed after the study at the follow-up visit (please refer to Chapter 10 of the information booklet). The volunteer will be required not to have consumed any food or drinks (with the exception of water) during the 4 hours prior to screening visit and the follow-up visit.

The volunteer is expected at the clinical research center on Day -1 at 14:00 h in the afternoon. 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).

On Days 1 to 14, every day the vounteer will receive GLPG2737 or placebo as an oral suspension in sitting position. The study compound will be given with a syringe (without needle) due to the small volume. After intake of the study compound the volunteer is required to drink 240 milliliters (mL) of water. Each dosing day, the study compound will be administered within 30 minutes after the start of breakfast, which the volunteer will need to finish entirely within 20 minutes

Intervention

Part 1:

Group Day
Treatment
How often
A 1 25 milligrams (mg) GLPG2737 or
placebo Once
B 1 TBD, but not exceeding 75 mg GLPG2737 or
placebo Once
C 1 TBD, but not exceeding 150 mg GLPG2737 or placebo
Once
D 1 TBD, but not exceeding 300 mg GLPG2737 or placebo Once
E 1 TBD, but not exceeding 450 mg GLPG2737 or
placebo Once
TBD* 1 TBD1 mg GLPG2737 or
placebo Once
TBD* 1 TBD1 mg GLPG2737 or
placebo Once
TBD* 1 TBD1 mg GLPG2737 or
placebo Once

TBD: to be determined
*: these are additional groups which may possibly be dosed. The dose level of these groups will be based on results of previous groups in Part 1

Part 2:

Group Days Treatment How often
F 1-14 TBD, but not exceeding 75 milligrams (mg) GLPG2737 or placebo Once daily
G 1-14 TBD, but not exceeding 150 mg GLPG2737 or placebo Once daily
H 1-14 TBD, but not exceeding 300 mg GLPG2737 or placebo Once daily
TBD1 1-14 TBD mg GLPG2737 or placebo Once daily
TBD1 1-14 TBD mg GLPG2737 or placebo Once daily
TBD1 1-14 TBD mg GLPG2737 or placebo Once daily

TBD: to be determined
1: these are additional groups which may possibly be dosed

Study burden and risks

All potential drugs cause adverse effects; the extent to which this occurs differs. As GLPG2737 will be administered to humans for the first time in this study, adverse effects of GLPG2737 in humans have not been reported to date.

In animal safety studies in rats and dogs, administration of GLPG2737 was shown to cause effects on the lining of the stomach and redness of the skin associated with inflammation. These findings were seen at the middle and highest of 3 doses studied. GLPG2737 administration also modified some laboratory tests such as cholesterol and liver enzymes. In addition there was a slight, reduction in the activity of an enzyme (myeloperoxidase) of a type of white blood cell, the neutrophil, which is involved in the body*s response to infections. All of the abovementioned effects were reversible.

All these parameters, amongst many others, will be closely monitored during this clinical study by repeat blood and urine sampling for laboratory parameters, frequent ECGs and vital signs assessments (blood pressure, pulse rate and body temperature), frequent physical examinations and continuous adverse effect monitoring during the course of the study.

The volunteer should be aware that the aforementioned adverse effects and possibly other, still unknown adverse effects, may occur during the study. However, with the doses used in this study no serious adverse effects are expected.

Contacts

Public
Galapagos SASU

Avenue Gaston Roussel 102

Romainville 93230
FR
Scientific
Galapagos SASU

Avenue Gaston Roussel 102
Romainville 93230
FR

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy Males between 18-50 years of age, inclusive,
body mass index (BMI) between 18-30 kg/m2, inclusive
Non-smokers and non-users of any nicotine-containing products

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 start of the study. In case of donating more than 100 milliliters of blood in the 12 weeks prior 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):	25-11-2016
Enrollment:	112
Type:	Actual

Ethics review

Approved WMO Date:	09-11-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-11-2016
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	EUCTR2016-003626-17-NL
CCMO	NL59733.056.16