A Phase 1 Study to Assess the Mass Balance, Excretion, and Pharmacokinetics of [14C]-GBT021601, an Oral Hemoglobin S Polymerization Inhibitor, in Healthy Participants

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Red blood cell disorders
Study type	Interventional

Summary

ID

NL-OMON53865

Source
ToetsingOnline

Brief title
GBT021601 ADME Microtracer Study

Condition

- Red blood cell disorders

Synonym
sickle cell anemia, sickle cell disease

Research involving
Human

Sponsors and support

Primary sponsor: Global Blood Therapeutics, Inc.
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: [14C]-GBT021601, EXCRETION, MASS BALANCE, PHARMACOKINETICS

Outcome measures

Primary outcome

- To determine the whole blood and plasma concentrations of [14C]-GBT021601

total radioactivity.

- To assess the mass balance by determining [14C]-GBT021601 total radioactivity

excreted in urine and feces.

- To determine the PK of GBT021601 in whole blood, plasma, and urine.

Secondary outcome

- To assess the safety and tolerability of GBT021601 administration in healthy

participants.

- To characterize and identify metabolites of [14C]-GBT021601 in whole blood,

plasma, urine, and feces.

Study description

Background summary

GBT021601 is a new compound that may potentially be used for the treatment of sickle cell disease (also known as sickle cell anemia). This disease causes severe tiredness and attacks of pain, and increases susceptibility to infections. People with sickle cell disease generally have a lower life expectancy.

Sickle cell disease is an inherited form of anemia, because red blood cells

have the shape of a sickle. Sickle cells are less able to carry oxygen around the body than normal red blood cells.

GBT021601 is being developed with the aim of improving transport of oxygen around the body and preventing the formation of sickle cells.

Study objective

In this study we will investigate how quickly and to what extent GBT021601 is absorbed, transported, and eliminated from the body. For this study, GBT021601 is radioactively labelled with carbon-14 (14C). In this way, GBT021601 can be traced in blood, urine, and feces.

We also investigate how safe the new compound GBT021601 is and how well it is tolerated when it is used by healthy subjects. In addition, we look at breakdown products (metabolites) of GBT021601 in blood, urine, and feces.

GBT021601 has been administered to humans before. In addition, it has been extensively tested in the laboratory and on animals.

Study design

The study will take a maximum of 8 months from the screening until the follow-up visit.

In total the volunteer will visit the research center up to 13 times:
- once for the screening.
- once for a long stay in the research center.
- Up to 11 times for a 24 hours visit to the research center.

The volunteer will once receive 200 mg 14C radioactively labeled GBT021601.

Intervention

The volunteer will be given 200 milligrams (mg) 14C labeled GBT021601 as an oral solution of 400 milliliters (mL). This oral solution may have a bitter taste. After administration of the oral solution, the vial will be rinsed twice times with 50 mL of water, which the volunteer will also be required to drink.

Study burden and risks

Blood draw
Drawing blood may be painful or cause some bruising. The use of the indwelling cannula (a tube in a vein in the arm) can sometimes lead to inflammation, swelling, hardening of the vein, blood clotting, and bleeding in the environment (bruising) of the puncture site. In some individuals, a blood draw

can sometimes cause pallor, nausea, sweating, low heart rate, or drop in blood pressure with dizziness or fainting.

In total, we will take about 535 milliliters (mL) of blood from the volunteer from screening to follow-up. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time at once. If the investigator thinks it is necessary for the safety of a subject, extra samples might be taken for possible additional testing. If this happens, the total amount of blood drawn may be more than the amount indicated above.

Heart tracing
To make a heart tracing, electrodes (small, plastic patches) will be placed on the volunteers arms, chest and legs. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Fasting
If the volunteer have to fast for a prolonged time during the study, this may lead to symptoms such as dizziness, headache, stomach upset, or fainting.

Coronavirus test
Samples for the coronavirus test will be taken from the back of the volunteers nose and throat using swabs. Taking the samples only takes a few seconds, but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of the volunteers throat may cause the volunteer to gag. When the sample is taken from the back of the volunteers nose, the volunteer may experience a stinging sensation and the volunteers eyes may become watery.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Sex: Male or female.
2. Age: 18 to 55 years, inclusive, at screening.
3. Body mass index (BMI): 18.0 to 27.0 kg/m2, inclusive, at screening.
4. Body weight: >=50 kg at screening.
5. Good physical and mental health on the basis of medical and surgical history, physical examination, clinical laboratory (including clinical chemistry, hematology, urinalysis, and coagulation), 12 lead electrocardiogram (ECG), and vital signs, as judged by the Investigator.

Further criteria apply

Exclusion criteria

1. Employee of ICON or the Sponsor.
2. History or presence of clinically significant allergic diseases (except for untreated, asymptomatic, seasonal allergies at time of dosing), in the opinion of the Investigator.
3. History or presence of conditions which, in the opinion of the Investigator, are known to interfere with the ADME of drugs, such as previous surgery on the gastrointestinal tract (including removal of parts of the stomach, bowel, liver, gall bladder, or pancreas). Participants who have a history of appendectomy are eligible for enrollment.
4. History of chronic constipation, or recent complaints of an irregular defecation pattern (ie, less than once per day on average) in the opinion of the Investigator.
5. History of surgery requiring general anesthesia (not including local procedures) or major trauma within 12 weeks of screening, or a planned surgery during participation in the study.

Further criteria apply

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-11-2022
Enrollment:	9
Type:	Actual

Ethics review

Approved WMO Date:	13-10-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-11-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-03-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	03-04-2023
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	EUCTR2022-003108-34-NL
CCMO	NL82705.056.22