A phase I, randomized, double-blind, placebo-controlled, single-center study designed to evaluate the safety, pharmacokinetics, and pharmacodynamic effects of single and multiple ascending doses of GDC-6599 and the effect of food on the pharmacokinetics and pharmacodynamics of GDC-6599 in healthy adult subjects

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Ethical review	Approved WMO
Status	Completed
Health condition type	Respiratory tract infections
Study type	Interventional

Summary

ID

NL-OMON52277

Source
ToetsingOnline

Brief title
GDC-6599 SAD, FE and MAD study

Condition

- Respiratory tract infections

Synonym
Asthma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: FE, GDC-6599, MAD, SAD

Outcome measures

Primary outcome

- Incidence and severity of adverse events, with severity determined according

to the DAIDS toxicity grading scale

- Change from baseline in targeted vital signs

- Change from baseline in targeted clinical laboratory test results

- Change from baseline in ECG parameters

Secondary outcome

- Plasma concentration of GDC-6599 at specified timepoints

- Plasma concentration of GDC-6599 at specified timepoints in subjects

receiving GDC-6599 under fasting and fed conditions

Study description

Background summary

Asthma is a chronic inflammatory disease in the lungs. Asthma results in narrowed airways and extra mucus production in the airways. This can trigger coughing, make breathing difficult and shortness of breath. Asthma prevalence seems to be increasing worldwide. At the moment there is no cure for asthma, but current treatment can help control the symptoms. Development of new therapies targets towards patients which respond poorly to current treatment methods. Patients with asthma and other respiratory diseases often say cough is a bothersome symptom and significantly contributes to disease burden. Cough is called chronic if it persists for longer than 8 weeks. Chronic cough may be a result of asthma or another lung disease. There may also be no clear reason why slight irritation causes coughing.
GDC-6599 is a new compound that may potentially be used for the treatment of asthma and chronic cough. GDC6599 is a so-called TRPA1 inhibitor and targeting TRPA1 is expected to reduce airway obstruction and sensitivity. The aim of GDC-6599 is reducing the (worsening of) symptoms in patients with asthma and reducing the symptoms in patients with chronic cough.

Study objective

In this study we will investigate how safe the new compound GDC-6599 is and how well it is tolerated when it is used by healthy participants.

We also investigate how quickly and to what extent GDC-6599 is absorbed, transported, and eliminated from the body (this is called pharmacokinetics). In addition, we look at the effect of GDC-6599 on an itch/pain test (this is called pharmacodynamics).

GDC-6599 has not been administered to humans before. It has been extensively tested in the laboratory and on animals. GDC-6599 will be tested at various dose levels.

We will compare the effects of GDC-6599 with the effects of a placebo. A placebo is a compound without any active ingredient. Please note that when the term *study compound* is used in this document, we mean GDC-6599, placebo, or both.

For this study we are looking for 92 healthy male or female participants. The study will consist of 3 parts.

The first part of this study will consist of taking a single dose of GDC-6599 or placebo, where the dose is increased per group. This is called a *single ascending dose* (SAD) study. The second part of this study will consist of taking a single dose of GDC-6599 or placebo when fasting, and then 1 or 2 more times with food. This is called a *food effect* (FE) study. The third part of this study consists of taking repeat doses of GDC-6599 or placebo for up to 29 days, where the dose is increased per group. We call this a *multiple ascending

dose* (MAD) study.

Study design

SAD:
For the study it is necessary that the volunteer stays in the research center for 1 period of 6 days (5 nights). This will be followed by 3 short visits to the research center. These short visits will take place on Day 6, Day 8 and Day 15.

Day 1 is the day when the volunteer receives the study compound. The volunteer is expected at the research center 2 days before administration of the study compound. The volunteer will leave the research center on Day 4 of the study.

FE:
For the study it is necessary that the volunteer stays in the research center for at least 1 period of 13 days (12 nights). This will be followed by 3 short visits to the research center. These short visits will take place on Day 13, Day 15 and Day 22

Day 1 and Day 8 are the days when the volunteer receives the study compound. The volunteer is expected at the research center 2 days before the first administration of the study compound. The volunteer will leave the research center on Day 11 of the study.

Based on the results of the first 2 doses, it will be decided if a third dose is needed. If a third is needed, it is necessary that the volunteer stays in the research center for a second period of 5 days (4 nights). This will be followed by 3 short visits to the research center. These short visits will take place on Day 6, Day 8 and Day 15. Day 1 is the day when the volunteer receives the third administration of the study compound. The volunteer is expected at the research center 1 day before administration of the study compound. The volunteer will leave the research center on Day 4 of the study.

MAD:
For the study it is necessary that the volunteer stays in the research center for 1 period of 13 days (12 nights). This will be followed by 2 short visits to the research center. These short visits will take place on Day 15 and Day 22. Day 1 is the day when the volunteer receives the study compound. The volunteer is expected at the research center 2 days before administration of the study compound. The volunteer will leave the research center on Day 11 of the study.

Intervention

SAD:
The volunteer will be given GDC-6599 or placebo as tablets orally with 240 mL

of water or as a suspension (a drink). After administration of the suspension, the vial will be rinsed twice with 30 mL of water, which the volunteer will also be required to drink. Thereafter he/she are also required to drink an additional amount of water, for a total administration of 240 mL of liquid.

FE:
The volunteer will be given GDC-6599 or placebo as tablets orally with 240 milliliters (mL) of water.

GDC 6599 will be given after a fasting period of 10 hours, or 30 minutes after a high-fat breakfast, or possibly 30 minutes after a low-fat breakfast.

MAD:
The volunteer will be given GDC-6599 or placebo as tablets orally with 240 milliliters (mL) of water.

In Group MAD-1, GDC-6599 will be given in a fasted state. In Groups MAD-2 and MAD-3, GDC-6599 will be given in a fasted or fed state, depending on the results of the FE part.

Study burden and risks

Blood draw
Drawing blood may be painful or cause some bruising. The use of the indwelling cannula can sometimes lead to inflammation, swelling, hardening of the vein, blood clotting, and bleeding in the environment 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 260 (SAD) 450 to 500 (FE) 370 (MAD) milliliters (mL) (8 days), 420 mL (15 days), or 500 mL (29 days) (MAD) of blood from the volunteer. If the investigator thinks it is necessary for the safety of a participant, 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 will be placed on the arms, chest and legs. To monitor your heart rate, electrodes will be placed on the chest and abdomen. Prolonged use of these electrodes can cause skin irritation.

Itch/pain test
A small amount of a liquid test agent is applied to areas about the size of 1 centimeter on the forearm. These areas are then scanned with a laser imaging camera for up to 21 minutes. The test agent, a mustard oil allyl isothiocyanate (AITC), may cause some mild skin redness, change in skin color, blistering, or pain and itching at the area of skin where it is applied. Most of the reactions

described above should resolve within a few hours. However, in some individuals, the skin changes (eg, redness and/or swelling) can last for 2 weeks, sometimes even up to several months. An example of the latter is a risk of *scarring*, ie, one participant (out of 86 total) had skin discoloration of the skin tested, which lasted 79 days. There is a rare risk of having an allergic skin reaction to AITC (contact dermatitis, which is a type of eczema triggered by contact with some chemicals).

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

The high-fat breakfast is a big breakfast containing eg, 2 fried eggs, fried potatoes and bacon. The volunteer must consume the whole breakfast. It can be difficult to consume the entire breakfast, particularly for light eaters.

Coronavirus test
Samples for the coronavirus test will be taken from the back of the 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 throat may cause the volunteer to gag. When the sample is taken from the back of the nose, the volunteer may experience a stinging sensation and the eyes may become watery.

Contacts

Public
Genentech, Inc.

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South San Francisco CA 94080
US
Scientific
Genentech, Inc.

DNA Way 1
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US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Signed Informed Consent Form
- Age 18*75 years at time of signing Informed Consent Form
- Ability to comply with the study protocol, in the investigator*s judgment
- Body mass index of 18*30 kg/m2 at screening
- Veins suitable for venipuncture and/or cannula insertion to accommodate blood sample collection at multiple timepoints during the study

Exclusion criteria

- Pregnant or breastfeeding, or intending to become pregnant during the study or within 14 days after the final dose of study drug during the SAD/FE stage and for 28 days after the final dose of study drug during the MAD stage, unless a longer period is required by local regulations or ethics committee
Women must have a negative serum pregnancy test result within 1 day prior to initiation of study drug.
- History of easy bruising or bleeding (i.e., bruising or bleeding out of proportion to the degree of trauma)
- Use of anticoagulant or anti-platelet therapies
- History of significant hepatic impairment, defined as Child-Pugh Class B or C, corresponding to a Child-Turcotte-Pugh Score >= 7
- History of abuse, in the investigator's judgment, of drugs including, but not limited to the following: amphetamines, barbiturates, benzodiazepines, cocaine, marijuana/cannabis, methadone, methamphetamine, ecstasy, morphine/opiates, phencyclidine, and tricyclic antidepressants within 12 months prior to screening and clinic admission
A positive drug screen test for any of the drugs listed above at screening is exclusionary.

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:	Completed
Start date (anticipated):	19-08-2021
Enrollment:	92
Type:	Actual

Ethics review

Approved WMO Date:	06-07-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-07-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	07-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-06-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-08-2023
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	EUCTR2021-002464-48-NL
CCMO	NL78223.056.21