A PHASE I, RANDOMIZED, DOUBLE BLINDED, PLACEBO CONTROLLED STUDY TO EVALUATE THE SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF SINGLE AND MULTIPLE ASCENDING DOSES OF ORAL GDC-8264 AND THE EFFECT OF FOOD ON THE PHARMACOKINETICS OF GDC-8264 IN HEALTHY VOLUNTEERS

Published: 09-12-2019
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Ethical review	Approved WMO
Status	Completed
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON55161

Source
ToetsingOnline

Brief title
GDC-8264 SAD/MAD/FE Study

Condition

- Gastrointestinal inflammatory conditions
- Autoimmune disorders

Synonym
Inflammatory Bowel Disease, irritable bowel syndrome

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Food effect, GDC-8264, Pharmacokinetics, Randomized

Outcome measures

Primary outcome

The safety objective for this study is to evaluate the safety and tolerability

of single and multiple doses of GDC 8264 compared with placebo in healthy

subjects

Secondary outcome

To characterize the pharmacokinetics of GDC 8264.

Study description

Background summary

GDC-8264 is a new compound that may potentially be used for the treatment of inflammatory bowel disease (IBD). IBD includes two main conditions: ulcerative colitis and Crohn*s disease. These diseases are characterized by chronic inflammation and increased cell death in parts of the intestines. The gastrointestinal tract can therefore not work normally anymore. Patients who suffer from IBD thus show symptoms such as abdominal pain, diarrhea and a

reduced appetite. Many of these patients require hospitalization and surgery. In the Netherlands approximately 1 in 200 people suffer from this disease. GDC-8264 works by preventing cell death and inflammation by blocking RIP1 kinase from performing its action. This protein plays an important role in regulating cell death and blocking it can result in reduced inflammation.

Study objective

The purpose of this study is to investigate how safe the new compound GDC-8264 is and how well it is tolerated when it is administered to healthy volunteers. GDC-8264 has not been administered to humans before. It has been previously tested in the laboratory and on animals. GDC-8264 will be tested at various dose levels. It will also be investigated how quickly and to what extent GDC-8264 is absorbed and eliminated from the body. The effects of GDC-8264 will be compared to the effects of a placebo.

DDI:
In at least one group of the MAD part, we will investigate whether GDC-8264 can influence how other compounds are handled by the body. This is called a drug-drug interaction (DDI) study. For this purpose, GDC-8264 will be given together with midazolam. Midazolam is not a new medication; it has been used in clinical practice since the mid-1980s. It is currently approved to treat sleep disorders and is sometimes used during anesthesia. In this study midazolam will be used as a model to measure the activity of CYP3A4, an enzyme that helps to break down chemicals in the body. First, we will examine how fast your body breaks down midazolam. Second, we will measure to what extent GDC-8264 influences this break down process.

Study design

SAD:
The study will consist of 1 period during which the subjects will stay in the research center for 6 days (5 nights). This will be followed by 1 day during which they will visit the research center for a short visit.
FE:
The study will consist of 3 periods during each the subjects will stay in the research center for 6 days (5 nights). They can return home in between these periods. This will be followed by 1 day during which they will visit the research center for a short visit.
MAD:
The study will consist of 1 period during which the subjects will stay in the research center for up to 19 days (18 nights). This will be followed by 2 days during which they will visit the research center for a short visit.
DDI:
The study will consist of 1 period during which the subjects will stay in the research center for up to 15 days (14 nights). This will be followed by 2 days

during which they will visit the research center for a short visit.

Intervention

The subjects will receive a single or multiple doses of GDC-8264 or placebo as tablets orally with 240 milliliters (mL) of water, or as a suspension. The starting dose is 5 mg.

Midazolam is given through a syringe without a needle in the mouth, after which it can be swallowed. One also gets 200 ml of water to rinse the mouth and to swallow. Midazolam is given after 8 hours of fasting. In addition, fasting continues for up to 4 hours after ingestion. Two single doses of midazolam of 5 mg each are given: once on Day 1 and once on Day 10.

Study burden and risks

As GDC-8264 will be administered to humans for the first time in this study, side effects of GDC-8264 in humans have not been reported to date. GDC-8264 has been studied extensively in the laboratory and in animals. The compound was generally well tolerated and did not result in significant changes in measurements of blood pressure, heart rate, heart tracings, behavior and respiratory function. Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Age 18 to 55 years, inclusive
- Body mass index between 18 and 30 kg/m2, inclusive
- Ability to comply with the study protocol, in the investigator's judgment
- Expressed willingness to participate in the entire study
- For women of childbearing potential: use contraception as described in protocol.
For men: use a condom, and agreement to refrain from donating sperm, as defined in protocol
- For subjects screened at PRA Health Sciences: meeting of site-specific COVID-19 criteria

Exclusion criteria

- Pregnant or breastfeeding, or intending to become pregnant during the study or within 90 days or 5 half-lives of GDC-8264, whichever is longer, after the final dose of study drug
- Treatment with investigational therapy within 90 days prior to initiation of study drug
- Participation in more than four other drug studies in the 12 months prior to drug administration in the current study
- Subjects who have been previously enrolled in this study
- Study site employees or immediate family members of a study site or Sponsor employee

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):	20-12-2019
Enrollment:	114
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Midazolam
Generic name:	n.a.
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	09-12-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	20-12-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	15-01-2020
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-08-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-08-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-03-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	09-07-2021
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	EUCTR2019-002613-19-NL
CCMO	NL72106.056.19

Study results

Date completed:	13-10-2021
Results posted:	20-05-2022

First publication
28-02-2022