A Phase 1, Open-label, Single Intravenous Infusion Dose Study to Evaluate the Mass Balance, Pharmacokinetics, Metabolism, and Excretion of TAK-954 Containing Microtracer ([14C]-TAK-954)in Healthy Male Subjects

Published: 16-04-2018
Last updated: 11-04-2024

TAK-954 is an investigational drug which means that it has not yet been approved for use. The main purpose of this study is to understand how the body handles TAK-954 (how it is absorbed, processed by and removed from the body). TAK-954 will be...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal conditions NEC
Study type	Interventional

Summary

ID

NL-OMON46703

Source
ToetsingOnline

Brief title
Microtracer TAK-954 Healthy Adult Male Subjects

Condition

- Gastrointestinal conditions NEC

Synonym
Gastrointestinal motility disorders

Research involving
Human

Sponsors and support

Primary sponsor: Millennium Pharmaceuticals Inc
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: ADME, Open-label, TAK-954

Outcome measures

Primary outcome

To determine the mass balance and routes of elimination of a single IV dose of

TAK-954 containing microtracer ([14C]-TAK-954).

To characterize the metabolic profiles following single-dose IV administration

of TAK-954 containing microtracer ([14C]-TAK-954) and identify major

circulating and excreted metabolites.

To determine the single-dose pharmacokinetics (PK) of total radioactivity,

TAK-954, THRX513466, and THRX 913682, where possible.

Secondary outcome

The secondary objective of the study is to evaluate the safety and tolerability

of a single IV dose of TAK-954 containing microtracer ([14C]-TAK-954) in

healthy male subjects.

Study description

Background summary

TAK-954 is being developed for the short-term treatment of critically ill patients that have developed difficulty receiving feedings through a tube leading into the stomach. TAK-954 activates the so-called 5-HT4 receptor. In animal studies it has been shown, that it has a positive effect on the gastrointestinal tract.

Study objective

TAK-954 is an investigational drug which means that it has not yet been approved for use. The main purpose of this study is to understand how the body handles TAK-954 (how it is absorbed, processed by and removed from the body). TAK-954 will be minutely radioactive labelled (with 14 Carbon [14C]) so that it can be traced in blood, urine and feces. The radiation dose is considered to be lower than that of background.

In addition, the safety and tolerability of TAK-954 will be investigated.

Study design

Participation in the entire study depends on the amount of radioactivity measured in volunteers blood, feces and urine. The volunteer will stay in the research center at least from Day -1 (the day before study compound is given) until the afternoon of Day 8. If, from Day 8 onwards, the radioactivity levels in urine and feces are below the pre-defined levels, the volunteer will be allowed to leave the research center. At the latest the volunteer will be allowed to leave the research center on the afternoon of Day 15.

Intervention

A total of 0.5 mg TAK-954 with trace amount of radioactivity will be given as an intravenous infusion over a 1-hour period during the morning of Day 1.

When TAK-954 is given, the volunteer should have fasted for at least 2 hours (no eating and drinking). Water is permitted until 1 hour prior to the start of dosing and may be consumed without restriction beginning 1 hour after the end of dosing.

During the first 4 hours after starting the drug infusion, the volunteer has to remain in a semi-recumbent (lying down with head of bed tilted up) position (except when indicated as such by one of the investigators).

Study burden and risks

The study compound may cause side effects.

In general, doses up to 0.5 mg once daily for 5 consecutive days as IV infusions, were well tolerated in healthy subjects.

Approximately 80 subjects have been exposed to different doses of TAK-954 in clinical trials. Based on the results of those studies, the known side effects that occurred for TAK-954 are as follows:
•headache (reported by 38% of the subjects)
•diarrhea (reported by 14% of the subjects)
•dizziness that may occur while standing or sitting up (reported by 10% of the subjects)
•irregular heartbeat (reported by 10% of the subjects)
•low blood pressure when sitting or standing (reported by 7% of the subjects)

Other side effects observed when TAK-954 was taken by mouth were nausea (reported by of the 56% subjects) and vomiting (reported by 29% of the subjects).

Side effects that have occurred with other medications with in the same class but were not reported with TAK-954 are as follows:
•abdominal pain with bloody diarrhea and increased size of abdomen
•heart attack or severe chest pain that may or may not spread into shoulders and arms, and stroke or temporary stroke symptoms
•serious irregular heart rhythms

If the volunteer has a known hypersensitivity to TAK-954 or to any ingredient in it, the volunteer will not be allowed to take part in the study.

The study compound can also have side effects that are not known yet.

Tests
Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising.
In total, we will take about 400 mL of blood from the volunteer. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time.

To make a heart tracing, electrodes (small, plastic patches) will be pasted at specific locations on your arms and legs. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Exposure to radiation
This study involves using radioactive markers. The additional amount of radiation the volunteer will be exposed to in this study is negligible (that is, less than the natural background radiation in 1 month) compared to the background radiation in the Netherlands, which is ~2.5 mSv per year. If the volunteer participate in scientific research involving exposure to radiation more often, the volunteer should discuss with the investigator whether

participation at this moment would be safe.

Procedures: pain, minor bleeding, bruising, possible infection.

Contacts

Public
Millennium Pharmaceuticals Inc

Landsdowne Street 40
Cambridge 02139
US
Scientific
Millennium Pharmaceuticals Inc

Landsdowne Street 40
Cambridge 02139
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-healthy male subjects
-18-55 yrs, inclusive
-BMI: >=18 and <=30 kg/m2 and a body weight >50 kg at the screening visit.
-non-smoking

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 the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study.

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):	30-04-2018
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO Date:	16-04-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-04-2018
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	EUCTR2018-001181-42-NL
CCMO	NL65503.056.18