A PHASE 1, OPEN-LABEL, NON-RANDOMIZED, 2-PERIOD, FIXED SEQUENCE STUDY TO INVESTIGATE THE ABSORPTION, DISTRIBUTION, METABOLISM AND EXCRETION OF 14C-PF-06835919 AND TO ASSESS THE ABSOLUTE BIOAVAILABILITY AND FRACTION ABSORBED OF PF-06835919 IN HEALTHY MALE PARTICIPANTS USING A 14C-MICROTRACER APPROACH.

Published: 17-08-2020
Last updated: 08-04-2024

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Hepatic and hepatobiliary disorders
Study type	Interventional

Summary

ID

NL-OMON49734

Source
ToetsingOnline

Brief title
A Phase 1 ADME Study of 14C-PF-06835919 in Healthy Male Participants.

Condition

- Hepatic and hepatobiliary disorders

Synonym
a liver disease., non-alcoholic steatohepatitis (NASH)

Research involving
Human

Sponsors and support

Primary sponsor: Pfizer Inc.
Source(s) of monetary or material Support: Pharmaceutical Industry.

Intervention

Keyword: 14C-PF-06835919, ADME, Bioavailability, Healthy male participants

Outcome measures

Primary outcome

Mass Balance: Cumulative recovery of radioactivity over time in urine, feces

and total excreta (urine + feces) as percentage of total radioactive

dose administered.

Secondary outcome

-Metabolic profiling/metabolite identification and determination of relative

abundance of 14C-PF-06835919 and metabolites in plasma, urine and feces (Period

1).

- PF-06835919 plasma (Period 1 and Period 2): Cmax, AUClast, Tmax, and if data

permit, t*, AUCinf, CL/F, Vz/F.

-14C-PF-06835919 plasma (Period 2): Cmax, AUClast, AUCinf, and if data permit,

Tmax, t*, CL and Vss.

-Total 14C radioactivity in plasma (Period 1): Cmax, AUClast, Tmax, t*.

-PF-06835919 AUCinf from both oral PF-06835919 and IV 14C-PF-06835919 (Period 2 only) plasma data.

-Total 14C urine data following both IV (Period 2) and oral (Period 1) administration of 14C-PF-06835919 (quantification by AMS).

-AE monitoring, physical examination, clinical laboratory measurements, vital signs and 12-lead ECG.

Study description

Background summary

PF-06835919 is an investigational compound that may eventually be used for the treatment of non-alcoholic steatohepatitis (NASH), a liver disease. NASH is characterized by inflammation (localized reaction that produces redness, warmth, swelling, and pain) and the build-up of fat in the liver. There are no therapies currently approved for the treatment of NASH.

PF-06835919 is a potent, reversible inhibitor of the enzyme ketohexokinase (KHK) that is currently being developed for the treatment of NASH. KHK is the enzyme (a protein that speeds up a chemical reaction in the body) responsible for the first step of fructose metabolism (break down). By blocking fructose metabolism, KHK may have the potential to reduce liver fat and inflammation.

Study objective

The purpose of this study is to investigate how quickly and to what extent PF-06835919 is absorbed and eliminated from the body.
PF-06835919 will be labelled with Carbon-14 (14C) and is thus radioactive. In this way, PF-06835919 can be traced in blood, urine, and feces.

This study will also investigate how safe the new compound PF-06835919 is and how well it is tolerated when it is administered to healthy volunteers. In addition, the taste of the oral solution of PF-06835919 will be assessed. PF 06835919 has been administered to humans before.

This study will be performed in 6 healthy male volunteers.

Study design

The participation from screening until the final follow-up phone call will last about 20 weeks.

The actual study will consist of 2 periods. Day 1 is the day of administration of the study compound in each period. In both periods, the volunteers are expected at the research center at 14:00 h in the afternoon 1 day before the administration of study compound (so on Day -1). The time of entry may be changed.

During Period 1, they will stay in the research center for a minimum of 8 days (7 nights) and a maximum of 15 days (14 nights).

The amount of radioactivity in urine and feces will be measured daily from Day 1 onwards. If, from Day 7 onwards, the radioactivity levels in urine and feces are below the pre-defined levels, volunteer will be allowed to leave the research center in the afternoon. The discharge criteria are met when more than 90% of the administered radioactivity has left the body or less than 1% of radioactivity is excreted in a 24-hour period on 2 consecutive days, and if there are no medical objections. In Period 1, the volunteer will leave the research center no later than Day 14. There are approximately 10 to 17 days between administration of the study compound in Period 1 and administration of the study compound in Period 2. In Period 2, the volunteer will leave the research center on Day 5.

When the volunteer enters the research center, 2 coronavirus samples will be collected at the same time to test if the volunteer is a carrier of SARS-CoV-2.
The coronavirus test will be done on the following days:
Day -1 of each period
Day 2 of each period
Before leaving the research center in Period 2
It may be decided that more tests are needed (eg, if the volunteer has COVID 19 symptoms).

Intervention

In Period 1 on Day 1, the volunteers will be given 300 mg of 14C-labeled PF-06835919 as an oral suspension of 100 mL. After administration of the study compound, the vial will be rinsed 3 times with approximately 47 mL of water, which the volunteers will also be required to drink.

In Period 2 on Day 1, they will be given 300 mg PF-06835919 without the radioactive label as an oral suspension of 240 mL. Approximately 1 hour later, they will receive 100 microgram (µg) PF-06835919 with radioactive label as an intravenous infusion of 10 mL. The infusion will last about 15 minutes.

During the first 4 hours after oral administration of the study compound, they will not be allowed to lie down (except when indicated as such by one of the

investigators), as this may influence the uptake of the study compound.

All volunteers will receive the same treatment.

Study burden and risks

The following side effects (non-severe and non-serious) have been reported in at least 2 participants treated with PF-06835919, when given alone, in any single human study completed to date:
- Headache
- Low blood sugar
- Acne
- Abdominal pain, discomfort and/or distension
- Change in bowel habit
- Constipation
- Loose stools
- Joint or muscle pain
- Pain in hands or feet
- Dry mouth
- Dry skin
- Rash or itch
- Difficulty sleeping
- Fatigue
- Increased urinary frequency
- Urinary tract infections

Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising.
In total, there will taken about 440 milliliters (mL) of blood from the volunteer. This amount does not cause any problems in adults.

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

A sample for the coronavirus test will be taken from the back of ther nose and throat using a swab. Taking the sample 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, they may experience a stinging sensation and the eyes may become watery.

Contacts

Public
Pfizer Inc.

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US
Scientific
Pfizer Inc.

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New York NY 10017
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Male participants must be nonsmoking, 18 to <55 years of age, inclusive
2. Male participants who are overtly healthy as determined by medical evaluation including medical history, physical examination, laboratory tests, and cardiac tests.
3. Participants who are willing and able to comply with all scheduled visits, treatment plan, laboratory tests, lifestyle considerations, and other study procedures.
4. BMI of 17.5 to 30 kg/m2; and a total body weight >50 kg (110 lb).
5. Capable of giving signed informed consent

Exclusion criteria

1. Evidence or history of clinically significant hematological, renal, endocrine, pulmonary, gastrointestinal, cardiovascular, hepatic, psychiatric,

neurological, or allergic disease (including drug allergies, but excluding untreated, asymptomatic, seasonal allergies at the time of dosing).
2. Any condition possibly affecting drug absorption (eg, gastrectomy, cholecystectomy,
appendectomy).
3. History of irregular bowel movements including irritable bowel syndrome or frequent
episodes of diarrhea or constipation defined by less than 1 bowel movement on average per 2 days or lactose intolerance.
4. History of HIV infection, hepatitis B, or hepatitis C; positive testing for HIV, HBsAg, or HCVAb. Hepatitis B vaccination is allowed.
5. Other medical or psychiatric condition including recent (within the past year) or
active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation or, in the investigator*s judgment, make the participant inappropriate for the study.
Further criteria apply, referring to protocol.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO

Date:	17-08-2020
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-09-2020
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	EUCTR2020-002837-14-NL
CCMO	NL74785.056.20