A phase 1, open label, 2-period, fixed sequence, study to assess the mass balance, absolute bioavailability of 14C-PF-06826647 in healthy male participants

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

Summary

ID

NL-OMON50100

Source
ToetsingOnline

Brief title
Mass balance and absolute bioavailability of 14C-PF-06826647 in men.

Condition

- Gastrointestinal inflammatory conditions
- Autoimmune disorders

Synonym
Psoriasis and ulcerative colitis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: 14C-PF-06826647, Bioavailability, Healthy male participants, Mass balance

Outcome measures

Primary outcome

Total recovery of radioactivity in urine and feces separately, and both routes

combined, expressed as a percent of total oral radioactive dose administered.

Secondary outcome

Safety: laboratory tests, AE reporting, ECG and vital signs.

The ratio of dose normalized AUCinf of PF-06826647 (LCMS) and 14C-PF-06826647

(AMS) in plasma in Period 2.

Study description

Background summary

PF-06826647 is a new experimental compound that may potentially be used for the treatment of the skin diseases psoriasis and hidradenitis suppurativa, and the digestive tract conditions that are part of inflammatory bowel disease (IBD). Cytokines are chemical messengers that help control the immune system and fight diseases. Some of these cytokines play an important role in the progression of these diseases. PF-06826647 is a molecule that has the potential to reduce the activity of these cytokines and may therefore be a treatment option for these diseases.

Study objective

The purpose of this study is to investigate how quickly and to what extent PF-06826647 is absorbed and eliminated from the body (pharmacokinetics).

PF-06826647 will be labelled with Carbon-14 (14C) and can be traced in blood, urine, and feces.

This study will also investigate how safe the new compound PF-06826647 is and how well it is tolerated when it is administered to healthy volunteers. In addition, the taste of the oral solution of PF-06826647 will be assessed. PF 06826647 has been administered to humans before.

Study design

The study will last about 11 weeks.

The study consist of 2 periods. Day 1 is the day of administration of the study compound in each period. During Period 1, the volunteer will stay in the research center for a minimum of 6 days (5 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 5 onwards, the radioactivity levels in urine and feces are below the pre-defined levels, the volunteer is allowed to leave the research center. If the discharge criteria are not met until Day 13 in Period 1, the volunteer will stay in the research center and Period 2 will start the next day. Period 2 will start at least 14 days after administration of the study compound in Period 1. In Period 2, the volunteer will leave the research center if the stay in Period 2 equals the period of stay in Period 1. Volunteer will receive a follow-up phone call at least 28 days after the last administration of the study compound in Period 2.

When the volunteer enters the research center, two 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 each Period
It may be decided that more tests are needed.

Intervention

In Period 1 on Day 1, volunteer will be given 600 mg of 14C-labeled PF-06826647 as a drink of 100 mL. After administration of the study compound, the cup will be rinsed 3 times with 47 mL of water, which the volunteer will also be required to drink.

In Period 2 on Day 1, volunteer will be given 600 mg PF-06826647 without the radioactive label as 6 tablets that contain 100 mg PF-06826647 each. The tablets will be ingested with a minimum of 240 mL of water. If necessary additional water to ingest the tablets is allowed. After ingestion of the tablets, one of the investigators will inspect volunteers hands and mouth to

check whether volunteer ingested the tablets. Approximately 3 hours later, volunteer will receive 100 microgram (µg) PF-06826647 with radioactive label as an intravenous infusion of 20 mL. The infusion will last about 1 hour.

During the first 4 hours after taking the drink containing the study compound, volunteer 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.

Study burden and risks

PF-06826647 has been studied in animals and humans, but not all product safety information is known at this time. There may be rare and unknown side effects, including serious or severe reactions that have not yet been discovered.

Human studies with PF-06826647 consist of one completed Phase 1 study (C2501001). A total of 69 healthy participants volunteers and 40 patients with plaques psoriasis received study treatments. All reported adverse events were mild in severity except for one adverse event that was moderate in a psoriasis patient receiving placebo. There were no serious or severe adverse events observed.

Animal studies have been conducted in animals to try to identify risks that may occur in people given PF-06826647. In some animals given high doses of PF-06826647, increases in blood pressure and heart rate occurred. Some animals had discolored feces and gastric reflux. These effects occurred generally at high dose levels of PF-06826647.
Based on animal studies, PF-06826647 may increase levels of certain proteins in the blood, which may indicate inflammation or injury to the liver. Rats and monkeys given PF-06826647 had increases in liver enzymes. However, these increases were not associated with signs of liver injury in animals. There is also the potential for changes in blood lipid levels (cholesterol and triglycerides) with PF-06826647. Lipid changes seen in animals were small and not associated with evidence of liver or other tissue injury. Decreases in certain immune cells (white blood cells) also occurred in some animals receiving PF-06826647. These immune cells normally help protect against infection.

Potential Side Effects:

Reactivation of viruses:
Certain viruses can remain in a sleeping form in the body and they may reactivate and cause negative effects. In studies with PF-06826647 or other similar medications, reactivation of the chicken pox virus (herpes zoster) has caused shingles and reactivation of the herpes simplex virus has caused cold sores or fever blisters in the mouth or genital ulcers. It is not known if PF-06826647 could lead to the reactivation of hepatitis viruses. Volunteer will not be allowed to participate in the study if the blood tests show that

volunteer have had hepatitis types B or C viruses (unless demonstrated to be completely cured from Hepatitis C).

Serious or Unusual infections:
PF-06826647 is a study drug that affects your immune system. It may lower the ability of your body to fight infections, leading to more serious infections or infections that usually don*t occur in people with a normal immune system. There were no infections observed in the previous healthy volunteer study with PF-06826647. Some people have had serious infections or unusual infections while taking medications similar to PF-06826647. Volunteer should not start PF-06826647 if volunteer have any kind of infection.

Cancer:
PF-06826647 may increase the risk of certain cancers by changing the way the immune system defends against cancer. No formation of cancers has been reported in the previous healthy volunteer study with PF-06826647. Lymphoma and other cancers, including skin cancers, have been reported in patients taking medications that work in a similar way to PF-06826647. Most people with a history of cancer will not be eligible for this study, except for those who have had successfully treated skin cancers that were not of the melanoma type.

Changes in certain laboratory test results. Some changes in blood tests that have occurred in animal or human studies with PF-06826647:
•Decreases in lymphocyte counts.
•Decreases in neutrophil counts.
•Increases in platelet counts.
•Changes in other laboratory tests, such as a rise in muscle enzymes (creatine kinase), kidney function parameters (serum creatinine), blood cholesterol or a drop in hemoglobin (red blood cells) levels.

Deep vein thrombosis and pulmonary embolism:
Pulmonary emboli have occurred in patients taking medications that work in similar ways to PF-06826647. PF-06826647 may increase the risk of developing a blood clot, including in legs (deep vein thrombosis) and lungs (pulmonary embolism). A serious adverse event of deep vein thrombosis occurred in a female healthy volunteer taking both PF-06826647 600 mg daily and high dose oral contraceptive (30 µg ethinyl estradiol + 150 µg of levonorgestrel) daily in C2501005, a Phase 1 Drug-Drug Interaction Study. If volunteer have had a history of recent blood clots in legs or lungs or a history of repeated blood clots in legs or lungs, or have other risk factors for clotting, volunteer may not be eligible for this study.

Possible discomforts:
Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising.
In total, about 390 milliliters (mL) of blood will be taken from the volunteer.

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

Radiation:
This study involves using radioactive markers. The additional amount of radiation the volunteer will be exposed to in this study is below 0.1 mSv.

A sample for the coronavirus test will be taken from the back of the 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, the volunteer may experience a stinging sensation and the eyes may become watery.

Contacts

Public
Pfizer Inc.

East 42nd Street 235
New York NY 10017
US
Scientific
Pfizer Inc.

East 42nd Street 235
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. Healthy male participants must be 18 to 55 years of age, inclusive, at the time of signing the ICD.
2. Male participants who are overtly healthy as determined by medical evaluation including medical history, physical examination, including BP and pulse rate measurement, laboratory tests, and 12-lead ECG.
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 30.0 kg/m2; and a total body weight >50 kg (110 lb).
5. Capable of giving signed informed consent as described in Appendix 1 of the protocol, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol.

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).
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.
-For hepatitis B, all participants will undergo testing for HBsAg and HBcAb during screening. Participants who are HBsAg positive will not be eligible for this study. Participants who are HBsAg negative but HBcAb positive will be reflex tested for HBsAb. The participant will be eligible if HBsAb is positive.
-For hepatitis C, all participants will undergo testing for HCVAb during screening.Participants who are HCVAb positive will be reflex tested for hepatitis C ribonucleic acid (HCV RNA). Participants who are HCVAb and HCV RNA positive are not eligible for the study. Participants who are HCVAb positive but HCV RNA negative will be considered eligible.
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.

11. A positive COVID-19 test or suspected of having SARS-CoV2 infection.

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:	Recruitment stopped
Start date (anticipated):	10-11-2020
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO

Date:	19-08-2020
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	EUCTR2019-004024-38-NL
CCMO	NL73843.056.20