A phase I, open-label, randomized, three-way cross-over study comparing bioavailability of two formulations and assessing the food effect on tablet formulation after PXL770 single oral dose in healthy subjects

Published: 31-08-2020
Last updated: 17-01-2025

The purpose of this study is compare a tablet formulation of PXL770 to the capsule formulation of PXL770. It will be investigated how quickly and to what extent PXL770 in each formulation is absorbed and eliminated from the body. To limit the...

Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON49206

Source
ToetsingOnline

Brief title
Bioavailability of two formulations of PXL770 after a single dose in HV

Condition

- Other condition
- Hepatic and hepatobiliary disorders

Synonym
Non-alcoholic steatohepatitis

Health condition

NASH

Research involving
Human

Sponsors and support

Primary sponsor: Poxel SA
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Bioavailability, PXL770

Outcome measures

Primary outcome

To assess and compare PXL770 relative bioavailability (rBA) and primary pharmacokinetic (PK) parameters (Cmax, tmax, AUC0-t, AUCinf) between tablet and capsule formulations after a single oral dose of 250 mg

Secondary outcome

- To compare PXL770 secondary PK parameters between tablet and capsule formulations after a single oral dose of 250 mg

- To assess the effect of food on the PK parameters (Cmax, tmax, AUC0-t, AUCinf) of the tablet formulation

- To assess the safety and tolerability of PXL770 after a single oral dose of tablet and capsule formulations

Study description

Background summary

PXL770 is a new compound that may eventually be used for the treatment of non-alcoholic fatty liver disease (NAFLD). NAFLD is the accumulation of fat in the liver which is not caused by excessive alcohol consumption. Some patients with NAFLD also develop inflammation in the liver, this is called non-alcoholic steatohepatitis (NASH). The inflammation leads to damage and scar tissue (fibrosis) in the liver. This can lead to liver cirrhosis, cancer and eventually liver failure. PXL770 works by activating a protein (AMPK) that results, among other things, in a decrease in the uptake of fat by the liver, which can be beneficial for patients that suffer from NASH. PXL770 was first developed as a capsule formulation. The Sponsor is now developing a tablet formulation that is intended to be used for further clinical studies.

Study objective

The purpose of this study is compare a tablet formulation of PXL770 to the capsule formulation of PXL770. It will be investigated how quickly and to what extent PXL770 in each formulation is absorbed and eliminated from the body. To limit the differences between the participants, only Caucasian participants can participate in this study.

Furthermore, we will assess whether the consumption of a meal just after administration of the tablet formulation has an effect on the pharmacokinetics of PXL770.

It will also be investigated how safe the new compound PXL770 is and how well it is tolerated when it is administered to healthy volunteers.

PXL770 has been administered to humans before. It has also been extensively tested in the laboratory and on animals. PXL770 will be tested at a fixed dose of 250 milligrams (mg).

Study design

The actual study will consist of 3 periods. In each period the volunteer will stay in the research center for 5 days (4 nights).

During the participation in the study, the volunteer will follow the scheme below:

Screening * Period 1 * Period 2 * Period 3 * Follow-up

In each period, Day 1 is the day of administration of the study compound. In each period, the volunteer is expected at the research center at 14:00 h in the afternoon prior to the day of each administration of the study compound (Day 1). The volunteer will leave the research center on Day 4 of each period.

The volunteer will receive 250 mg PXL770, 3 times over the course of 3 periods. PXL770 will be administered twice as a tablet formulation and once as a capsule formulation. Each administration will be given with 240 milliliters (mL) of (tap) water. The study compound must not be chewed prior to swallowing. Which treatment the volunteer will receive in each period will be determined by drawing lots. The volunteer will be assigned to one of the following 6 sequences:

Sequence Period 1 Period 2 Period 3
1 Capsule Tablet Tablet (with a meal)
2 Tablet (with a meal) Capsule Tablet
3 Tablet Tablet (with a meal) Capsule
4 Tablet (with a meal) Tablet Capsule
5 Tablet Capsule Tablet (with a meal)
6 Capsule Tablet (with a meal) Tablet

Intervention

The volunteer will receive 250 mg PXL770, 3 times over the course of 3 periods. PXL770 will be administered twice as a tablet formulation and once as a capsule formulation. Each administration will be given with 240 milliliters (mL) of (tap) water. The study compound must not be chewed prior to swallowing. Which treatment the volunteer will receive in each period will be determined by drawing lots. The volunteer will be assigned to one of the following 6 sequences:

Sequence Period 1 Period 2 Period 3
1 Capsule Tablet Tablet (with a meal)
2 Tablet (with a meal) Capsule Tablet
3 Tablet Tablet (with a meal) Capsule
4 Tablet (with a meal) Tablet Capsule
5 Tablet Capsule Tablet (with a meal)
6 Capsule Tablet (with a meal) Tablet

There will be a period of at least a 8 days between PXL770 administration in each period, to make sure the study compound has left the body.

Study burden and risks

The study compound may cause side effects.

PXL770 has been administered to 104 humans before in 3 previous clinical trials with different doses up to 500 mg during 10 days. Only a limited amount of side effects of PXL770 in humans have been reported to date. However, PXL770 has also been studied extensively in the laboratory and in animals.

No serious complaints have been observed, only mild and moderate complaints. The following complaints were most frequently observed:
- headache, observed in 5 volunteers
- abdominal complaints (abdominal pain, diarrhea), observed in 7 volunteers

The study compound may also have side effects that are still unknown. In addition to unknown side effects, there is a small chance that an allergic reaction will occur. This can be caused by the study compound or other ingredients used to make the formulation.

Possible discomforts due to procedures

Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising. On these days, blood will be sampled regularly to determine the course of the concentration of the study compound in the blood over time.

In total, we will take about 370 milliliters 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 will be pasted at specific locations on your arms, chest and legs. Prolonged use of these electrodes can cause skin irritation.

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
Poxel SA

Avenue Jean Jaurès 259-261
Lyon 69007
FR
Scientific
Poxel SA

Avenue Jean Jaurès 259-261

Lyon 69007
FR

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Gender : male or female.
2. Age : 18 to 55 years, inclusive, at screening.
3. Body mass index (BMI) : 18.0 to 30 kg/m2, inclusive, at screening.
4. Weight : >=50 kg at screening.
5. Status : healthy subjects.

Exclusion criteria

1. Previous participation in any clinical study with PXL770 (only if subject received study drug).
2. Employee of PRA or the Sponsor.
3. Mental handicap, legal incapacity, or any history of clinically important emotional and/or psychiatric illness.
4. Vulnerable subjects (e.g. persons kept in detention).
5. History of relevant drug and/or food allergies.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	17-09-2020
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO Date:	31-08-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-09-2020
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	EUCTR2020-003511-10-NL
CCMO	NL75054.056.20

Study results

Date completed: 12-11-2020

Results posted: 02-07-2021

First publication
01-06-2021