An open-label study to characterize the absorption, distribution, metabolism and elimination of a single oral dose of 14C-leniolisib in healthy male subjects

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Ethical review	Approved WMO
Status	Completed
Health condition type	Immune system disorders congenital
Study type	Interventional

Summary

ID

NL-OMON50412

Source
ToetsingOnline

Brief title
Leniolisib ADME Study

Condition

- Immune system disorders congenital

Synonym
Activated Phosphoinositide 3-kinase DeltaSyndrome (APDS), Immune disorder

Research involving
Human

Sponsors and support

Primary sponsor: Pharming Technologies B.V.

Source(s) of monetary or material Support: Ministerie van OC&W,Pharmaceutical Industry

Intervention

Keyword: 14C, ADME, Leniolisib

Outcome measures

Primary outcome

To determine the total recovery and relative excretion of radioactivity in

urine and feces after a single dose of 70 mg 14C-leniolisib, containing 40 µCi

of 14C-radioactivity administered as a solution for oral administration.

Secondary outcome

To determine the plasma PK parameters of total 14C-radioactivity and of

leniolisib;

To evaluate the safety profile of a single 70 mg dose of 14C-leniolisib.

Study description

Background summary

Leniolisib is a new compound that may potentially be used for the treatment of Activated Phosphoinositide 3 kinase Delta Syndrome (APDS). APDS is a disorder that impairs the immune system. Individuals with this condition often have low levels of white blood cells, which normally recognize and attack foreign invaders, such as viruses and bacteria, to prevent an infection. Beginning in childhood, people with APDS develop recurrent infections, particularly in the lungs, sinuses, and ears. Over time, recurrent respiratory tract infections can lead to a condition called bronchiectasis, which damages the passages leading from the windpipe to the lungs (bronchi) and can cause breathing problems. APDS affects approximately 1-2 per million persons globally and there is currently no approved treatment available. Leniolisib works by inhibiting a specific protein that is not functioning normally and believed to be the cause of the progression of this disease.

Study objective

In this study we will investigate how safe the new compound leniolisib is and how well it is tolerated by healthy male participants.

We also investigate how quickly and to what extent leniolisib is absorbed, transported, and eliminated from the body. Leniolisib is radioactively labelled with carbon-14 (14C). In this way leniolisib can be traced in blood, urine, and feces.

Leniolisib has been investigated in humans before in previous drug studies. In addition, it has been extensively tested in the laboratory and on animals.

Study design

For the study it is necessary that subjects stay in the research center for at least 9 days (8 nights) and at most 13 days (12 nights). The length of their stay depends on the amount of radioactivity that has left their body. From Day 8 onwards, the amount of radioactivity in their feces and urine is checked daily. If the predetermined criteria have been reached, they will be informed about this in the late afternoon and they may then leave the research center. They will leave the research center on Day 12 the latest. If they do not yet meet the set criteria then, 1 to 3 weekly 24-hour visits (1 night stay per 24 hour visit) will follow, until the radioactivity is low enough. These potential visits will take place on Day 19/20, 26/27 and 33/34. There is also a follow-up visit within 5 days after last visit. If the amount of radioactivity in blood and urine on Day 8-12 is so low that it cannot be measured, then they only have to collect a feces sample at home once weekly and bring it to the research center on Day 19, 26, and 33.

Day 1 is the day when they receive the study compound. They will leave the research center on Day 12 of the study.

During this study we will measure the amount of radioactivity left in blood, urine, and feces. This means that we will take regular blood samples and that we will collect all feces and urine from study compound intake until subjects leave the research center. We will also ask them to collect a feces sample at home from within 24 hours prior to entry in the research center.

If the radioactivity levels in feces and urine have not yet reached the pre-defined criteria on Day 12, they will return to the research center for 24-hour visits for the collection of urine and feces on Day 19 and, if applicable, also on Day 26 and 33. For the additional visits, they are expected at the research center at 11:00h in the morning and they can leave after the 24 hours have passed (Day 20, 27, and 34). They will also be asked to collect their feces at home within 24 hour prior to the start of these visits. They will receive material for this.

During the 24-hour visit, their urine and feces will be collected, and blood

will be sampled to measure the amount of radioactivity. Depending on the test results of the amount of radioactivity left in their blood, urine and feces, remaining 24-hour visits can be cancelled. They will be contacted by phone as soon as possible and be told if they have to come back for the additional 24-hour visits or not.

Below is an overview of the days they stay at the research center, or when they visit the research center.
Screening -> Day -28 till -2
Stay - Arrival -> Day -1
Stay - In-house stay -> Day -1 till Day 8-12**
Stay - Departure -> Day 8-12**
24-hour visits* -> Day 19
24-hour visits* -> Day 26
24-hour visits* -> Day 33
Follow-up visit -> Within 5 days after last visit

* The 24 hour visits are only needed if subjects have not yet reached the pre-defined criteria at the previous stay or visit.
** The length of the stay depends on the amount of radioactivity that has left the body.

Subjects will be given leniolisib as an oral solution of 50 milliliters (mL). After intake of the study compound, the vial will be rinsed three times with 50 mL of water, which they will also be required to drink.

Intervention

Subjects will receive 70 mg of 14C radioactively labeled leniolisib once (as an oral solution of 50 milliliters (mL)).

Study burden and risks

Blood draw
Drawing blood may be painful or cause some bruising. The use of the indwelling cannula can sometimes lead to inflammation, swelling, hardening of the vein, blood clotting, and bleeding in the environment (bruising) of the puncture site. In some individuals, a blood draw can sometimes cause pallor, nausea, seating, low heart rate, or drop in blood pressure with dizziness or fainting.

In total, we will take about 390 milliliters (mL) of blood. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time. If the investigator thinks it is necessary for the safety of a participant, extra samples might be taken for possible additional testing. If this happens, the total amount of blood drawn may be

more than the amount indicated above.

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

Coronavirus test
Samples for the coronavirus test will be taken from the back of the nose and throat using swabs. Taking the samples 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 subjects 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

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Male between 18 and 45 years of age (both inclusive) at the screening visit;
2. Subject has Dutch or English as native language
3. Body mass index between 18.5 and 30.0 kg/m2 (both inclusive);
4. Subject is judged to be in good health based on medical history, physical examination, vital sign measurements, and laboratory safety tests performed at the screening visit and prior to administration of the initial dose of study drug;
5. Subject has regular (daily) bowel movements;

Exclusion criteria

1. Employee of PRA or the Sponsor;
2. History of known sensitivity or intolerability to leniolisib or to any related compound or excipients in the formulation, or history of significant multiple and/or severe allergies (including latex allergy) or has had an anaphylactic reaction or significant intolerability to prescription or non-prescription drugs or food;
3. The radiation exposure from the previous 3 year period is over 10 mSv for subjects who had been exposed to ionizing radiation above background as a result of their work with radiation as Category A (classified) workers or as a result of research studies they might have been involved in. Clinical (therapeutic or diagnostic) exposure will not be included;
4. An occupation which requires monitoring for radiation exposure, nuclear medicine procedures or excessive x-rays within the past 12 months;
5. History of clinically significant endocrine, gastrointestinal, cardiovascular, haematological, hepatic, immunological, renal, respiratory, neoplastic or genitourinary abnormalities or diseases;

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	15-10-2021
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	14C-Leniolisib
Generic name:	Leniolisib

Ethics review

Approved WMO Date:	20-09-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-10-2021
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	EUCTR2021-001807-33-NL
CCMO	NL78964.056.21

Study results

Date completed: 26-11-2021

Results posted: 22-03-2022

First publication
14-03-2022