A Phase 0, Open-label Study to Evaluate the Release and Absorption of the Polymer-bound Form of [14C]-PL8177 in the Distal Gastrointestinal Tract Following a Single Oral Dose in Healthy Male Subjects

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

Summary

ID

NL-OMON46068

Source
ToetsingOnline

Brief title
PL8177 Microtracer study

Condition

- Gastrointestinal inflammatory conditions

Synonym
Colitis Ulcerosa, Inflammatory Bowel

Research involving

Human

Sponsors and support

Primary sponsor: Palatin Technologies, Inc.
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: Absorption, Microtracer, Open-label, PL8177

Outcome measures

Primary outcome

To demonstrate release of [14C]-PL8177 from the polymer-bound form of [14C] PL8177 in the colon after oral administration. This will be accomplished by observation of the formation of metabolite PL8435.

To confirm that the orally administered, polymer-bound form of [14C] PL8177 does not result in systemic exposure to [14C]-PL8177 and/or metabolite [14C]-PL8435 (in healthy male subjects).

To establish the relationship between an oral dose of polymer-bound [14C] PL8177 and the amount of [14C] PL8177 and/or metabolite [14C]-PL8435 in the colon.

Secondary outcome

To evaluate the safety and tolerability of the orally administered, polymer-bound form of [14C] PL8177 in healthy male subjects.

Study description

Background summary

PL8177 is a new compound that may eventually be used for the treatment of ulcerative colitis. Ulcerative colitis is an inflammatory bowel disease. It is characterized by abdominal pain, persistent diarrhea and loss of appetite. The compound PL8177 is a protein-like structure with anti-inflammatory properties as shown in studies with animals. PL8177 has recently been administered to humans via an injection under the skin (subcutaneous) to investigate how safe it is and how well it is tolerated. The Sponsor has now developed a capsule of PL8177 that can be orally administered and would thus facilitate the administration of the compound. PL8177 in capsule format is formulated in such a way that it should exclusively reach the site where action takes place, i.e., the colon (large intestine) and not reach the circulation. This will be assessed in this study.

In addition to the study compound, also a strong laxative will be administered in this study. This laxative will be given at different time points after administration of the study compound. The laxative is used to remove the contents of the colon in order to examine the level of PL8177 at certain specific time points. Without the laxative, the timing of naturally occurring defecation is highly variable. The highly variable aspect of natural defecation makes it difficult to study how much and also when PL8177 reaches the colon. In addition, PL8177 degrades in feces which complicates measurement of how much study compound actually reached the colon.

Study objective

The purpose of this study is to investigate how quickly and to what extent the new compound PL8177 is absorbed and eliminated from the body (this is called pharmacokinetics) when it is administered to healthy volunteers. PL8177 will be labelled with 14 Carbon (14C) and is thus radioactive. In this way PL8177 can be traced in blood, urine and feces. The additional radiation the volunteer will be exposed to in this study is negligible (that is, it is less than the natural background radiation during 1 month). It will also be investigated how safe PL8177 is and how well it is tolerated.

Study design

The actual study will consist of 1 period during which the subject will stay in the research center for 5 days (4 nights) if he participates in Groups 1 to 5, or for 7 days (6 nights) if he participates in Group 6.

Day 1 is the day of administration of the study compound. The subject is

expected at the research center at 14:00 h in the afternoon prior to the day of administration of the study compound (so on Day -1). He will leave the research center on Day 4 (Groups 1 to 5) or Day 6 (Group 6) of the study, depending on the group he is in.

The subject will receive a single dose of 70 microgram (µg)/33.3 kBq radiolabeled PL8177 as an oral capsule with 240 milliliters (mL) of (tap) water on Day 1. In addition to the study compound, volunteers in Groups 1 to 5 will receive a strong laxative and volunteers in Group 6 will not receive any laxative.

Intervention

The subject will receive a single dose of 70 microgram (µg)/33.3 kBq radiolabeled PL8177 as an oral capsule with 240 milliliters (mL) of (tap) water on Day 1. In addition to the study compound, volunteers in Groups 1 to 5 will receive a strong laxative and volunteers in Group 6 will not receive any laxative.

Study burden and risks

Disadvantages of participation in the study may be:
• possible side effects
• possible discomforts of the evaluations in the study

Participation in the study also means:
• time requirements
• tests you will have to do
• instructions you need to follow

Drawing blood and/or insertion of the indwelling cannula (tube in an arm vein) may be painful or cause some bruising.
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).

In this study radiolabeled PL8177 will be used. The amount of radioactivity in this dose will be approximately 18.5 kBq (kBq=kiloBecquerel, this is a unit to express the amount of radioactivity in the study compound). The average environmental background radiation in The Netherlands is approximately 2.5 mSv per year (mSv=miliSievert, this is the unit which indicates the burden on the human body thus the effect on the human body of the amount of radioactivity administered). The additional radiation you will be exposed to in this study is negligible (that is, it is less than the natural background radiation during 1 month).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1.Males of any race, between 18 and 55 years of age, inclusive, at screening. ;2.Body mass index between 18.0 and 30.0 kg/m2, inclusive, at screening.;3.In good health, determined by no clinically significant findings from medical history, physical examination, 12-lead ECG, vital sign measurements, and clinical laboratory evaluations (congenital nonhemolytic hyperbilirubinemia [eg, Gilbert*s syndrome] is not acceptable) at screening or admission (Day -1) as assessed by the Investigator (or designee).;4.Blood pressure at screening must be within the following ranges (measured with subjects in the supine position after they have rested for at least 5 minutes): systolic blood pressure >=90 and <=139 mmHg and diastolic blood pressure >=45 and <=89 mmHg. If blood pressure readings are out of range, the Investigator (or designee) may obtain 1 additional reading, so that up to 2 consecutive assessments are made within 1 hour.

Exclusion criteria

1. Employee of PRA or the Sponsor.
2. Significant history or clinical manifestation of any metabolic, allergic, dermatological, hepatic, renal, hematological, pulmonary, cardiovascular, GI, neurological, respiratory, endocrine, or psychiatric disorder, as determined by the Investigator (or designee).
3. History of irritable bowel syndrome, Crohn*s disease, or ulcerative colitis.
4. History of chronic constipation.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-09-2018
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	29-08-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	14-09-2018
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□002495□41-NL
CCMO	NL67194.056.18