A Phase 1 Study to Investigate the Absorption, Metabolism, and Excretion of PTC857 Following Oral Administration of a Single Dose of 14C-PTC857 at Steady-State Conditions in Healthy Male Volunteers.

Published: 23-07-2022
Last updated: 07-04-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neuromuscular disorders
Study type	Interventional

Summary

ID

NL-OMON51552

Source
ToetsingOnline

Brief title
AME study with 14C-PTC857.

Condition

- Neuromuscular disorders

Synonym
neurological diseases, progressive nervous system diseases

Research involving

Human

Sponsors and support

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

Intervention

Keyword: 14C, AME, PTC857

Outcome measures

Primary outcome

• To assess the rates and routes of excretion and calculate the mass balance of total radioactivity(TRA) following a single oral dose of 250 mg 14C-PTC857 containing ~3.7 MBq (100 µCi) TRA, during repeated PTC857 dosing*.

• To assess the pharmacokinetics (PK) of TRA in whole blood and plasma following a single oral dose of 250 mg 14C-PTC857 containing ~3.7 MBq (100 µCi) TRA, during repeated PTC857 dosing*.

• To assess the metabolite profiles and the distribution of 14C-PTC857 and its metabolite(s) in plasma, urine, and feces, following a single oral dose of 250 mg 14C-PTC857 containing ~3.7 MBq (100 µCi) TRA, during repeated PTC857 dosing*.

*6 days of oral dosing with 250 mg PTC857 BID before, and 7 days of oral dosing with 250 mg PTC857 BID after the 14C-PTC857 dose.

Secondary outcome

• To assess the safety and tolerability of multiple oral doses of PTC857.

Study description

Background summary

PTC857 is a new compound that is being studied f or the treatment of neurological diseases, such as amyotrophic lateral sclerosis (ALS). ALS is a progressive nervous system disease that affects nerve cells in the brain and spinal cord, causing loss of muscle control. There is currently no cure f or this disease. Treatment is aimed at reducing the symptoms.

In neurological diseases, there is an overproduction of highly reactive compounds that can damage cell structures, which can result in inf lammation in the brain. PTC857 aims to reduce overproduction of the highly reactive compounds by inhibiting a specific protein (15-lipoxygenase).

PTC857 has been given to humans bef ore in medical-scientific studies. PTC857 has also been studied extensively in the laboratory and in animals with higher doses than those that will be given in this study. No major or clinically relevant side effects were found.

In a previous clinical study (with 82 subjects), single PTC857 doses of 100 mg to 1000 mg were administered and multiple doses of 250 mg twice daily, 500 mg once daily, and 150 mg once or twice daily were administered for 14 days. In another previous clinical study (with 16 subjects), 2 single doses of 150 mg with 7 days between doses were administered. All these doses were overall well tolerated and only mild side effects were reported.

Study objective

In this study, we will investigate how quickly and to what extent the new compound PTC857 is absorbed, metabolized, and eliminated from the body. Both unlabeled and radioactively labeled PTC857 will be administered. Unlabeled PTC857 will be given multiple times to reach a steady exposure level.

Furthermore, we will investigate how safe PTC857 is and how well it is tolerated when it is used by healthy subjects.

Study design

In total the volunteer will visit the research center 3 times:
• Once for the screening.
• Once for a stay in the research center. For the study, it is necessary that the volunteer stays in the research center for at least 15 days (14 nights) and at most 22 days (21 nights). Day 1 is thef irst day when the volunteer receives the study compound. The volunteer is expected at the research center the day

before the day of first administration of the study compound, so on Day -1. The volunteer will leave the research center at the latest on Day 21.
• Once for a follow-up visit.

Intervention

The volunteer will receive multiple doses of unlabeled PTC857 and a single dose of 14C-labeled PTC857 as oral solutions using dosing syringes. The volunteer is required to drink 240 mL water after each administration to rinse the mouth.

Below is an overview of the treatments:

Day 1 up to Day 6: PTC857 twice daily 250 mg
Day 7: 14C-PTC857 in the morning 250 mg 250 mg radioactively labeled PTC857
Day 7: PTC857 in the evening 250 mg
Day 8 up to Day 14: PTC857 twice daily* 250 mg

* The evening dose on Day 14 is not needed if it appears on Day 14 that the volunteer has already reached the predetermined criteria.

On Day 7, after an overnight f ast, the volunteer will have to consume an adapted breakfast within approximately 30 minutes prior to the 14C-PTC857 dose.

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 of the puncture site. In some individuals, a blood draw can sometimes cause pallor, nausea, sweating, low heart rate, or drop in blood pressure with dizziness or fainting.
In total, we will take about 394 mL to 485 mL of blood from screening to follow-up. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken at once 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.

Fasting:
If someone has to fast for a prolonged time during the study, this may lead to symptoms such as dizziness, headache, stomach upset, or fainting.

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 gagging. When the sample is taken from the back of the nose, The volunteer may experience a stinging sensation and 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. Healthy male participants between 18 and 65 years of age, inclusive, at Screening.
2. Body mass index (BMI) between 18.0 and 32.0 kg/m2, inclusive, and total body weight >=50 kg, at Screening and Check-In.

3. Participants must understand the nature of the study and must provide a signed and dated written informed consent before the conduct of any study-related procedures.
4. Male participants sexually active with women of childbearing potential who have not had a vasectomy must agree to use a barrier method of birth control from check-In until 90 days after discharge. Males must also refrain from sperm donations during this time period.
5. In good health, determined by no clinically significant findings from medical history, physical examination, 12-lead electrocardiogram (ECG), vital sign measurements, and clinical laboratory evaluations (congenital nonhemolytic hyperbilirubinemia [eg, suspicion of Gilbert*s syndrome based on total and direct bilirubin] is not acceptable) at Screening and/or Check-In as assessed by the Investigator (or designee).
6. Willing and able to comply with the protocol.
7. History of on average 1 bowel movement per day (ie, no recent history of constipation and/or irregular bowel movement).

Exclusion criteria

1. Significant history or clinical manifestation of any metabolic, allergic, dermatologic, hepatic, renal, hematologic, pulmonary, cardiovascular, gastrointestinal, neurological, respiratory, endocrine, or psychiatric disorder, as determined by the Investigator (or designee).
2. History of significant hypersensitivity, intolerance, or allergy to sesame oil, gelatin (bovine and/or porcine), titanium dioxide, or red iron oxide, unless approved by the Investigator (or designee).
3. History of stomach or intestinal surgery or resection that would potentially alter absorption and/or excretion of orally administered drugs (uncomplicated appendectomy and hernia repair are allowed).
4. History of alcohol or drug/chemical abuse within 2 years prior to Screening, or current evidence of substance dependence or self-reported alcoholic intake >21 units per week. One unit of alcohol equals 360 mL beer, 45 mL liquor, or 150 mL wine.
5. Positive drug screen at Screening or Check-In or positive alcohol screen at Check-In.
6. Use of tobacco- or nicotine-containing products within 1 month prior to Check-In, or positive cotinine screen at Screening or Check-In. A positive cotinine screen may be repeated once.
7. QT-interval corrected using Fridericia*s formula (QTcF) >=450 msec (based on the mean of triplicate measurements taken at Screening).

Further criteria apply, see 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):	18-08-2022
Enrollment:	8
Type:	Actual

Ethics review

Approved WMO Date:	23-07-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	12-08-2022
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	EUCTR2022-002302-25-NL
CCMO	NL82099.056.22