Single-center, open-label study with 14C-radiolabeled cenerimod to investigate the mass balance, pharmacokinetics, and metabolism following single oral administration to healthy male subjects

Published: 05-09-2016
Last updated: 14-04-2024

The purpose of the study is to investigate how quickly and to what extent cenerimod is absorbed, distributed, metabolized (broken down) and eliminated from the body (this is called pharmacokinetics).

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

Summary

ID

NL-OMON42951

Source
ToetsingOnline

Brief title
Mass balance 14C-radiolabeled cenerimod in healthy volunteers

Condition

- Autoimmune disorders

Synonym
Autoimmune disorder, SLE

Research involving
Human

Sponsors and support

Primary sponsor: Actelion Pharmaceuticals Ltd.
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: 14C ADME, Immune disorder, PK, safety

Outcome measures

Primary outcome

- Change from baseline to each time point of measurement in vital signs (supine BP and pulse rate) after study treatment administration.

- Change from baseline to each time point of measurement in ECG variables: HR, and the intervals: PR, QRS, QT, QTc calculated according to Bazett*s correction (QTcB), and QTc calculated according to Fridericia*s correction (QTcF) after study treatment administration.

- Change from baseline to each time point of measurement in clinical laboratory variables after study treatment administration.

- Change from baseline to EOS in body weight.

- Treatment-emergent ECG abnormalities from study treatment administration up to EOS.

- Treatment-emergent AEs from study treatment administration up to EOS.

- Treatment-emergent SAEs from study treatment administration up to EOS.

- Mass balance (Cumulative excretion of radioactivity in urine, feces, and expired air (if applicable))

- PK of 14C radioactivity in whole blood and plasma.

- PK of cenerimod and its metabolites in plasma.

- Metabolic profiling (profiles, identification, and quantification of

cenerimod metabolites in plasma, urine, and feces).

Secondary outcome

Not applicable

Study description

Background summary

Cenerimod (also known as ACT-334441) is a new investigational compound that may eventually be used for the treatment of several autoimmune disorders such as systemic lupus erythematosus (SLE) or disorders ensuing from organ transplantation. The immune system is normally the first line of defense against illness and bad health. However, sometimes immune systems function abnormally due to deficiencies and disorders where the body either loses its natural immunity or the immune system turns against the body it is supposed to protect: these are called autoimmune diseases.

The study compound reduces the amount of specific types of white blood cells (T and B lymphocytes) in the blood, and thus at the sites of inflammation where they would usually act, by modulating a specific receptor (sphingosine 1-phosphate receptor 1, S1P1) involved in the release of white blood cells in the system. Cenerimod is in development and is not registered as a drug, but has been given to humans before.

Study objective

The purpose of the study is to investigate how quickly and to what extent cenerimod is absorbed, distributed, metabolized (broken down) and eliminated from the body (this is called pharmacokinetics).

Study design

The study will consist of 1 period during which the volunteer will stay in the clinical research center in Groningen for 23 days (22 nights).

The volunteer will leave the clinical research center in the morning of Day 22.

The volunteer may be required to come back to the clinical research center in Groningen for a maximum of 7 additional visits (extended observation period) which will be 24 hours for each visit.

The participation of the volunteer in the extended observation period will depend on the amount of radioactivity left in his urine, feces, and expired air at the end of the in-clinic stay (Day 22). This amount of radioactivity will be measured after Day 22 and before the first planned 24-hour stay of the extended observation period.
- If the radioactivity recovered during these 22 days meets the pre-defined stopping criteria for continuing participating in the study, the volunteer will not be required to come back to the clinical research center for the extended observation period, but you will be asked to come back for the post-study screening visit (see below).
- If the radioactivity recovered during these 22 days does not meet the pre-defined stopping criteria, the volunteer will be required to come back to the clinical research center for the extended observation period. These visits are planned on Days 28, 35, 42, 49, 63, 77, and 98. The volunteer will leave after each 24-hour stay (respectively on Days 29, 36, 43, 50, 64, 78 and 99). The participation of the volunteer in the extended observation period will end as soon as the radioactivity recovery meets the pre-defined stopping criteria (this means that the volunteer may not be required to come to the clinical research center 7 times). The volunteer will then be asked to come back only for the post-study screening visit.

Intervention

The volunteer will receive a single dose of 2 mg/3.7 MBq radiolabeled cenerimod as an oral solution of 25 mL.

Study burden and risks

In this study radiolabeled cenerimod will be used. The amount of radioactivity in this dose will be approximately 3.7 MBq (MBq = megaBecquerel, this is a unit to express the amount of radioactivity in the study compound). The average environmental background radiation burden in The Netherlands is approximately 2 mSv per year (mSv = milliSievert, this unit indicates the burden on the human body; thus the effect on the human body of the amount of radioactivity administered). The additional radiation burden in this study due to the administration of approximately 3.7 MBq radiolabeled cenerimod is calculated to be 0.26 mSv. This is approximately 13% of the average annual radiation burden in the Netherlands.

All potential drugs cause adverse effects; the extent to which this occurs differs. Cenerimod has been given to 64 healthy volunteers as single doses (up to 25 mg) and as multiple doses for 35 days (up to 4 mg once daily) as well as to 36 patients (up to 2 mg once daily) for 12 weeks. The most frequently observed adverse effects in man were: decreases of blood pressure and pulse rate with a maximal effect between 4 and 8 hours and which resolved within 12 hours after administration, a transient elevation of liver enzymes when the

study compound was given as multiple dose, and one event of mild dyspnea (shortness of breath) which also occurred after multiple dosing. One healthy volunteer suffered from a severe circulatory collapse after a single dose of 25 mg, which was treated using the standard care for circulatory shock. In this study a dose of 2 mg will be given. subjects should be aware that the aforementioned adverse effects and possibly other, still unknown adverse effects, may occur during the study. However, with the dose used in this study no serious adverse effects are expected. Potential adverse "effects" of catheter insertion, venipuncture and ECG electrodes are infection of injection site or rash. No risk of radiation illness are expected with he current radiation burden.

Contacts

Public
Actelion Pharmaceuticals Ltd.

Gewerbestrasse 16
Allschwil CH-4123
CH
Scientific
Actelion Pharmaceuticals Ltd.

Gewerbestrasse 16
Allschwil CH-4123
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

healthy male subjects
45-65 yrs, inclusive
BMI : 18.0-30.0 kg/m2, inclusive
SBP 100-145 mmHg, DBP 50-90 mmHg, and heart rate 55-90 bpm
Signed informed consent in a language understandable to
the subject prior to any study-mandated procedure.
No clinically significant findings on the physical
examination at screening.
Regular (daily) defecation pattern.

Exclusion criteria

No cardiac significant disorders, no asthma, no chronic obstructive pulmonary disease, no tuberculosis. No HIV, hepatitis B and C. No immunosuppressive treatment within 6 weeks. No other investigational drug within 3 months or not more than 4 studies with investigational drugs within 1 year. No study with a radiation burden of >0.1 mSv and =<1 mSv within 1 year (add 1 msv per year).

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):	19-09-2016
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cenerimod
Generic name:	N/A

Ethics review

Approved WMO Date:	05-09-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-09-2016
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	EUCTR2016-000192-25-NL
CCMO	NL58500.056.16