Phase I, Open Label, Single Dose Study to Determine the Pharmacokinetics, Metabolism, and Excretion of [14C]-Evobrutinib in Healthy Participants

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

Summary

ID

NL-OMON46168

Source
ToetsingOnline

Brief title
Human ADME of 14C-Evobrutinib

Condition

- Autoimmune disorders

Synonym
Multiple Sclerosis, Rheumatoid Arthritis

Research involving
Human

Sponsors and support

Primary sponsor: PRA Health Sciences

Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: ADME, Evobrutinib, Open-label, Pharmacokinetics

Outcome measures

Primary outcome

To determine the rates and routes of excretion of total radioactivity,

including mass balance of total drug-related radioactivity in urine and feces

To determine the PK of total radioactivity in blood and plasma

To characterize the plasma PK of evobrutinib

Secondary outcome

To assess the safety and tolerability of a single oral 75 mg dose of

[14C]-evobrutinib administered to healthy male participants

Study description

Background summary

Evobrutinib is a new compound that may eventually be used for the treatment of autoimmune diseases (eg. multiple sclerosis (MS), rheumatoid arthritis (RA), and systemic lupus erythematosus (SLE). Evobrutinib inhibits the response of a certain type of immsystune cell: B-cells, which play an important role in diseases such as MS, RA, and SLE.

Study objective

The purpose of this study is to investigate how quickly and to what extent evobrutinib is absorbed, distributed, metabolized (broken down) and eliminated from the body (this is called pharmacokinetics). Part of the evobrutinib will be labelled with 14 Carbon (14C) and is thus radioactive. In this way

evobrutinib can be traced in blood, urine, and feces and it can be measured when the radioactivity levels in blood, urine and feces reaches the level below a pre-defined threshold.

Study design

The actual study will consist of one period during which the subject will stay in the clinical research center for 9 days (8 nights). If the level of radioactivity in urine and feces is above a pre-defined threshold, this may be extended up to 6 days (and 6 nights) more during which the subject will stay in the clinical research center, as is described below.

Day 1 is the day of administration of the study compound. The subjects will leave the research center on Day 8 up to 14 of the study.

The subject should be aware that when the radioactivity levels are still above the pre-defined levels on Day 14, he has to return to the clinical research center on Day 17, 21, 28 and 35 until the radioactivity levels in urine and feces are below the pre-defined levels.

Intervention

Evobrutinib will be given as an oral solution of 30 milliliters (mL) which will be administered orally in a syringe after an overnight fast (no eating for at least 10 hours). After administration of the study compound on Day 1, the subject will be required to fast for an additional 4 hours. Then he will be served lunch. Drinking of water is allowed except for from 1 hour before administration of the study compound until 1 hour after administration of the study compound.

Study burden and risks

The study compound may cause side effects.

An approximate number of 361 participants (consisting of 183 healthy volunteers and 178 patients with MS, RA, and SLE) have been exposed to evobrutinib. Evobrutinib was well tolerated and no relevant adverse events were reported.

Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising.

In total, about 475 milliliters (mL) blood will be taken per 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 (small, plastic patches) will be pasted at

specific locations on the volunteers arms and legs. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Exposure to radiation
This study involves the use of radioactive markers. The amount of radioactivity will be approximately 3.6 MBq. The average environmental background radiation burden in The Netherlands is approximately 2.5 mSv per year. The amount of radiation burden in this study is calculated to be 0,02 mSv. This is below the limit of 1.0 mSv as determined by the Dutch regulation on radiation protection and is considered acceptable.

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. 18-55 years of age at the time of signing the informed consent.
2. Are overtly healthy as determined by medical evaluation, including medical history, physical examination, laboratory tests, and cardiac monitoring.
3. Have a body weight within 50.0 and 120.0 kg (inclusive) and Body Mass Index (BMI) within the range 19.0 - 30.0 kg/m2 (inclusive).
4. Male

Exclusion criteria

1. History or presence of clinically relevant respiratory, gastrointestinal, renal, hepatic, hematological, lymphatic, neurological, cardiovascular, psychiatric, musculoskeletal, genitourinary, immunological, dermatological, connective tissue diseases or disorders.
2. Prior history of cholecystectomy or splenectomy, and any clinically relevant surgery within 6 months prior to screening.
3. Any surgical or medical condition which might significantly alter the absorption, distribution, metabolism, or excretion of drugs, or which may jeopardize the subject in case of participation in the study.
4. History of any malignancy.

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):	30-10-2018
Enrollment:	6
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	01-10-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-10-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-01-2019
Application type:	Amendment
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	EUCTR2018-003371-35-NL
CCMO	NL67350.056.18