An Open-label, Randomized, Crossover, Single Ascending Dose Pharmacokinetic Study of Continuous Subcutaneous Infusion of Lenalidomide Compared with Revlimid® Oral Capsules in Healthy Adult Male Subjects

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Ethical review	Approved WMO
Status	Completed
Health condition type	Lymphomas NEC
Study type	Interventional

Summary

ID

NL-OMON50544

Source
ToetsingOnline

Brief title
Lenalidomide single ascending dose study in healthy male subjects

Condition

- Lymphomas NEC

Synonym
blood cancer, multiple myeloma

Research involving

Human

Sponsors and support

Primary sponsor: Starton Therapeutics
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Lenalidomide, Revlimid®, SAD

Outcome measures

Primary outcome

To assess and compare the pharmacokinetics (PK) of a 24-hour continuous subcutaneous (SC) infusion of lenalidomide versus lenalidomide oral capsules (Revlimid) in healthy adult male subjects at 3 escalating infusion rates and reference oral doses.

Secondary outcome

- To evaluate the relative bioavailability of a 24-hour continuous SC infusion of lenalidomide versus Revlimid oral capsules in healthy adult male subjects

- To evaluate the safety and tolerability of a 24-hour continuous SC infusion of lenalidomide versus Revlimid oral capsules in healthy adult male subjects

Study description

Background summary

Lenalidomide is a compound that is used for the treatment of multiple myeloma, a type of blood cancer. The exact mechanism of action of lenalidomide is still being studied. Researchers know that lenalidomide targets myeloma cells by binding to a specific protein called cereblon. This protein is involved in regulating the activity of proteins related to cell adhesion, metabolism, and cell division. The binding of lenalidomide to cereblon triggers the death of cancer cells as it affects the above processes. Lenalidomide also activates a

type of immune cell called a T cell. In addition, lenalidomide also inhibits the formation of blood vessels in the vicinity of a tumor, affecting the blood supply needed to fuel the tumor*s growth.

Study objective

The purpose of this study is to investigate how quickly and to what extend lenalidomide is absorbed and eliminated from the body (this is called pharmacokinetics). In this study the pharmacokinetics will be compared when lenalidomide is administered subcutaneous (under the skin) for a period of 24-hours continuously versus an oral dose with capsules.

We also investigate how safe the compound lenalidomide is and how well it is tolerated when it is used by healthy participants.

Lenalidomide is not a new compound; it is already being used by patients. Lenalidomide is already available on the market as an oral capsule under the name Revlimid.

Study design

For the study it is necessary that subjects stay in the research center for 1 period of 6 days (5 nights). This will be followed by 1 short visit to the research center. This short visit will take place between 3 and 7 days after they leave the research center. In addition, we will call 1 time approximately 28 days after they leave the research center. They will then be asked about your health.

Day 1 is the first day when they receive the study compound. They will leave the research center on Day 5 of the study.

Below is an overview of the days you stay at the research center, or when they visit the research center.

Screening -> Day -21 up to Day -1

Treatment Period - Arrival -> Day -1
Treatment Period - In-house stay -> Day -1 up to Day 5
Treatment Period - Departure -> Day 5

Follow-up - Visit -> 3 to 7 days after departure
Follow-up - Phone call -> Day 33 or Day 34

How will the study compound be administered?
Subjects will be given lenalidomide as an infusion (subcutaneous) under the

skin for 24 hours and as oral capsule(s) with 240 milliliters (mL) of water.
For the subcutaneous administration, you will have a cannula inserted under the skin on your abdomen with a pump.

They will receive each administration once, so 2 administrations in total. The order in which these administrations are given are shown in the table below. They will be randomly assigned to Administration Sequence TR or RT.

Sequence | First administration (Day 1) | Second administration (Day 3)
Sequence TR | A 24-hour subcutaneous infusion, Administration T (Test Administration) | Oral capsule(s), Administration R (Reference Administration)
Sequence RT | Oral capsule(s), Administration R | A 24-hour subcutaneous infusion, Administration T

During the first 4 hours after administration of the oral capsule(s) they will not be allowed to lie down (except when instructed to do so by one of the investigators), as this may influence the uptake of the study compound.

One of the investigators will inspect hands and mouth after the intake of the oral capsule(s). This it to check if they have taken the study compound.

Intervention

The dose for the next group will only be increased if the lower dose of the previous group was found to be well tolerated and in case of no objection by the Medical Research Ethics Committee. The study will be discontinued if, in the opinion of the investigators, unacceptable side effects appear.

The planned dose levels for the study are as follows:

Group 1 Day 1: once Lenalidomide 2.4 mg/day (100 µg/hour) subcutaneous infusion or lenalidomide 5 mg oral capsule (1x5 mg)
Group 1 Day 3: once Lenalidomide 2.4 mg/day (100 µg/hour) subcutaneous infusion or lenalidomide 5 mg oral capsule (1x5 mg)

Group 2 Day 1: once Lenalidomide 4.8 mg/day (200 µg/hour) subcutaneous infusion or lenalidomide 10 mg oral capsules (2x5 mg)
Group 2 Day 3: once Lenalidomide 4.8 mg/day (200 µg/hour) subcutaneous infusion or lenalidomide 10 mg oral capsules (2x5 mg)

Group 3 Day 1: once Lenalidomide 9.6 mg/day (400 µg/hour) subcutaneous infusion or lenalidomide 20 mg oral capsules (4x5 mg)
Group 3 Day 3: once Lenalidomide 9.6 mg/day (400 µg/hour) subcutaneous infusion or lenalidomide 20 mg oral capsules (4x5 mg)

Study burden and risks

Blood draw
Drawing blood may be painful or cause some bruising. The use of the indwelling cannula (a tube in a vein in the arm) 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 290 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 (small, plastic patches) 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 them 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

Public
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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Gender : Male.
2. Age : 18 years to 55 years, inclusive, at screening.
3. Body mass index (BMI) : 18.0 kg/m2 to 32.0 kg/m2, inclusive at screening.
4. Weight : 50 kg to 110 kg, inclusive, at screening.
5. Status : Healthy subjects.
6. Creatinine clearance >61 mL/min (by Chronic Kidney Disease Epidemiology Collaboration).

Exclusion criteria

1. Employee of PRA or the sponsor.
2. History of relevant drug and/or food allergies.
3. History of alcohol abuse or drug addiction (including soft drugs like cannabis products).
4. Positive drug and alcohol screen (opiates, methadone, cocaine, amphetamines [including ecstasy], cannabinoids, barbiturates, benzodiazepines, tricyclic antidepressants, and alcohol) at screening and admission to the clinical research center.
5. Average intake of more than 24 units of alcohol per week (1 unit of alcohol equals approximately 250 mL of beer, 100 mL of wine, or 35 mL of spirits).
6. Positive screen for hepatitis B surface antigen (HBsAg), anti-hepatitis C virus (HCV) antibodies, or anti-human immunodeficiency virus (HIV) 1 and 2 antibodies.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	30-03-2022
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Revlimid
Generic name:	Lenalidomide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	21-10-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-01-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-04-2022
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-04-2022
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	EUCTR2021-004607-41-NL
CCMO	NL79355.056.21

Study results

Date completed:	04-07-2022
Results posted:	06-12-2022

First publication
17-11-2022