A phase 1 open-label study to characterize the metabolism and excretion of a single dose of radiolabeled AL-335 administered in combination with Odalasvir and Simeprevir and administered alone in healthy male subjects

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON44638

Source
ToetsingOnline

Brief title
64294178HPC1011 ADME study

Condition

- Viral infectious disorders

Synonym
chronic hepatitis C infection.

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag International NV
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: AL-335, chronic hepatitis C infection

Outcome measures

Primary outcome

The primary objective of this study is to characterize the metabolic pathways of AL-335 and the routes of excretion of the compound and its metabolites, after single oral dosing of AL-335 in combination with ODV and SMV and after single oral dosing of AL-335 alone, in healthy male subjects.

Secondary outcome

The secondary objective of this study is to determine the short-term pharmacokinetics (PK), safety, and tolerability of a single oral dose of radiolabeled (14C-)AL-335 administered in combination with ODV and SMV and administered alone, in healthy male subjects.

Study description

Background summary

AL-335 is a new investigational compound that may eventually be used for the treatment of chronic hepatitis C infection. AL-335 works by inhibiting the replication of the hepatitis C virus. AL-335 is being developed for use in combination with odalasvir and simeprevir. These compounds have a similar mechanism of action, but act on a different protein involved in the replication of the virus. It is hypothesised that the 3 compounds will complement each

other and may thereby reduce the risk of resistance against these compounds.

Odalasvir and AL-335 are not registered as a drug but have been given to humans before. Simeprevir is no new drug; it is already available in the market under several dosages.

Study objective

The purpose of the study is to investigate how quickly and to what extent AL-335 is absorbed, distributed, metabolized (broken down) and eliminated from the body (this is called pharmacokinetics). AL-335 to be administered will be labeled with 14-Carbon (14C) and is thus radioactive (also called radiolabeled). This radioactive version is called 14C-AL-335 and can be traced in blood, urine, feces and your breath. It will also be investigated to what extent AL-335 is tolerated when administered alone or in combination with odalasvir and simeprevir. In addition, the influence of genetic factors on the pharmacokinetics of AL-335 will be explored.

This study will be performed in 10 healthy male volunteers, divided over 2 groups (Group 1 and Group 2).

Study design

The actual study will consist of 1 period during which the volunteers will stay in the clinical research center in Groningen (location Martini Hospital). They are expected at the clinical research center at 14:00 h in the afternoon of Day -1, one day prior to the (first) day of administration of the study compound (Day 1). They will be required not to have consumed any food or drinks during the 4 hours prior to arrival in the clinical research center (with the exception of water).

If they are assigned to Group 1, they will stay in the clinical research center for 20 to 25 days (19 to 24 nights). They will leave the clinical research center between Day 19 and Day 24, depending on the amount of radioactivity found in their blood, expired air and the excreted urine and feces. In order to measure the amount of radioactivity in urine and feces, you will be required to collect all your urine and feces from Day 12 until discharge.
If you are assigned to Group 2, you will stay in the clinical research center for 7 to 12 days (6 to 11 nights). You will leave the clinical research center between Day 6 and Day 11, depending on the amount of radioactivity found in your blood, expired air and your excreted urine and feces. In order to measure the amount of radioactivity in urine and feces, they will be required to collect all the urine and feces throughout the stay in the clinic. They are also required to collect a feces sample at home prior to admission to the clinical research center on Day -1.

The volunteer should be aware that when radioactivity levels are still above pre-defined levels at discharge on Day 24 (Group 1) or Day 11 (Group 2), or if they were not able to produce at least 5 feces samples since administration of AL-335, they may have to continue the collection of urine and/or feces samples at home. They will be asked to return these samples to the clinical research center every other day until the radioactivity levels are below the pre-defined levels. They will receive instructions on how to deliver these samples to the clinical research center.
A post-study screening will take place 10 to 14 days after the last intake of study drug. If needed in case of adverse events, they may need to return for an additional post-study screening 30 to 35 days after the last intake of study drug. The appointment for the post-study screening(s) will be made as soon as it is known when the study will end for the volunteer.
The participation to the entire study, from the pre-study screening until the post-study screening (excluding an additional post-study screening or any other visits), will be up to 59 days (Group 1) or 35 days (Group 2).

If the volunteers are assigned to Group 1, they will receive once daily treatment with odalasvir alone (Days 1-7) or in combination with simeprevir (Days 8-13; see Table 1 above). On Day 14 they will once receive radiolabeled AL-335, followed by a dose of odalasvir and simeprevir; the investigational compounds will be administered within 10 minutes after completion of breakfast in the morning. Thereafter, the once daily treatment with odalasvir and simeprevir will be continued on Days 15 and 16.

If they are assigned to Group 2, they will receive radiolabeled AL-335 once, within 10 minutes after completion of a breakfast on Day 1.
On the day of AL-335 administration (Day 14 in Group 1 or Day 1 in Group 2), breakfast will be served approximately 30 minutes before administration of AL-335 and after an overnight fast (no eating or drinking) of at least 10 hours. During fasting, they are allowed to drink water with the exception of 2 hours before and after administration of the study compound (except for the fluids served with breakfast). Fasting will continue until 4 hours after administration of the study compound. Then they will receive a standardized lunch. From approximately 10 hours after administration of the study compound, they are allowed to resume their normal diet (taking into consideration the restrictions mentioned in the section *Are there any rules for volunteers?* below). Except for that night during which they will need to fast one more time for at least 10 hours until breakfast will be served the next day (on Day 15 in Group 1, or Day 2 in Group 2).

The volunteers will also be required to fast for at least 4 hours before they will leave the clinical research center, which will be ultimately on Day 24 in Group 1 or Day 11 in Group 2.

Intervention

Group 1;
Days 1-7; 25 mg odalasvir; once daily
Days 8-13; 25 mg odalasvir + 75 mg simeprevir, once daily
Day 14; 25 mg odalasvir + 75 mg simeprevir + 800 mg radiolabeled AL-335; once
Days 15-16; 25 mg odalasvir + 75 mg simeprevir; once daily

Group 2; Day 1; 800 mg radiolabeled AL-335; once

Study burden and risks

Infection/pain, minor bleedings, bruises, possibly an infection.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

healthy male subjects
18 - 55 years of age
BMI 18 - 30 kilograms/meter2
weight at least 50 kilograms
non smokers

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	10
Type:	Anticipated

Ethics review

Approved WMO

Date:	19-07-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	21-07-2017
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	EUCTR2017-002015-34-NL
CCMO	NL62526.056.17