A single-center, open-label study to investigate the absorption, distribution, metabolism and excretion (ADME) of HDM201 (Siremadlin) after a single oral dose of 25 mg [14C]HDM201 in healthy subjects

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON49451

Source
ToetsingOnline

Brief title
[14C]HDM201

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
Cancer

Research involving

Human

Sponsors and support

Primary sponsor: Novartis Pharma AG
Source(s) of monetary or material Support: Pharmaceutical/Biotechnological Industry

Intervention

Keyword: a single dose of [14C]HDM201, Human ADME study, pharmacokinetics

Outcome measures

Primary outcome

To determine the routes and rates of excretion of [14C]HDM201 related

radioactivity, including mass balance of total drug-related radioactivity in

urine,

feces, and excretion of radioactivity via expired air, following the

administration of a single 25 mg oral dose of [14C]HDM201 in healthy subjects.

To determine the PK of total radioactivity in blood and plasma.

To characterize the single dose plasma PK of HDM201 and/or known key

metabolite(s) if applicable.

Secondary outcome

To evaluate the safety and tolerability of a single 25 mg oral dose of

[14C]HDM201 administered in healthy male and/or female subjects.

Study description

Background summary

HDM201 is a new compound that may eventually be used for the treatment of cancer. p53 is a protein that controls the expression of a large number of genes involved in DNA repair, apoptosis (programmed cell death), and stopping the cell cycle. Approximately half of all cancers have inactivated p53 which is caused by a mutation (change in DNA). HDM201 leads to p53 activation which leads to an increase in p53 and thereby HDM201 can inhibit the cell growth. The effect of HDM201 on p53 is seen as a way to treat various types of cancers.

Study objective

The purpose of this study is to investigate how quickly and to what extent HDM201 is absorbed, broken down and eliminated from the body (this is called pharmacokinetics). HDM201 will be labeled with 14-carbon (14C) and is thus radioactive. In this way HDM201 can be traced in blood, urine, feces, and expired air. HDM201 has been administered to humans before. It has also been previously tested in the laboratory and on animals.

It will also be investigated how safe the new compound HDM201 is and how well it is tolerated when it is administered to healthy volunteers.

Furthermore, the effect of your genetic information on your body*s response to HDM201 will be investigated (this is called pharmacogenetics). This part of the study is optional.

Study design

The volunteer will once receive 25 milligram (mg) of 14C-labeled HDM201 as an oral capsule with 240 milliliters (mL) of (tap) water. This amount contains 3.7 MBq (100 µCi) radioactivity. One of the investigators will inspect the volunteers hands and mouth after intake of the study treatment, to check whether you have actually taken the study treatment. All subjects will receive the same study treatment.

Intervention

The volunteer will once receive 25 milligram (mg) of 14C-labeled HDM201 as an oral capsule with 240 milliliters (mL) of (tap) water. This amount contains 3.7 MBq (100 µCi) radioactivity.

Study burden and risks

The study treatment may cause side effects.

So far, a total of 383 subjects have been treated with HDM201 (331 patients and 52 healthy volunteers) in 7 completed or ongoing studies (6 studies with patients and 1 study with healthy volunteers) as monotherapy or together with

other drugs.

The most common side effects considered related to the study treatment were:
- Hematological (blood related) side effects:
- Anemia (decrease in the amount of red blood cells or hemoglobin in the blood, or a lowered ability of the blood to carry oxygen)
- Leukopenia (decrease in the amount of white blood cells in the blood) including neutropenia (abnormally low concentration of neutrophils [a type of white blood cells] in the blood)
- Thrombocytopenia (abnormally low concentration of thrombocytes, also known as platelets, in the blood)
- Gastrointestinal (stomach and gut related) side effects:
- Nausea
- Vomiting
- Diarrhea
- Decreased appetite
- Fatigue
- Rash

The side effects were overall manageable and generally mild to moderate in severity.

The study treatment may also have side effects that are still unknown.

Possible discomforts due to procedures
Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising.

In total, we will take up to 500 mL of blood from the 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 will be pasted at specific locations on your arms, chest and legs. Prolonged use of these electrodes can cause skin irritation.

A sample for the coronavirus test will be taken from the back of the nose and throat using a swab. Taking the sample only takes a few seconds, but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of your throat may cause the volunteer to gag. When the sample is taken from the back of the nose, the volunteer may experience a stinging sensation and the eyes may become watery.

Contacts

Public
Novartis Pharma AG

Lichtstrasse 35
Basel 4056
CH
Scientific
Novartis Pharma AG

Lichtstrasse 35
Basel 4056
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy males and/or females age 18 to 54 years included
Weighy at least 55 kg and no more than 120 kg
BMI 18.0 - 30 kg/m2

Exclusion criteria

Females of childbearing potential (WOCBP).
Exposure to radiation at a level of 0.1 to1.0 mSv over the past year, 1.1 to 2.0 mSv over the past 2 years, or 2.1 to 3.0 mSv over the past 3 years, etc., e.g., due to systemic administration of radioactive substances, or to external irradiation (e.g., by x-rays) for diagnostic,

therapeutic, job-related, or research purposes.
Use of other investigational drugs within 5 half-lives, or within 6 months (in case of therapeutics with expected long half-lives such as immunoglobulin G antibodies), or within 30 days prior to dosing (for
small molecule drugs with daily dosing scheme), or longer if required by local regulations.
Any surgical or medical condition which might significantly alter the ADME of drugs, or which may jeopardize the subject in case of participation in the study.
Has absence of regular defecation pattern (subjects with a mean defecation frequency of less than once per 2 days or chronic diarrhea).
Positive for Hepatitis B surface antigen (HBsAg), Hepatitis C virus (HCV), and/or human immunodeficiency virus (HIV).
Smokers (use of tobacco/nicotine products in the previous 3 months).
History or presence of clinically significant ECG abnormalities or a family history or presence of prolonged QT-interval syndrome.

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):	13-07-2020
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	HDM201
Generic name:	N/A

Ethics review

Approved WMO Date:	13-03-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-03-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-07-2020
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	EUCTR2019-000472-42-NL
CCMO	NL72933.056.20