An open-label, single center study to determine the absorption, distribution, metabolism, and excretion (ADME) of a single oral dose of [14C]LDE225 (74 kBq) to healthy male subjects

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Primary:To evaluate the extent of absorption of unchanged drug and total radioactivity from available blood and plasma exposure, urinary, and fecal excretion dataTo determine the mass balance, routes of excretion and extent of metabolism in humansTo...

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

Summary

ID

NL-OMON37376

Source
ToetsingOnline

Brief title
LDE225 ADME study

Condition

- Other condition

Synonym
malignant tumors

Health condition

kwaadaardige tumoren

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: ADME, LDE225, malignant tumors

Outcome measures

Primary outcome

Pharmacokinetics: blood and plasma concentrations of radioactivity, plasma

concentrations of LDE255 and LGE899,

metabolite patterns in plasma, excretion of radioactivity, metabolite patterns

in urine and feces, metabolite identity,

absorption of LDE255

Pharmacogenetics

Safety: adverse events, vital signs, ECG, clinical laboratory and physical

examination.

Secondary outcome

n/a

Study description

Background summary

LDE225 is a new investigational compound that may eventually be used for the treatment of malignant tumors. LDE225 inhibits the activity of Smo that is involved in the development of a wide range of malignancies. LDE225 is not

registered as a drug but has been given to humans before.

Study objective

Primary:
To evaluate the extent of absorption of unchanged drug and total radioactivity from available blood and plasma exposure, urinary, and fecal excretion data
To determine the mass balance, routes of excretion and extent of metabolism in humans
To determine the pharmacokinetic parameters of total radioactivity, LDE225, LGE899, and any other major metabolites as feasible

Secundary:
To generate metabolite profiles in plasma, urine and feces using accelerator mass spectrometry, to identify the major metabolites, and to elucidate the major metabolic pathways
To evaluate the systemic exposure to the major metabolites in plasma and excreta, as feasible using reference standards and metabolite profiles
To evaluate the safety and tolerability of a single oral dose of 800 mg LDE225 plus tracer amount of 14C-radioactivity (74 KBq) to healthy male volunteers

Study design

This ADME study aims to provide understanding of absorption, pharmacokinetics, distribution, metabolism and elimination
of 800 mg of LDE225+tracer amount of 14C (74 kBq) after a single oral dose in healthy male subjects.

Procedures and assessments:
Screening and follow-up: physical examination, vital signs (weight, body temperature, blood pressure), pulse rate, clinical laboratory (serum chemistry, haematology and urinalysis), and ECG
Only at screening: demography, medical history, prior and concomitant medication, HBsAg, anti HCV, anti-HIV *, alcohol and drug screen, body height
Repeated at entry op Day -1: alcohol and drug screen, physical examination, vital signs (weight, body temperature, blood pressure), pulse rate, clinical laboratory (serum chemistry, haematology and urinalysis), ECG

Blood samples:
For PK LDE225, total radioactivity and metabolite profiles: pre-dose and until 85 days post-dose, with a possible extension up to Day 183 post-dose, maximally
Pharmacogenetics: On Day -1

Urine collection:
For PK LDE225, total radioactivity and metabolite profiles: Day 1-22 and during the 24 hr visits (Day 28-85 with a possible extension up to Day 183 maximally)

Feces collection:
For PK LDE225, total radioactivity and metabolite profiles: Day 1-22 and during the 24 hr visits (Day 28-85 with a possible extension up to Day 183 maximally)

Vomitus collection:
For total radioactivity: up to 72 hrs post-dose.

Intervention

One oral dose of 800 mg LDE225 plus tracer amount of radioactivity (74 kBq) made up of 16 50 mg capsules.

Study burden and risks

The most important adverse events of LDE225 reported in previous clinical studies were: nausea, decreased sense of taste, decreased appetite, fatigue, vomiting, muscle pain, loss of hair, decreased weight, diarrhea, headache, lack or loss of strength and energy, inflammation of the muscle, and pain in extremity.

In this study radio labeled LDE225 will be used. The amount of radioactivity in this dose will be 74 KBq (KBq = kiloBecquerel, this is a unit to express the amount of radioactivity in the study drug). The average environmental background radiation burden in The Netherlands is approximately 2 mSv per year (mSv = miliSievert, this is the unit which 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 74 KBq 14C-labeled LDE225 is calculated to be negligible (that is, less than the natural background radiation in one month).

Registration of adverse effects: During the entire investigation all adverse effects will be documented.

Blood draw, indwelling canula: During this study approximately 700 ml of blood will be drawn. It is anticipated that on Day -1 an indwelling canula will be inserted for most of the blood sampling on Day 1 and 2. On the other days during this study, blood will be drawn by direct puncture of the vein.

Collection of urine: A pre-dose urine sample of approximately 100 ml will be collected at anytime before administration of LDE225 on either Day -1 or Day 1. Further 24-hour urine samples will be collected on Day 1 until Day 22 and on the 24-hour visits (Day 28-85 with a possible extension up to Day 183, maximally).

Collection of feces: One stool sample will be collected at any time before administration of LDE225 (within 48 hours prior to dosing). Further all feces

will be collected completely on Day 1 until Day 22 and on the 24-hour visits (Day 28-85 with a possible extension up to Day 183, maximally)

Collection of vomitus: If a participant vomits within 72 hours following LDE225 dosing, the vomitus will be collected and analyzed to confirm the level of radioactivity.

Heart trace (ECG*s): ECG*s will be made regularly.

Blood sample for DNA tests: On Day -1 a blood sample will be taken for possible DNA tests.

Contacts

Public
Novartis

Fabrikstrasse 2
Basel 4056
CH
Scientific
Novartis

Fabrikstrasse 2
Basel 4056
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy male volunteers
18-55 years, inclusive
BMI: 18.0 * 32.9 kg/m2, inclusive
non-smoking

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:	Recruitment stopped
Start date (anticipated):	28-06-2012
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO

Date:	13-06-2012
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-06-2012
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	EUCTR2011-005388-26-NL
CCMO	NL39935.056.12