An open-label, non-randomized, single-center, Phase I trial to investigate the mass balance and the metabolite profile of cilengitide in five healthy subjects

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Primary:- To evaluate the mass balance of total 14C radioactivity, i.e. PK parameters of cilengitide and potential metabolites,- To quantify the route(s) of excretion in urine (14C and cilengitide) and feces (14C), - To profile potential metabolites...

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

Summary

ID

NL-OMON37147

Source
ToetsingOnline

Brief title
Cilengitide mass balance study

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
angiogenesis, cancer

Research involving
Human

Sponsors and support

Primary sponsor: Merck
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Cancer, Cilengitide, Mass balance

Outcome measures

Primary outcome

Pharmacokinetics/Mass balance

Metabolite profiling

Safety

Blood/Plasma Ratio

Secondary outcome

NA

Study description

Background summary

Cilengitide is a new investigational compound that may eventually be used for the treatment of cancer. The compound reduces a part of the angiogenesis (the growth of new blood vessels) limiting the growth of tumors. Cilengitide is not registered as a drug but has been given to humans before.

Study objective

Primary:
- To evaluate the mass balance of total 14C radioactivity, i.e. PK parameters of cilengitide and potential metabolites,
- To quantify the route(s) of excretion in urine (14C and cilengitide) and feces (14C),
- To profile potential metabolites of 14C-cilengitide in plasma, and
- To assess and compare the pharmacokinetic (PK) profiles of cilengitide and total radioactivity in plasma, after a single dose of 2.2 MBq 14C-cilengitide

administered together with a single dose of 2000 mg of unlabeled cilengitide in healthy subjects by a 1-hour intravenous (i.v.) infusion.

Secondary:
-To assess the safety and tolerability of cilengitide in healthy subjects.
-To assess the metabolite profile in urine and in feces.
-To structurally identify potential relevant metabolite(s).
-To determine blood/plasma ratio of total 14C radioactivity.

Exploratory:
- To determine the influence of genetic variants in genes potentially involved in the pharmacokinetics of cilengitide.

Study design

The purpose of the study is to investigate how quickly and to what extent cilengitide is distributed, metabolized (broken down) and eliminated from the body (this is called pharmacokinetics). The compound to be administered will be labeled with 14-Carbon (14C) and is thus radioactive. This enables the investigator to trace the compound in blood, urine and feces. The safety and tolerability of the compound will also be evaluated.

Screening and follow-up:
clinical laboratory, full physical examination, ECG; at eligibility screening: medical history, drug screen, HBsAg, anti-HBc, anti HCV, anti-HIV 1/2

Observation period:
one period in clinic from -18 h up to 96 h after start of drug administration with possible extension to 144 h, 192 h, 240 h. Additional ambulatory visits possible on Days 13 and 15.

Blood sampling:
Plasma samples for determination of total radioactivity will be taken at pre-dose, 0.5 h after SOI (Start Of Infusion), 1 h (at EOI (End Of Infusion)), 2 h, 4 h, 6 h, 12 h and 24 h, after SOI, and every further 12 h after SOI until 96 hours after administration, and, if necessary every 24 h until End-of-Hospitalization as defined above. Whole Blood samples for determination of total radioactivity will be taken at 0.5 h, 1 h (at EOI), 2 h, 4 h, 6 h, and 12 h after SOI. Plasma samples for determination of cilengitide will be taken at pre-dose, 0.5 h after SOI, 1 h (at EOI), 2 h, 4 h, 6 h, 12 h, and 24 h after SOI.
Plasma samples for metabolite profiling will be taken at pre-dose, 1 h (at EOI), 2 h, 4 h, 6 h, 12 h, 24 h, and 96 h after SOI.

Urine sampling:
Urine samples will be collected before dosing (-12 to 0 h) and at 0-4 h, 4-8, 8-12, 12-24 h after SOI. Collection will continue in further 12-hour intervals

until 96 h after SOI and in 24-hour intervals until End-of-Hospitalization as defined above.

Feces sampling:
Feces samples will be taken before dosing and every 24 hours after SOI until End-of-Hospitalization as defined above. If release criteria are not met at End-of-Hospitalization, subject will be asked to continue collecting urine and feces at home and hand in the samples every 2nd day.

Safety assessments:
AEs, CM, from inclusion until follow-up, 12-lead ECG, vital signs, clinical laboratory, at screening, pre-dose, and 1 h, 5 h, 24 h, and 48 h after start of infusion and at discharge on Day 5, if the stay is prolonged at Day 7 and 9 when relevant, physical examination at screening, end of hospitalization and follow-up.

Intervention

One intravenous infusion of 2000 mg 14C labeled cilengitide in 250 ml over 60 minutes

Study burden and risks

The additional radiation burden in this study due to the administration of 2.2 MBq 14C-labeled cilengitide is calculated to be approximately 0.5- 0.7 mSv. This is approximately 25 % of the average annual radiation burden and can be compared with two return flights to Australia.

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

Blood draw, indwelling canula: During this study less than 500 ml of blood will be drawn. It is anticipated that an indwelling canula will be used on Day 1 and regular blood draws will be drawn by direct puncture of the vein. It is anticipated that a maximum of 19 punctures will be done with a volume of 8.2 mL each.

IV dosing: For the iv administration you will have an indwelling canula inserted specifically for this purpose in addition to the indwelling canula used for blood sampling on Day 1. Thus you will have a canula inserted in both arms during dosing. The canula for the infusion will be removed immediately after dosing.

Collection of urine and feces: Urine and feces will be collected until 96 hours after administration of cilengitide (thus until Day 5) with a possible maximum extension to Day 11 (240 hours).

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

Blood sample for DNA tests: For general information on DNA tests, please refer to section 4.6 of the information booklet. On Day 1 a blood sample of 6 mL will be taken for DNA tests. Participation in this part of the study is mandatory and double coding will be used. This means that the blood samples will be given a first code assigned to you at the start of the Main Study (your coded trial subject number). Specific Sponsor personnel will assign a second code (double-coding) to these blood samples, only they will have the link between the two codes. The laboratory analyzing your blood will only use your second code and will not have access to the first code or the link to the first code.

Contacts

Public
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Scientific
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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 volunteers
18-45 years, inclusive
BMI: 18.5 * 29.9 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):	02-11-2012
Enrollment:	5
Type:	Actual

Ethics review

Approved WMO

Date:	16-10-2012
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-10-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-11-2012
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-01-2013
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	EUCTR2012-003301-94-NL
CCMO	NL42211.056.12