A single-center, open-label study to investigate the absorption, distribution, metabolism and excretion (ADME) of LEE011 after a single oral dose of 600 mg [14C]LEE011 (0.37 MBq) in healthy male subjects

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

Summary

ID

NL-OMON40904

Source
ToetsingOnline

Brief title
Human metabolism and mass balance study of LEE011

Condition

- Other condition

Synonym
advance cancer

Health condition

gevorderde kanker

Research involving
Human

Sponsors and support

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

Intervention

Keyword: 14C, cancer, LEE011

Outcome measures

Primary outcome

* To determine the rates and routes of excretion of [14C]LEE011 related radioactivity, including mass balance of total drug-related radioactivity in urine and feces, following the oral administration of a single 600 mg dose of [14C]LEE011 to healthy male subjects.

* To determine the pharmacokinetics of total radioactivity in blood and in plasma.

* To characterize the plasma pharmacokinetics of LEE011 and known key metabolites, if applicable.

* To characterize the urine concentrations of LEE011 and known key metabolites, if applicable.

Secondary outcome

* To assess the safety of a single 600 mg oral dose of [14C]LEE011 administered to healthy male subjects.

Study description

Background summary

LEE011 is a new investigational compound that may eventually be used for the treatment of advanced cancers. LEE011 is a specific inhibitor of protein complexes (the cyclin-dependent kinase enzyme complexes) which play an important role in the development and progression of cancer. LEE011 is not registered as a drug but has been given to humans before.

Study objective

The purpose of the study is to investigate how quickly and to what extent LEE011 is absorbed, 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 (also called radiolabeled).

Study design

The actual study will consist of 1 period during which you will stay in the clinical research center in Zuidlaren for 23 days (22 nights). After this period it is possible that you may have to come back for a maximum of 4 additional visits during which you will stay in the clinical research center in Zuidlaren for 2 days (1 night).

During the study the volunteers will receive the study medication after an overnight fast (at least 10 hours) as 3 capsules of 200 mg each, together with approximately 250 milliliters of water.

Fasting will continue until 4 hours after administration of the study medication. During fasting and after intake of the study medication, the volunteers are allowed to drink water as they wish with the exception of 2 hours prior to until 2 hours after administration of study medication.

During the first 4 hours after study medication intake the volunteers will have to rest in an upright seated position. The volunteers will not be allowed to lie down, except when indicated as such by one of the investigators, as this may influence the uptake of the drug.

Intervention

The volunteer will receive a single dose of 600 mg radiolabeled study medication in the form of 3 capsules of 200 mg each

Study burden and risks

All potential drugs cause adverse events; the extent to which this occurs differs.

LEE011 is an investigational drug and not all of the side effects are known. Serious side effects, including death, are a possibility. The long-term effects of LEE011 are also unknown. Risks are possible side effects of study medicine given alone or in combination with other medication(s), and those related to any of the study procedures (e.g. taking blood, biopsy, and imaging scans).

Based on the data from ongoing studies in cancer patients who received multiple doses of LEE011 alone or in combination with other medications, the following are the possible risks with taking LEE011.

Most frequent side effects of LEE011 (> 20% incidence):
* Low white blood cell count which can increase the risk for infections
* Low red blood cell count which can lead to tiredness and weakness
* Low platelets count which can lead to easy bruising and bleeding.
* Nausea and/or vomiting
* Diarrhea
* Tiredness or fatigue

Frequent side effects of LEE011 (10 to 20% incidence):
* Changes in electrical activity of the heart called QTc prolongation. This is an abnormality of the heart rhythm and may cause dizziness, palpitations, fainting and in severe cases loss of consciousness and death
* Mouth sores, or pain, inflammation and/or infection of the of the mouth and throat
* Increase in creatinine (a waste product) and a decrease in the kidneys* ability to handle the body*s waste
* Decrease in appetite

Less frequent side effects of LEE011 (5-9% incidence):
* Low levels of protein in the blood
* High blood sugar
* Skin rash
* General aches including headache, stomach ache, back ache, or joint pain
* Fever
* Nosebleeds
* Dizziness

Infrequent but important side effects of LEE011 (<5% incidence):
* Low levels of sodium in the blood
* Low levels of calcium in the blood

* High levels of potassium in the blood
* High blood pressure
* Blockage in the blood vessels of the lung usually caused by blood clot(s)
* High blood levels of liver enzymes and bilirubin (yellow pigment found in bile which is made by the liver) and possible liver damage
* Potential accumulation of LEE011 in the thyroid gland. In rats, LEE011 was found to accumulate in the thyroid gland but there was no evidence of damage to the thyroid gland. There have been no reports of abnormal thyroid function in any patient so far.
* One patient participating in a trial (CMEK162X2114) combining LEE011 with MEK162 (another investigational drug) died from bleeding in the brain. The treating physician considered the fatal brain bleed to be related to the combination of MEK162 and LEE011.

We do not know the side effects of LEE011 when given either alone or in combination with other drugs. A combination of drugs might result in serious or even life-threatening side effects. Some over the-counter and prescription medications can reduce the effectiveness or increase the side effects of LEE011. Likewise, LEE011 can increase the side effects or lessen the effectiveness of some medications. This might result in serious or even life-threatening side effects.

Procedures: pain, minor bleeding, bruising, possible infection

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 subjects
45 - 65 yrs, inclusive
BMI: 18.0 - 30.0 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 0.4 liters of blood in the 8 weeks 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):	06-10-2014

Enrollment:	6
Type:	Actual

Ethics review

Approved WMO Date:	18-09-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-09-2014
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	EUCTR2014-001873-15-NL
CCMO	NL50615.056.14