A STUDY OF THE SAFETY, TOLERABILITY, PHARMACOKINETICS AND PHARMACODYNAMICS OF LY3045697 AFTER MULTIPLE ORAL DOSING IN HEALTHY SUBJECTS

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Primary: To evaluate the safety and tolerability of LY3045697 after multiple oral dosing in healthy subjectsSecondary: To investigate the pharmacokinetics of LY3045697 after multiple oral dosing in healthy subjects

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Renal disorders (excl nephropathies)
Study type	Interventional

Summary

ID

NL-OMON38581

Source
ToetsingOnline

Brief title
ASEB

Condition

- Renal disorders (excl nephropathies)

Synonym
Chronic Kidney Disease, Kidney Disease

Research involving
Human

Sponsors and support

Primary sponsor: Chorus, Eli Lilly and company
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: LY3045697, Multiple rising doses, PK, Safety

Outcome measures

Primary outcome

Safety and tollerability of LY3045697

Secondary outcome

Pharmacokinetics of LY3045697

Study description

Background summary

LY3045697 is a new investigational compound that may eventually be used for the treatment of chronic kidney disease. LY3045697 is not registered as a drug but has been given to humans before.

Study objective

Primary:
To evaluate the safety and tolerability of LY3045697 after multiple oral dosing in healthy subjects

Secondary:
To investigate the pharmacokinetics of LY3045697 after multiple oral dosing in healthy subjects

Study design

This is a randomized, double blind, placebo and positive comparator (spironolactone) controlled, multiple dose escalating, incomplete cross-over design study in 24 healthy males and females of non-child bearing potential. Subjects will be divided into 2 groups of 12 subjects, which will be dosed in an alternating fashion during 3 separate admission periods per group. There

will be a wash-out period of at least 7 days between dosing periods for an individual subject. Dosing will be in the fed state. Within each treatment period, subjects will be randomized 8:2:2 to LY3045697:placebo:spironolactone, and each subject will have received 2 LY3045697 levels and either placebo or spironolactone at the end of the study. To maintain the blind, the study will be conducted in a double dummy format, with subjects taking a solution vial (either LY3045697 or placebo) and a capsule (either spironolactone or placebo) on each day of dosing. There will be an oral K+ challenge on Day 7 and an intravenous (IV) ACTH challenge on Day 8 in each period.

Intervention

Multiple oral doses of LY3045697 or placebo,
spironolactone or placebo

Study burden and risks

The study where LY3045697 was given to humans for the first time is still ongoing. Thus far, subjects were treated with a single oral dose of 0.1 mg, 0.3 mg and 1 mg of LY3045697. The most reported adverse events include tiredness, headache, common cold and abdominal pain. All adverse events were of mild intensity and none were considered to be related to the study medication by the investigator.

Animal studies showed that LY3045697 was well tolerated in rats for 28 days at very high doses (1000 mg/kg). In monkeys this was the case for doses of 30 mg/kg. In both species there was a slight increase in weight and volume of the liver and adrenal glands. LY3045697 may reduce a substance in your blood called aldosterone. Aldosterone helps your body to regulate sodium and potassium levels and blood pressure. LY3045697 may cause increased potassium levels, which could cause abnormal heart rhythm. LY3045697 may also cause your blood pressure to drop. LY3045697 may reduce a substance in your blood called cortisol which helps your body survive stressful situations. Lack of cortisol can result in abdomen pain, nausea and vomiting, muscles aches, loss of appetite and weight, lack of energy and a low blood pressure. LY3045697 may reduce the amount of sodium in your blood. You may also experience increased urination.
LY3045697 has not been studied in animals for any effects on pregnancy or on sperm function. In women who get pregnant while taking LY3045697, there may be bad effects on the embryo or fetus.
Women of childbearing potential or who are breast-feeding must not take LY3045697.

The most frequently reported adverse effect of the registered drug spironolactone is hyperkalemia (abnormally high levels of potassium in the blood). Symptoms of hyperkalemia are muscle weakness, nausea, dizziness and

headache. Please refer to page 8 of the instruction manual of spironolactone for more information on adverse effects.

With the dose(s) used in this study no serious adverse effects are expected. The occurrence of known or other effects cannot be excluded. All potential drugs cause adverse events to some extent. Therefore you should take into account that some risks are still unknown at this moment.

Contacts

Public
Chorus, Eli Lilly and company

Lilly Corporate Center n/a
Indianapolis IN 46285
US
Scientific
Chorus, Eli Lilly and company

Lilly Corporate Center n/a
Indianapolis IN 46285
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Healthy males or females (females must be postmenopausal or surgically sterile)
-Postmenopausal female subjects must be between the ages of 45 and 65 years, inclusive
-Male subjects and surgically sterile females must be between the ages of 18 and 65 years,

inclusive
-BMI between 18.0 and 32.5 kg/m2 , inclusive

Exclusion criteria

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

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-05-2013
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	spironolactone
Generic name:	spironolactone
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	20-03-2013
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-04-2013
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-05-2013
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	EUCTR2013-000475-32-NL
CCMO	NL43925.056.13