Study of the Safety, Tolerability, Pharmacokinetics and Effect on Renal Potassium Clearance after Multiple Oral Dosing of LY2623091 in Healthy Volunteers

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Primary:- to investigate the safety and tolerability of the study drug after multiple oral dosing in healthy volunteersSecondary:- to investigate the effect of the study drug on potassium clearance upon oral potassium challenge after multiple oral...

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

Summary

ID

NL-OMON36630

Source
ToetsingOnline

Brief title
LY2623091 MAD study

Condition

- Renal disorders (excl nephropathies)

Synonym
chronic kidney disease, Kidney failure

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Kidney disease, LY2623091, MAD

Outcome measures

Primary outcome

Pharmacodynamics

Pharmacokinetics

Safety

Secondary outcome

n.a.

Study description

Background summary

The drug to be given LY2623091 is a new, investigational compound that may eventually be used for the treatment of chronic kidney disease. This compound is in the development phase. Chronic kidney disease is characterized by ongoing deterioration of kidney function. Ultimately, total loss of kidney function may occur, requiring patients to use dialysis or renal transplant to survive. Current treatments do not counter the deterioration of kidney function sufficiently. Consequently, new therapies are urgently needed for these patients. The experimental drug used in this study, LY2623091 is being developed to safely improve kidney function in chronic kidney disease patients, using a novel mechanism.

Study objective

Primary:
- to investigate the safety and tolerability of the study drug after multiple oral dosing in healthy volunteers

Secondary:
- to investigate the effect of the study drug on potassium clearance upon oral potassium challenge after multiple oral dosing in healthy volunteers
to further explore the pharmacokinetics of the study drug after multiple oral dosing in healthy volunteers

Exploratory:
- blood samples for DNA extraction will be collected and stored from all subjects in this study to enable exploratory future analyses and pharmacogenomic evaluations related to the compound activity/exposure during later phase clinical development

Study design

Design:
a double-blind (for the study drug), placebo-controlled, four treatment, two-period incomplete crossover, multiple-ascending dose study in two groups of sixteen healthy male and/or healthy female (postmenopausal/sterilized) subjects each receiving the study drug (eight subjects) or eplenerone (four subjects) or placebo (four subjects) once daily for seven days, in the fed state on Day 1-6 and in the fasted state on Day 7; a washout of at least seven days between dosing periods; each subject will follow a restricted sodium/potassium diet from Day 2 until the end of the dosing period; a potassium challenge will take place on Day 7 in fasted state

Procedures and assessments
Screening and follow-up:
clinical laboratory (including urinary albumin/creatinine ratio at screening), vital signs, physical examination, weight, urine alcohol and drug screen, 12-lead ECG; at eligibility screening: medical history, height, temperature, respiratory rate, serum pregnancy test (females only), HBsAg, anti HCV, anti-HIV 1/2; clinical laboratory, directed physical examination, vital signs, urine pregnancy test (females only), urine alcohol and drug screen to be repeated upon each admission

Observation period:
2 periods, each period in clinic from -41 h drug administration on Day 1 up to 72 h after drug administration on Day 7; in each period, subjects will be on a restricted 150 mEq/day sodium and 125 mEq/day potassium diet on Days 2 - 7

Blood sampling:
for pharmacokinetics of the study drug in plasma: pre-dose and 1, 2, 3, 4, 8, 12 and 24 h post-dose on Day 1, pre-dose and 1, 2, 3, 4, 8 and 12 h post-dose on Day 6 and 24, 48 and 72 h post-dose on Day 7, during the 3rd dose level the following additional samples will be taken: 1, 2, 3, 4, 8 and 12 h post-dose on Day 7
for pharmacodynamics of sodium and potassium: -1.5 h pre-oral K+ challenge and

0 h (baseline) and 1, 2, 3, 4 and 5 h post-oral K+ challenge on Day 7
for future DNA extraction and genomics: pre-dose on Day 1 (Period 1 only)

Urine sampling:
for pharmacodynamics of sodium and potassium: 24 h pool starting at -2 h on Day 6 (relative to oral K+ challenge) and intervals -2 to -1, -1 to 0 h pre-oral K+ challenge and 0-1, 1-2, 2-3, 3-4, and 4-5 h post-oral K+ challenge on Day 7
for pharmacodynamics of aldosterone: 24 h pool starting at -2 h on Day 6 (relative to oral K+ challenge)

Safety assessments:
adverse events: throughout the study; clinical laboratory: pre-dose on Days 1, 2, 4 and 8; 12-lead ECG (in triplicate): pre-dose and at approximately Tmax and 24 h post-dose on Days 1 and 7; vital signs (blood pressure in triplicate): pre-dose and 1, 4 and 24 h post-dose on Days 1, 3 and 7

Bioanalysis:
analysis of plasma LY2623091 samples using a validated method by PRA
analysis op serum and urine potassium and sodium samples using a clinical chemistry method by PRA
analysis of urine aldosterone samples using a non-validated method by PRA
DNA extraction and genomics by Sponsor

Intervention

Active substance: LY2623091
Comparator: eplerenone

Study burden and risks

Procedures: pain, light bleeding, heamatoma, possibly an infection.

Contacts

Public
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US
Scientific
Eli Lilly

Lilly Corporate Centre

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US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Healthy males and/or healthy females (postmenopausal/sterilized)
- 18-65 years, inclusive
- BMI: 19.0-32.5 kg/m2, inclusive
- non-smoking, or smoking a maximum of10 cigarettes/day

Exclusion criteria

Suffering from: hepatitis B, cancer or HIV/AIDS. In case of participation in another drug study within 60 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 (for men) / more than 1.0 liters of blood (for women) in the 10 months prior the start of this study.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial

Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-10-2010
Enrollment:	32
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Inspra
Generic name:	Eplerenone
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	08-10-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-10-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-01-2011
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	EUCTR2010-022707-22-NL
CCMO	NL34111.056.10