A First in Human, Single-dose Escalation Study of LY2562175 In Healthy Subjects

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lipid metabolism disorders
Study type	Interventional

Summary

ID

NL-OMON33901

Source
ToetsingOnline

Brief title
LY2562175 single dose escalation study in humans

Condition

- Lipid metabolism disorders

Synonym
lipids, metabolism

Research involving
Human

Sponsors and support

Primary sponsor: Chorus, Lilly Research Laboratories
Source(s) of monetary or material Support: Chorus;Lilly Research Laboratories

Intervention

Keyword: Dyslipidemie, LY2562175

Outcome measures

Primary outcome

Pharmacokinetics:

plasma LY2562175 concentrations, pharmacokinetic parameters

Safety:

adverse events, vital signs, ECG-parameters, laboratory parameters, physical

examination

Secondary outcome

Pharmacodynamics :

bile acid panel, fasting lipid panel (TG, LDL-C, VLDL-C, directed HDL, HDL-C

and TC) and target engagement as measured by changes in TG, LDL-C and HDL-C.

Study description

Background summary

The drug to be given, LY2562175, is a new, investigational compound that may eventually be used in the treatment of high cholesterol (too high percentage of fat in the blood). High cholesterol is associated with a higher risk of developing Coronary Heart Disease (CHD).

Cholesterol can build up in the walls of your arteries. This buildup of cholesterol is called plaque. Over time, plaque can cause narrowing of the arteries. This is called atherosclerosis, or hardening of the arteries. Narrowing of your coronary arteries due to plaque can stop or slow down the flow of blood to your heart. When the arteries narrow, the amount of oxygen-rich blood is decreased. This is called coronary heart disease (CHD). By lowering the percentage of fat in the blood, LY2562175 reduces the risk of high

cholesterol and subsequently the risk of CHD.

Study objective

The purpose of the study is to investigate how safe the compound is and how well the compound is tolerated. The study will also investigate how quickly and to what extent the drug is absorbed, metabolised (broken down into smaller parts) and eliminated from the body (this is called pharmacokinetics). This study is not intended to improve your health, but is necessary for the further development of the drug.

Study design

Design:
a double-blind, placebo-controlled, single-dose escalation study with two groups of nine healthy male and/or female (postmenopausal/sterilized) subjects each receiving a single oral dose of LY2562175 or placebo (six verum and three placebo) on three occasions; a wash-out of at least fourteen days between dosing within a cohort
Procedures and assessments

Screening and follow-up:
clinical laboratory, creatinine, hepatic profile, blood glucose, total cholesterol, vital signs, physical examination, ECG (in triplicate at screening);
at eligibility screening: medical history, oral temperature and respiratory rate height, weight, BUN, PT, aPTT, alcohol and drug screen, HBsAg, anti HCV, anti-HIV 1/2 and pregnancy test (females only); urinalysis and drug screen to be repeated upon each admission

Observation period:
3 periods, each period in clinic from -17 h up to 48 h after drug administration

Blood sampling:
for pharmacokinetics of LY2562175 in plasma: pre-dose and 0.25, 0.5, 1, 2, 4, 6, 7, 8, 11, 12, 24, 36, and 48 h post-dose
for pharmacodynamics of fasting lipid panel (TG, LDL-C, VLDL-C, directed HDL, HDL-C and TC): once on Day 1 and 24 h post-dose
for pharmacodynamics of bile acid panel: once on Day 1 and 24 h post-dose and at follow-up

Safety assessments :
adverse events: throughout the study; physical examination, biochemistry, haematology, PT and aPTT and vital signs: once on Day 1 and 24 and 48 h post-dose (including oral temperature and respiratory rate: pre-dose); weight: once on Day 1; ECG (in triplicate): pre-dose, 0.5, 1, 2, 4, 6, 8, 12 and 24 h

post-dose;

Bioanalysis:
analysis of plasma LY2562175 samples using LC/MC method by PRA
analysis of fasting lipid panel using a clinical laboratory method by PRA
analysis of bile acid panel using a validated method by PRA

Intervention

Study medication
Active substance: LY2562175
Activity : potent farnesoid x receptor agonist
Indication : dyslipidemia
Strength : 5, 25 and 100 mg
Dosage form: capsules

Treatments
Group 1
period 1: a single oral dose of 5 mg LY2562175 or placebo on Day 1 in the fasted state
period 2: a single oral dose of 75 mg LY2562175 or placebo on Day 1 in the fasted state
period 3: a single oral dose of 400 mg LY2562175 or placebo on Day 1 in the fasted state

Group 2
period 1: a single oral dose of 25 mg LY2562175 or placebo on Day 1 in the fasted state
period 2: a single oral dose of 200 mg LY2562175 or placebo on Day 1 in the fasted state
period 3: a single oral dose of 600 mg LY2562175 or placebo on Day 1 in the fasted state

Study burden and risks

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

Contacts

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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 men or women of non child bearing potential
18 - 60 years inclusive

Exclusion criteria

18 - 60 years inclusive
BMI 18 - 30 kg/m
By screening no abnormalities found

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):	23-03-2009
Enrollment:	18
Type:	Actual

Ethics review

Approved WMO Date:	18-03-2009
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-03-2009
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	EUCTR2008-006338-89-NL
CCMO	NL25420.056.09