Onderzoek naar, de farmacologie, de effecten van voedsel en geneesmiddel interactie met meervoudige oplopende doseringen van LY2562175 in gezonde vrijwilligers

Gepubliceerd: 17-07-2009 Laatst bijgewerkt: 04-05-2024

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Ethische beoordeling	Goedgekeurd WMO
Status	Werving gestopt
Type aandoening	Lipidenmetabolismestoornissen
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON32962

Bron
ToetsingOnline

Verkorte titel
LY2562175 MAD/DDI/FE studie

Aandoening

- Lipidenmetabolismestoornissen

Synoniemen aandoening
lipiden, metabolisme

Betreft onderzoek met
Mensen

Ondersteuning

Primaire sponsor: Chorus, Lilly Research Laboratories
Overige ondersteuning: Chorus;Lilly Research Laboratories USA

Onderzoeksproduct en/of interventie

Trefwoord: Dyslipidemia, LY2562175

Uitkomstmaten

Primaire uitkomstmaten

Pharmacodynamics:

Parts 1 and 2: bile acid panel (GCDCA, GCA, TCDCA, TCA, CA, CDCA, TDCA and GDCA) and fasting lipid panel (TG, LDL-C, VLDL C, HDL-C and TC)

Part 1 only:

TG levels, NMR lipoprofile, ApoB48 and ApoB100 levels during an MMTT, fasting glucose and insulin (homeostatic model assessment to quantify insulin resistance)

Part 2 only:

NMR lipoprofile and palmitoleic acid (C-16-1) levels

Pharmacokinetics:

Plasma concentrations of LY2562175 (Parts 1 and 2), midazolam and its metabolites (Part 2 only), and pravastatin (Part 2 only). PK parameters: Cmax, tmax, kel, t*, AUC0-t, AUC0-inf, %AUC, Rac (Part 1 only), CL/F, Vz/F.

Safety:

AEs, vital signs, 12-lead ECG and clinical laboratory

Secundaire uitkomstmaten

NVT

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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 and eliminated from the body. The influence of other drugs on the compound and the effect of food will also be investigated. This study is not intended to improve your health, but is necessary for the further development of the drug.

Onderzoeksopzet

Design:
This is a 2-part, single center study in healthy male and/or female subjects. Part 1 will be a randomized, double-blind, placebo-controlled, multiple ascending dose study with 4 groups of 12 healthy subjects (males and/or females of non-child bearing potential [NCBP]). In each group, 9 subjects will receive LY2562175 and 3 subjects will receive placebo orally once daily for a period of 14 days in the fasted state. Each subject will participate in one 14-day multiple dose treatment period. A Mixed Meal Tolerance Test (MMTT) will be performed at breakfast and lunch on Days -2 and 10.
Part 2 will be an open-label study with 9 healthy male and/or NCBP female subjects. Subjects will receive LY2562175 orally once daily for a period of 14 days in the fed state. Midazolam (intravenous [iv] injection) and pravastatin (oral) will be administered as single doses on Day -2 and Day 12.
All subjects of both study parts will return for a follow-up visit on Days 21 and 28.
Procedures and assessments

Screening and follow-up:
Demographics, medical history, clinical laboratory (clinical chemistry, hematology, urinalysis and coagulation), urine drug and alcohol screen, pharmacodynamic (PD) assessments (fasting lipid panel: triglycerides [TG], low-density lipoprotein-bound cholesterol [LDL-C], very low-density lipoprotein-bound cholesterol [VLDL C], high-density lipoprotein-bound cholesterol [HDL C] and total cholesterol [TC]), antiviral serology (HBsAg, anti HCV, anti HIV 1/2), pregnancy test (females only), vital signs (blood pressure, pulse rate, oral body temperature and respiratory rate), 12 lead electrocardiogram (ECG) (triplicate), complete physical examination including body height and weight, previous and concomitant medication recording, and adverse events (AEs).
Follow-up Day 21: Clinical laboratory (clinical chemistry, hematology, urinalysis and coagulation), PD assessments (bile acid panel: glycochenodeoxycholic acid [GCDCA], glycocholic acid [GCA], taurochenodeoxycholic acid [TCDCA], taurocholic acid [TCA], cholic acid [CA], chenodeoxycholic acid [CDCA], taurodeoxycholic acid [TDCA] and glycodeoxycholic acid [GDCA]; fasting lipid panel: TG, LDL-C, VLDL C, HDL-C and TC; fasting glucose and insulin) and directed physical examination.
Follow-up Day 28:Clinical laboratory (only if clinically significant on Day 21 [clinical chemistry, hematology, urinalysis and coagulation]), PD assessments (bile acid panel: GCDCA, GCA, TCDCA, TCA, CA, CDCA, TDCA and GDCA; fasting lipid panel: TG, LDL-C, VLDL C, HDL-C and TC; fasting glucose and insulin), vital signs (blood pressure and pulse rate), ECG (single) and complete physical examination.
Observation period :
Part 1:1 period in clinic from Day -4 up to Day 16, and an ambulant visit on Day 18.
Part 2: 1 period in clinic from Day -3 up to Day 16, and an ambulant visit on Day 18.

Blood sampling:
Part 1:
For pharmacokinetics (PK) of LY2562175: at pre-dose and at 0.5, 1, 2, 4, 6, 8, 12 and 24 hours post-dose on Day 1, at pre-dose on Days 3, 5 and 10, and at pre-dose and at 0.5, 1, 2, 4, 6, 8, 12, 24, 48 and 96 hours post-dose on Day 14.
For PD (bile acid panel: GCDCA, GCA, TCDCA, TCA, CA, CDCA, TDCA and GDCA; fasting lipid panel: LDL-C, VLDL C, HDL-C and TC): at pre-dose on Days 1, 2, 4, 7, 10 and 14.
For PD (TG): at pre-dose on Days 1, 2, 4, 7 and 14.
For PD (MMTT: TG): Day 10: before starting breakfast (pre-dose), at 1, 2, 3, 4 and 5 hours (pre lunch) after starting breakfast, and at 1, 2, 3, 4 and 5 hours (pre-dinner) after starting lunch.
Blood sampling for this PD parameter will also be done on Day -2 at the same time points as on Day 10.
For PD (MMTT: nuclear magnetic resonance [NMR] lipoprofile): Day 10: before starting breakfast (pre-dose), at 1, 2, 3, 4 and 5 hours (pre-lunch) after

starting breakfast and at 1, 2, 3, 4 and 5 hours (pre dinner) after starting lunch.
Blood sampling for this PD parameter will also be done on Day -2 at the same time points as on Day 10.
For PD (MMTT: apolipoprotein B-48 [ApoB48] and apolipoprotein B-100 [ApoB100]): Day 10: before starting breakfast (pre-dose), at 3, 4 and 5 hours (pre-lunch) after starting breakfast and at 3, 4 and 5 hours (pre-dinner) after starting lunch.
Blood sampling for these PD parameters will also be done on Day -2 at the same time points as on Day 10.
For PD (fasting glucose and insulin): before starting breakfast (pre-dose) on Days 1, 2, 4, 7, 10 and 14.
Part 2:
For PK of LY2562175: at pre-dose and at 0.5, 1, 2, 4, 6, 8, 12 and 24 hours post-dose on Day 1, at pre-dose on Days 3, 5 and 10, and at pre-dose and at 0.5, 1, 2, 4, 6, 8, 12, 24, 48 and 96 hours post-dose on Day 14.
For PK of midazolam, midazolam metabolites, and pravastatin: at pre-dose and at 0.25, 0.5, 1, 2, 4, 6, 8, 12, 24, and 48 hours post-dose on Day 12.
Blood sampling for PK of midazolam, midazolam metabolites, and pravastatin will also be done on Day -2 at the same time points as on Day 12.
For PD (bile acid panel: GCDCA, GCA, TCDCA, TCA, CA, CDCA, TDCA and GDCA; fasting lipid panel: TG, LDL-C, VLDL C, HDL-C and TC): at pre-dose on Days 1, 2, 4, 7, 10 and 14.
For PD (NMR lipoprofile): Day 10: before starting breakfast, at 2.5, 3.5, 4.5 and 5.5 hours (pre-lunch) after starting breakfast and at 1, 2, 3, 4 and 5 hours (pre dinner) after starting lunch.
Blood sampling for NMR lipoprofile will also be done on Day -2 at the same time points as on Day 10.
For PD (palmitoleic acid [C-16-1]): Day 10: before starting breakfast, at 2.5 and 3.5 hours after starting breakfast and at 2 and 3 hours after starting lunch.
Blood sampling for palmitoleic acid [C-16-1] will also be done on Day -2 at the same time points as on Day 10.
MMTT:
on Days -2 and 10 (Part A only)
Safety assessments :
AEs and concomitant medication: recorded from the time the Informed Consent Form is signed until completion of the follow up visit; physical examination (directed): on Day 7; vital signs (blood pressure and pulse rate): at pre-dose and at 3 hours post-dose on Days 1, 7 and 14; ECG (triplicate): at pre dose and at 2, 4 and 24 hours post dose on Days 1 and 14; clinical laboratory (clinical chemistry, hematology, urinalysis and coagulation): at pre-dose on Day 7 and at 48 hours post-dose on Day 14.

Onderzoeksproduct en/of interventie

Study Medication Active substance: LY2562175 midazolam pravastatin Activity : potent

farnesoid x receptor agonist sedative HMG-CoA reductase Inhibitors Indication : dyslipidemia anesthesia prevention of strokes/heart attacks Strength : 5, 25 and 100 mg 200 µg 40 mg Dosage form: capsules iv injection tablet

Inschatting van belasting en risico

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

Contactpersonen

Publiek

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USA

Wetenschappelijk

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Locaties

Landen waar het onderzoek wordt uitgevoerd

Netherlands

Deelname eisen

Leeftijd
Volwassenen (18-64 jaar)
65 jaar en ouder

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Gezond mannen en/of postmenopausal/gesteriliseerd
18 t/m 65 jaar inclusief
BMI 18-30 kg/m2

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Lijdend aan: ernstige aandoening zoals bijvoorbeeld hepatitis B, kanker of HIV/AIDS. Indien gedurende de 60 dagen voorafgaand aan de start van dit onderzoek aan een ander geneesmiddelenonderzoek is deelgenomen.
Indien gedurende de 60 dagen voor start van dit onderzoek bloed gegeven of plotseling bloedverlies gehad van een gelijkwaardige hoeveelheid bloed.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo
Doel:	Behandeling / therapie

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	06-08-2009
Aantal proefpersonen:	57
Type:	Werkelijke startdatum

Ethische beoordeling

Goedgekeurd WMO Datum:	17-07-2009
Soort:	Eerste indiening
Toetsingscommissie:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Goedgekeurd WMO Datum:	24-07-2009
Soort:	Eerste indiening
Toetsingscommissie:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
EudraCT	EUCTR2009-013167-19-NL
CCMO	NL28974.056.09