Een onderzoek naar de veiligheid en farmacologie van een enkelvoudige dosering LY2165766 waarbij LY2165766 voor het eerst aan de mens wordt toegediend waarbij ook de bezetting van dopamine D2 receptor in de hersenen wordt onderzocht door positron emissie tomografie (PET)

Gepubliceerd: 04-09-2008 Laatst bijgewerkt: 06-05-2024

Part APrimary: to evaluate the safety and tolerability of LY2165766 administered as a single oral dose in healthy volunteersSecondary: to determine the pharmacokinetics of LY2165766Part BPrimary: to explore the relationship between plasma...

Ethische beoordeling	Goedgekeurd WMO
Status	Werving gestopt
Type aandoening	Schizofrenie en andere psychotische stoornissen
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON33530

Bron
ToetsingOnline

Verkorte titel
LY2165766 SDSS/PET studie

Aandoening

- Schizofrenie en andere psychotische stoornissen

Synoniemen aandoening

schizofrenie

Betreft onderzoek met
Mensen

Ondersteuning

Primaire sponsor: Chorus LRL (devisie van Eli Lilly)
Overige ondersteuning: sponsor van dit onderzoek

Onderzoeksproduct en/of interventie

Trefwoord: LY2165766, schizofrenie

Uitkomstmaten

Primaire uitkomstmaten

Pharmacodynamics : dopamine D2 receptor occupancy (D2RO) based on

11C-raclopride PET scanning

Pharmacokinetics : plasma LY2165766 concentrations, pharmacokinetic parameters

Safety : adverse events, vital signs, ECG-parameters, laboratory parameters,

physical examination

Secundaire uitkomstmaten

nvt

Toelichting onderzoek

Achtergrond van het onderzoek

Schizophrenia is a serious chronic psychiatric disease that is characterized by auditory hallucinations and delusions (*positive symptoms*), and deficits (*negative symptoms*) including an inability to pay attention, loss of a sense of pleasure, loss of will or drive, disorganization or impoverishment of thought and speech, flattening of affect, social withdrawal, and cognitive dysfunction as manifested by a decreased ability to focus attention and deficiencies in short-term verbal and nonverbal memory. Patients are at risk for committing violent acts in response to hallucinations or delusions. The current pharmacologic therapy of schizophrenia is centered on drugs that cause

dopamine D2 receptor blockade. The first-generation antipsychotic drugs such as haloperiodol were shown to block D2 receptors and demonstrated therapeutic efficacy. However, these drugs were associated with significant adverse effects. A second generation of D2 blocking antipsychotics are now the preferred agents to treat schizophrenia, and these agents are less tightly bound to the D2 receptor. The first of these second generation antipsychotics known as *atypical antipsychotics* was associated with a decrease in the side effects associated with the first generation antipsychotics, but has been associated with agranulocytosis which initially caused a number of fatalities, but is now managed by frequent monitoring of blood cell counts. Newer atypical antipsychotics are now available, but these are, however, not devoid of adverse effects, including some adverse effects associated with the earlier drugs. These events include sedation, moderate degrees of EPS, hypotension, weight gain, hyperlipidemia and its consequences, and hyperprolactinemia, each of which occur at different frequencies for any given individual atypical antipsychotic. An atypical antipsychotic with appropriate D2 blocking properties and with no or a low incidence of the these adverse effects is a potentially attractive therapeutic agent.

Doel van het onderzoek

Part A
Primary:
to evaluate the safety and tolerability of LY2165766 administered as a single oral dose in healthy volunteers

Secondary:
to determine the pharmacokinetics of LY2165766

Part B
Primary:
to explore the relationship between plasma concentration and brain dopamine D2 receptor occupancy (D2RO) after a single dose of LY2165766 in healthy subjects

Part C
Primary:
to explore the relationship between plasma concentration and brain dopamine D2 receptor occupancy (D2RO) after a multiple dose of LY2165766 in healthy subjects

Secondary:
to characterize the brain dopamine D2 receptor occupancy (D2RO) relationship to LY2165766 dose and to further evaluate the safety and tolerability of LY2165766 after single dose

Onderzoeksopzet

A single-site, double-blind, placebo-controlled, alternating panel, single-dose escalation study with two cohorts of nine healthy male subjects each receiving a single oral dose of LY2165766 or placebo (six verum and three placebo) on three occasions; treatment periods for each cohort will be separated by a washout of at least seven days.

A multiple dose, open study with one cohort of 3 healthy male subjects each receiving a multiple dose of LY2165766 once daily on days 1 - 7.

Onderzoeksproduct en/of interventie

Part A Cohort 1 period 1: a single oral dose of 2 mg LY2165766 or placebo on Day 1 in the fasted state period 2: a single oral dose of 10 mg LY2165766 or placebo on Day 1 in the fasted state period 3: a single oral dose of 50 mg LY2165766 or placebo on Day 1 in the fasted state Cohort 2 period 1: a single oral dose of 4 mg LY2165766 or placebo on Day 1 in the fasted state period 2: a single oral dose of 25 mg LY2165766 or placebo on Day 1 in the fasted state period 3: a single oral dose of 100 mg LY2165766 or placebo on Day 1 in the fasted state Part B Cohort 1: a single oral dose of 4 mg LY2165766 on Day 1 in the fasted state Cohort 2: a single oral dose of 6 mg LY2165766 on Day 1 in the fasted state Cohort 3: a single oral dose of 10 mg LY2165766 on Day 1 in the fasted state Cohort 4: a single oral dose of 20 mg LY2165766 on Day 1 in the fasted state Part C Cohort 1: a multiple dose of 6 mg LY2165766 on days 1 - 7, in the fasted state

Inschatting van belasting en risico

Procedures: pain, light bleeding, heamatoma, possibly an infection
Medication: balance and tremors (shaking), reduced appetite, increase blood pressure, enlargement of breast

Contactpersonen

Publiek

Chorus LRL (devisie van Eli Lilly)

550 North University Blvd
Indianapolis, IN 46202
Verenigde Staten van Amerika

Wetenschappelijk

Chorus LRL (devisie van Eli Lilly)

550 North University Blvd

Indianapolis, IN 46202
Verenigde Staten van Amerika

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)

gezonde mannen
Deel A: 18 - 65 jaar.
Deel B: 35 - 65 jaar
Deel C: 35 - 65 jaar

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Relevante ziekten of aandoeningen in medische voorgeschiedenis

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind

Controle:	Placebo
Doel:	Behandeling / therapie

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	12-10-2008
Aantal proefpersonen:	38
Type:	Werkelijke startdatum

In onderzoek gebruikte producten en hulpmiddelen

Soort:	Geneesmiddel
Merknaam:	[11C]Raclopride
Generieke naam:	nvt
Registratie:	Geregistreerd voor een andere indicatie/dosering

Ethische beoordeling

Goedgekeurd WMO Datum:	04-09-2008
Soort:	Eerste indiening
Toetsingscommissie:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Goedgekeurd WMO Datum:	09-09-2008
Soort:	Eerste indiening
Toetsingscommissie:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Goedgekeurd WMO Datum:	16-03-2009
Soort:	Amendement
Toetsingscommissie:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Goedgekeurd WMO Datum:	17-03-2009
Soort:	Amendement

Toetsingscommissie:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Goedgekeurd WMO Datum:	17-04-2009
Soort:	Amendement
Toetsingscommissie:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Goedgekeurd WMO Datum:	20-04-2009
Soort:	Amendement
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	EUCTR2008-005287-14-NL
CCMO	NL24758.056.08