Evaluation of the cognitive and psychomotor effects of LY2624803 following bedtime dosing in healthy subjects

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This study is being performed to evaluate the cognitive and psychomotor effects of the new compound LY2624803 after bedtime dosing.

Ethical review	Approved WMO
Status	Pending
Health condition type	Sleep disorders and disturbances
Study type	Observational invasive

Summary

ID

NL-OMON31867

Source
ToetsingOnline

Brief title
Evaluation of CNS effects of LY2624803 following bedtime dosing

Condition

- Sleep disorders and disturbances

Synonym
insomnia, sleep disorders

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Cognition, Inverse agonist histamine H1 receptor, Sedation, Serotonin 2a receptor antagonist

Outcome measures

Primary outcome

To evaluate the cognitive and psychomotoric effects of LY2624803,

diphenhydramine and zolpidem after bedtime dosing in healthy volunteers.

Secondary outcome

-Determine the cognitive and psychomotor effects of LY2624803 at 5 and 8 hours

post-evening dose (after a first awakening at 2 hours post dose) on periods 1-4

-Determine the cognitive and psychomotor effects of LY2624803 at 5 and 8 hours

post-evening dose (after a first awakening at 5 hours post dose) on period 5

-Explore the relationship between the cognitive and psychomotor tests and

LY2624803, zolpidem and diphenhydramine doses and exposures.

Study description

Background summary

LY2624803 is a new research drug developed by Eli Lilly for the potential treatment of insomnia. It is believed to act in a more specific way than existing drugs. Therefore it is expected to have less unfavourable side-effects compared to existing drugs. Diphenhydramine and zolpidem are two examples of such existing drugs used commonly to treat insomnia. Since these drugs are taken at bedtime, their side-effects may cause problems when waking up unexpectedly during the night.
The purpose of this study is to investigate the cognitive and psychomotor effects of LY2624803 and zolpidem in part A and of diphenhydramine, zolpidem and LY2624803 in part B. Part A and part B consist of 5 separated study periods each.

Study objective

This study is being performed to evaluate the cognitive and psychomotor effects of the new compound LY2624803 after bedtime dosing.

Study design

This study is a phase I, single dose, randomized, double-blind, 5 periods cross-over, placebo-controlled, 2-cohort study to evaluate the Cognitive and Psychomotor effects of LY2624803 following bedtime dosing in healthy subjects.

Study burden and risks

Study drug side-effects:

LY2624803
As of March 2008, LY2624803 has been taken by 115 people (107 men and 8 women). The most common bad effects seen in more than 1 person who have taken LY2624803 include feeling worn out, headache, feeling dizzy, having an upset stomach (nausea), nosebleeds, runny nose, and nightmares. Additionally, an increase in the number of heartbeats each minute was observed in 9 out of 10 people who had been given a 10-mg dose. An increase in the number of heartbeats per minute may be noticeable as a fluttering or pounding in the chest, or may be accompanied by feelings of tiredness or dizziness. Taking LY2624803 could affect your ability to perform activities that require mental alertness, such as operating machinery or driving a car.

Zolpidem
Zolpidem is a registered sedative used for the treatment of insomnia. It may commonly cause drowsiness the following day, headache, dizziness, numbed emotions, reduced alertness, confusion, vertigo, gastro-intestinal disturbances, double vision, skin reactions and amnesia. Zolpidem could affect your ability to perform activities such as operating machinery or driving a car

Diphenhydramine
Diphenhydramine is a registered drug used for the treatment of nightly awakening and initial insomnia. It may commonly cause dizziness, drowsiness and grogginess. Diphenhydramine could affect your ability to perform activities such as operating machinery or driving a car.

Rare side effects:

LY2624803
LY2624803 has been studied in animals. Information on bad effects in animals may predict possible risks to humans. Animals treated with high doses of LY2624803 showed uncoordinated movement, problems with walking, uncontrollable

shaking (convulsions), or death. High doses of LY2624803 have also produced increased blood pressure in animals. The doses that you receive will be much lower than the doses given to animals at which the above bad effects were noted. Studies in animals also suggest that humans may be at risk for seizures. However, no seizures have been reported by subjects taking LY2624803 and are not expected in humans at the doses administered clinical trials. Taking LY2624803 may also cause dizziness when standing up. One may even faint when feeling dizzy if not sitting or lying down until the dizziness is gone. One man given a 6-mg dose of LY2624803 became dizzy and was observed to have a low blood pressure when standing. He did not faint or require special treatment. Another man given a 3 mg-dose of LY2624803 fainted shortly after standing up from bed. For a brief period of time medical personnel were unable to determine if his heart was beating. This is not unusual in such an event and was not life threatening. He regained consciousness without special treatment and recovered completely. If you have a history of fainting or dizziness upon standing you may be at greater risk for these problems if you receive LY2624803.

Zolpidem
Zolpidem is a registered drug. The risk of unforeseen side-effects is therefore not greater than with other drugs. Fatigue, muscle weakness, ataxia, decreased libido and paradoxical reactions occur seldomly.

Diphenhydramine
Diphenhydramine is a registered drug. The risk of unforeseen side-effects is therefore not greater than with other drugs. Dryness of the mouth, nausea and nervousness occur seldomly.

Burden (see also section E4 of this form):
-no chocolate, cola, coffee or tea during 8 hours prior to the study day and during the study day. It is also not allowed to administer more than 5 units within 48 hours prior to the study day;
-smoking is not allowed during each study day and it is not allowed to smoke more than 5 sigarettes a day within 21 days prior to the study;
-use of adequate contraceptives during the study and 3 months after the sudy;
-use of alcohol is not allowed during 24 hours prior to the study day and during the study day. Male subjects are not allowed to consume more than 28 units a week and female subjects are not allowed to consume more than 21 units a week;
-go to bed not more than one hour earlier or one hour later than usual for the 2 nights prior to each study period.
-subjects have to wear the actigraph during 24 hours prior to the study day.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Provision of written informed consent
2. Healthy male and female subjects aged 18 to 45 years or 65-85 years on sceening
3. Body Mass Index (BMI) >= 19 and <= 30 kg/m2

Exclusion criteria

1.Investigator site personnel or Lilly employees directly affiliated with this study and their immediate families. Immediate family is defined as a spouse, parent, child or sibling, whether biological or legally adopted.
2.Shift workers (those who shifted work within 7 days of any study night) or any person who has crossed (or will have crossed) more than one time zone by aircraft

within 3 days prior to each study night.
3.Rhinoconjunctivitis, urticaria, chronic pain or nocturia that, in the investigator*s opinion, would interfere with sleep assessment.
4.Previously diagnosed sleep disorder including chronic insomnia, sleep apnea, narcolepsy or restless leg syndrome, or current symptoms consistent with a sleep disorder.
5.Insomnia caused by a psychiatric, neurological or medical disease within the past 12 months.
6.Irregular or altered sleep/wake schedule interpreted by the investigator.
7.History of loss of consciousness due to explained or unexplained syncope or orthostatic signs and symptoms such as dizziness, tachycardia or hypotension. History of loss of consciousness due to cranial trauma will be discussed prior to including any such subject (See Section 6.4.1.3 for orthostatic measurement procedure).
8.Known history of epilepsy (except a single febrile convulsion) or a family history of seizures.
9.Use of prescription, over the counter or herbal medications (other than oral contraceptive treatment or hormonal replacement therapy) that can safely be discontinued within 21 days prior to enrollment. Subjects over 65 yrs of age, on a stable dose (>= 3 months prior to screening) of one medication for lowering cholesterol, triglycerides and/or one medication for lowering blood pressure and/or substitutive hormonal therapy in post menopausal women are allowed provided those treatments have no clinically significant central nervous system adverse effects. See Section 5.6 Concomitant Therapy, for sample list of acceptable medication.
10.Enrolment in another concurrent investigational study or intake of an investigational drug within 3 months prior to the start of the study or more than 4 times a year.
11. Known allergies or contraindications to LY2624803, zolpidem, diphenhydramine or related compounds.
12.Persons who have previously completed or withdrawn from this study or any other study investigating LY2624803 or HY10275
13.An abnormality in the 12-lead ECG that, in the opinion of the investigator, increases the risks associated with participating in the study.
14.History or presence of clinically significant cardiovascular, respiratory, hepatic, renal, gastrointestinal, endocrine, haematological, neurocardiogenic or neurological disorders capable of significantly altering the absorption, metabolism, or elimination of drugs; of constituting a risk when taking the study medication; or of interfering with the interpretation of data.
15.Any other condition which in the opinion of the investigator would preclude participation the study.
16.Current regular use (including "recreational uses") of any illicit drugs (including cannabis) confirmed by positive urine drug screen at screening or any study day, or a history of drug or alcohol abuse.
17.Positive Human Immunodeficiency Virus (HIV), hepatitis B or hepatitis C test.
18.Women who are lactating.
19.Blood donation of more than 500 mL within the last 3 months.

20.Subjects who have an average weekly alcohol intake that exceeds 28 units per week (males) and 21 units per week (females), or subjects unwilling to stop alcohol consumption for at least 24 hours prior to admission to the CRU until being discharged from the CRU (1 unit = 12 oz or 360 mL of beer; 5 oz or 150 mL of wine; 1.5 oz or 45 mL of distilled spirits).

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	18-08-2008
Enrollment:	40
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Betadorm-D, 50 mg Tabletten
Generic name:	Diphenhydramine
Product type:	Medicine
Brand name:	LY2624803 1 mg
Generic name:	LY2624803
Product type:	Medicine
Brand name:	LY2624803 3 mg
Generic name:	LY2624803
Product type:	Medicine

Brand name:	Zolpidem Tartrate 10 mg film coated tablets
Generic name:	Zolpidem
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Zolpidem Tartrate 5 mg film coated tablets
Generic name:	Zolpidem
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	04-07-2008
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	18-09-2008
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2008-001929-34-NL
CCMO	NL23384.058.08