A double-blind, randomized, placebo-controlled, double-dummy, four-way crossover study to investigate the drug-drug interactions of almorexant and ethanol in healthy subjects.

Published: 10-12-2008
Last updated: 05-05-2024

- To evaluate if co-administration of single-dose almorexant (200 mg) influences the psychomotor and cognitive impairing effects of ethanol (at a blood level of 0.6 g/L for 5 hours) in healthy subjects.-To evaluate the potential PK interactions...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Sleep disturbances (incl subtypes)
Study type	Observational invasive

Summary

ID

NL-OMON32705

Source
ToetsingOnline

Brief title
A study to investigate the interaction between almorexant and alcohol.

Condition

- Sleep disturbances (incl subtypes)

Synonym
insomia, sleeplessness

Research involving
Human

Sponsors and support

Primary sponsor: Actelion Pharmaceuticals
Source(s) of monetary or material Support: Actelion Pharmaceuticals

Intervention

Keyword: almorexant, ethanol, pharmacodynamics, pharmacokinetics

Outcome measures

Primary outcome

-Saccadic eye movements (saccadic reaction time, saccadic peak velocity, and saccadic inaccuracy) to assess sedation;

-Smooth pursuit eye movements (percentage of time the eyes of the subjects are in smooth pursuit of the target) to assess attention and eye movement coordination;

-Body sway (antero-posterior sway in mm/2min) to assess postural (in)stability;

-Adaptive tracking, to assess visuo-motor control and vigilance;

-Visual Analog Scales (VAS) according to Bond and Lader to assess mood, alertness, and calmness;

-VAS for alcohol intoxication to assess the subjective effects of ethanol;

- Visual verbal learning test to test memory;

- Almorexant and ethanol pharmacokinetics; and

- Safety endpoints (blood pressure, heart rate, electrocardiogram, clinical laboratory tests, (serious) adverse events).

Secondary outcome

-

Study description

Background summary

Almorexant (ACT-078573) is a oral, selective orexin antagonist. Orexin peptides play a central role in the sleep-wake rhythm. Pre-clinical data obtained from animal studies has shown that this drug (almorexant) increases REM and non-REM sleep. Earlier phase I studies in healthy volunteers revealed no serious side effects.

Anatomical and functional evidence suggests that the GABAergic and orexin systems interact. However, clinical evidence for this interaction is limited.
An almorexant and ethanol interaction study investigating the PK and PD effects has strong clinical relevance and is recommended by health authorities for the development of a hypnotic drug.

Study objective

- To evaluate if co-administration of single-dose almorexant (200 mg) influences the psychomotor and cognitive impairing effects of ethanol (at a blood level of 0.6 g/L for 5 hours) in healthy subjects.

-To evaluate the potential PK interactions between single-dose almorexant (200 mg) and ethanol (at a blood level of 0.6 g/L for 5 hours) in healthy subjects.

-To evaluate the safety and tolerability of co-administration of single-dose almorexant (200 mg) and ethanol (at a blood level of 0.6 g/L for 5 hours) in healthy subjects.

Study design

A double-blind, randomized, placebo-controlled, double-dummy, four-way crossover study.

Study burden and risks

Alcohol
The effects of alcohol are well-known and include a drunk feeling, sleepiness, headache or dizziness. In addition, the intravenous ethanol infusion could give local pain or irritation in the beginning of the infusion. This will be avoided by an extra diluting (glucose) infusion.

Almorexant
Double vision, nausea and muscle weakness (during emotional moments or at waking up) have been reported a few times. These symptoms may be frightening

for persons not familiar with them. Some healthy volunteers have reported dry and/or irritated eyes after multiple doses of almorexant.

Alcohol and almorexant combination
Theoretically, alcohol could exacerbate any rare side effects that are caused by almorexant. Rare side-effects of the combination of alcohol and almorexant would therefore be an increase of double vision, nausea and muscle weakness.

Contacts

Public
Actelion Pharmaceuticals

Gewerbestrasse 16
CH-4123 Allschwil
Nederland
Scientific
Actelion Pharmaceuticals

Gewerbestrasse 16
CH-4123 Allschwil
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Signed informed consent prior to any study-mandated procedure.
- Male or female aged between 18 and 65 years (inclusive) at screening.
- Women of childbearing potential must consistently and correctly practice (from screening,

during the entire study, and for at least 1 month after study drug intake) a reliable method of contraception with a failure rate of < 1% per year (such as implants, injectables, combined oral hormonal contraceptives, some intrauterine devices), sexual abstinence, or vasectomised partner. Women not of childbearing potential are defined as postmenopausal (i.e., amenorrhea at least 1 year), or surgically or naturally sterile.
- No clinically significant findings on the physical examination at screening.
- Body mass index (BMI) between 18 and 30 kg/m2 (inclusive) at screening.
- Systolic blood pressure (SBP) 100-145 mmHg, diastolic blood pressure (DBP) 50-90 mmHg, and heart rate (HR) 45-90 bpm (all inclusive), measured on the leading arm, after 5 minutes in the supine position at screening.
- 12-lead electrocardiogram (ECG) without clinically relevant abnormalities at screening.
- Hematology and clinical chemistry results not deviating from the normal range to a clinically relevant extent at screening.
- Negative results from urine drug screen at screening.
- Ability to communicate well with the investigator in the local language, and to understand and comply with the requirements of the study.

Exclusion criteria

- Known hypersensitivity to any excipients of the drug formulations.
- Previous treatment with any prescribed or over-the-counter (OTC) medications (including herbal medicines such as St John*s Wort) within 7 days prior to screening except for contraceptives for females.
- Treatment with another investigational drug within 3 months prior to screening or having participated in more than 4 investigational drug studies within 1 year prior to screening.
- History or clinical evidence of alcoholism or drug abuse within the 3-year period prior to screening.
- History of regular alcohol consumption within 6 months of the study defined as an average weekly intake of greater than 21 units or an average daily intake of greater than 3 units (males), or defined as an average weekly intake of greater than 14 units or an average daily intake of greater than 2 units (females). One unit is equivalent to a half-pint (220 mL) of beer or 1 (25 mL) measure of spirits or 1 glass (125 mL) of wine.
- Excessive caffeine consumption, defined as >= 800 mg per day at screening.
- History or clinical evidence of any disease, and/or existence of any surgical or medical condition, which might interfere with the absorption, distribution, metabolism or excretion of the study drugs.
- Smoking within 3 months prior to screening and inability to refrain from smoking during the course of the study.
- Loss of 250 mL or more of blood within 3 months prior to screening.
- Positive results from the hepatitis serology, except for vaccinated subjects, at screening.
- Positive results from the HIV serology at screening.
- Pregnant females as determined by positive urine hCG test at screening or prior to dosing.
- Breast-feeding females.
- Individuals of Asian descent or other individuals reporting ethanol intolerance (Asian descent defined as: either the individual, or 1 or more parent or grandparent of Asian origin).

- Any circumstances or conditions, which, in the opinion of the investigator, may affect full participation in the study or compliance with the protocol.
- Legal incapacity or limited legal capacity at screening.

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:	Recruitment stopped
Start date (anticipated):	04-02-2009
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Almorexant
Generic name:	Almorexant
Product type:	Medicine
Brand name:	ethanol
Generic name:	alcohol

Ethics review

Approved WMO

Date:	10-12-2008

Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	30-01-2009
Application type:	First submission
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	EUCTR2008-005844-18-NL
CCMO	NL26058.058.08