Double-blind, placebo- and active-controlled, randomized, single-ascending dose study to investigate the tolerability, safety, pharmacokinetics, and pharmacodynamics of ACT-462206 in healthy male subjects

Published: 07-10-2011
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- To evaluate the safety and tolerability of ascending single oral doses of ACT-462206 in healthy male subjects.- To investigate the single oral dose PK and PD of ACT-462206 in healthy male subjects.- To investigate dose proportionality across...

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

Summary

ID

NL-OMON35433

Source
ToetsingOnline

Brief title
First-in-man study of single, ascending doses of ACT-462206

Condition

- Sleep disturbances (incl subtypes)

Synonym
insomnia, sleep disturbance

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Dual orexin receptor antagonist, first-in-human

Outcome measures

Primary outcome

Safety:

- Vital signs (heart rate, blood pressure) and body weight

- ECG variables

- Changes in blood- and urine tests

- Occurence of (serious) adverse events

Pharmacokinetics:

- Cmax, Tmax, t1/2

- AUC

- dose-proportionality

Pharmacodynamics:

- Saccadic peak velocity

- Body sway

- Adaptive tracking

- VAS Bond and Lader

Secondary outcome

Pharmacokinetics:

- renal clearance

- percentage of dose excreted unchanged in urine

Study description

Background summary

In this study we investigate the effect of a new investigational drug (ACT-462206) on the body, during this study it will be the first time that it will be given to humans. The drug is being developed for the treatment of sleep disturbances and works via orexin. Orexin is a substance that is produced in the brain and plays a role in the sleep- wake cycle and alertness. ACT-462206, blocks temporarily the action of orexin. Laboratory animals that have been administered ACT-462206 fell asleep after taking it, but cou ld easily wake up (in contrast to other sleep medications) and then function normally.

Study objective

- To evaluate the safety and tolerability of ascending single oral doses of ACT-462206 in healthy male subjects.
- To investigate the single oral dose PK and PD of ACT-462206 in healthy male subjects.
- To investigate dose proportionality across different doses of ACT-462206.

Study design

Double-blind, placebo and active-controlled, randomised study with single-ascending doses.

Intervention

Single dose of ACT-462206, almorexant, or placebo.

Study burden and risks

The side-effects that are expected for ACT-462206 and Almorexant are associated with its sleep-promoting potential and consist of somnolence, dizziness,

fatigue and reduced vigilance.

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

- Signed informed consent prior to any study-mandated procedure.;- Healthy male subjects aged between 18 and 45 years (inclusive) at screening.;- Hematology, clinical chemistry, and urinalysis results not deviating from the normal range to a clinically relevant extent at screening.;- No clinically significant findings on physical examination at screening.;- Body mass index (BMI) between 18.0 and 28.0 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 (inclusive) measured at screening on the dominant arm after 5 minutes in supine position.;- 12-lead electrocardiogram (ECG) without clinically relevant abnormalities in supine position 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

- Previous history of fainting, collapse, syncope, orthostatic hypotension, or vasovagal reactions.;- Veins unsuitable for intravenous (i.v.) puncture on either arm (e.g., veins that are difficult to locate, access or puncture, veins with a tendency to rupture during or after puncture).;- Treatment with any prescribed medications (including vaccines) or over-the-counter (OTC) medications (including herbal medicines such as St John*s Wort) within 2 weeks prior to (first) study drug administration.;- Treatment with another investigational drug within 3 months prior to screening or having participated in more than four 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 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.;- Excessive caffeine consumption, defined as >= 800 mg per day at screening.;- Smoking within 3 months prior to screening and inability to refrain from smoking during the course of the study (from screening to End-of-Study [EOS]).;- Loss of 250 mL or more of blood, or an equivalent amount of plasma, within 3 months prior to screening.;- Positive results from the hepatitis serology, except for vaccinated subjects or subjects with past but resolved hepatitis, at screening.;- Positive results from the HIV serology at screening.;- Known hypersensitivity to any excipients of the drug formulations.;- Modified Swiss Narcolepsy Scale total score < 0 or history of narcolepsy or cataplexy. ;- 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:	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):	14-11-2011
Enrollment:	64
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ACT-462206
Generic name:	ACT-462206
Product type:	Medicine
Brand name:	Almorexant
Generic name:	Almorexant

Ethics review

Approved WMO Date:	07-10-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-11-2011
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	EUCTR2011-003752-39-NL
CCMO	NL38094.056.11