A phase 1, single centre, single dose, double-blind, double-dummy, four-way crossover, placebo-controlled, randomized study to investigate the effects of AZD7325 on sedation, cognition and EEG in comparison with lorazepam in healthy male volunteers.

Published: 08-05-2008
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This study is being performed to document the effects of the new compound AZD7325 on brain functions and to investigate whether it has fewer side-effects compared lorazepam.

Ethical review	Approved WMO
Status	Pending
Health condition type	Anxiety disorders and symptoms
Study type	Observational invasive

Summary

ID

NL-OMON32334

Source
ToetsingOnline

Brief title
Effects of AZD7325 on sedation, cognition and EEG.

Condition

- Anxiety disorders and symptoms

Synonym
anxiety, anxiety disorders

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: anxiolytic, cognition, sedation

Outcome measures

Primary outcome

To investigate the pharmacodynamic (PD) effects of single oral doses of AZD7325

on sedation and cognition in comparison with lorazepam, a widely used

non-selective GABA-A modulator for anxiolysis.

Secondary outcome

1. To evaluate the safety and tolerability of AZD7325 by assessing adverse

events, vital

signs, laboratory parameters, and ECGs.

2. To measure the effects of single oral doses of AZD7325 with

electroencephalogram (EEG)

and to assess whether the EEG power spectral changes of AZD7325 seen in animal

studies

are observed in humans.

3. To determine the effects of single oral doses of AZD7325 on body sway and to

compare

its effects to those of lorazepam.

4. To investigate the pharmacokinetic (PK) profile of AZD7325 after single oral

doses

administration. Mathematical PK/PD modelling to correlate the relationships

between

plasma concentration and effects for changes in CNS measurements will be

attempted.

Study description

Background summary

AZD7325 is a new investigational drug that is being developed for the treatment of anxiety disorders. The drug has not yet been registered in the Netherlands. Compared to the drugs presently on the market, it acts more selectively in the brain. It is therefore expected that AZD7325 will cause fewer side effects than the current drugs. Lorazepam is an example of such a drug that has already been registered for a number of years in the Netherlands. It belongs to the group of benzodiazepines. These drugs are used by physicians to treat people with anxiety disorders. Benzodiazepines are effective against anxiety. However, they cause unwanted side effects such as sleepiness and memory and concentration difficulties.

Study objective

This study is being performed to document the effects of the new compound AZD7325 on brain functions and to investigate whether it has fewer side-effects compared lorazepam.

Study design

A phase 1, single centre, single dose, double-blind, double-dummy, four-way crossover, placebo-controlled, randomized study to investigate the effects of AZD7325 on sedation, cognition and EEG in comparison with lorazepam in healthy male volunteers.

Study burden and risks

Study drug side-effects
AZD7325
The most frequently occurring side effects in study in animals and humans are feeling *high*, sleepiness, dizziness and numbness. All side effects were of

moderate severity and disappeared spontaneously within hours. AZD7325 has been tested before in healthy males up to a maximum dose of 100 mg per day and was well tolerated.

Lorazepam
Lorazepam is a sedative used for the treatment of anxiety disorders and tension in general. Some side effects of lorazepam may be sleepiness, dizziness and loss of memory.

Rare side-effects
Lorazepam:
Lorazepam is a registered drug. The risk of unforeseen side-effects is therefore not greater than with other drugs. Muscle weakness, headache, forgetfulness and intestinal disturbances occur seldomly.

AZD7325:
Until now the drug has been tolerated well and no dangerous side-effects have been reported. Blood pressure decrease, increased heart beat, slow respiration and confusion have incidentally been reported and may therefore occur.

Burden (see also section E4 of this form):
- No coffee/tea/chcolate at 22h00 prior to and during each study day;
- Refrain from smoking from 22h00 prior and during each study day;
- No alcohol use 24h prior and during each studie day;
- Refain from physical examination 72h prior and during each study day;
- Refrain from eating and drinking from 22h00 prior each study day. No grapefruit allowed from 7 days prior and during each study day;
-Use of contraception during the study and 3 months after the study;
-No blood donation for 3 months after the study.

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

1. Provision of written informed consent
2. Healthy male subjects aged 18 to 55 years (extremes inclusive) on sceening
3. Body Mass Index (BMI) >= 18 and <= 30 kg/m2

Exclusion criteria

1. Clinically relevant disease and/or abnormalities (past or present) which in the opinion of the investigator, may either put the subject at risk to participate in the study or may influence the results of the study or the subject*s ability to participate in the study
2. Psychiatric, medical, and surgical history that may interfere with the objectives of the study
3. Subject*s partner is planning pregnancy within 3 months of last dosing
4. Significant illness, as judged by the investigator, within 2 weeks of the first study day
5. Clinically relevant abnormalities in physical examinations, vital signs, clinical chemistry, thyroid function test, hematology or urinalysis at screening as judged by the investigator and/or sponsor
6. ECG with a QTcF interval of >450 or <360msec at screening
7. History of clinically significant arrhythmias (including II degree atrioventricular block and Wolff-Parkinson-White Syndrome)
8. Any other clinically significant abnormal baseline ECG and/or abnormalities in ECG as judged by the investigator and/or sponsor at the screening visit
9. Positive human immune deficiency virus (HIV), Hepatitis B or Hepatitis C test
10. Current manifestation of any clinically significant allergic disorder with the exception of seasonal allergies
11. Use of any medication or herbal preparation within 14 days of the first study day through the Follow-up Visit other than paracetamol (up to 3g/day) and incidental use of prescription or non-prescription medication approved by the investigator.

12. Enrollment 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.
13. Donation of blood in the past 3 months.
14. Smoking in excess of 5 cigarettes per day or the equivalent within 28 days prior to the first study day or inability to refrain from smoking from 22:00 prior to each study day
15. Current regular user (including *recreational uses*) of any illicit drugs or history of drug or alcohol abuse. Subjects who have a positive drug screen at screening are excluded.
16. Involvement in the planning and conduct of the study (applies to both AstraZeneca staff and staff at the CPU)
17. Prior randomization in a trial with AZD7325
18. Inability to understand or cooperate with the requirements of this study

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):	02-06-2008
Enrollment:	16
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Product type:	Medicine
Generic name:	lorazepam
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	08-05-2008
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	EUCTR2008-001756-51-NL
CCMO	NL22758.058.08