A randomized long-term safety study of Org 50081 in elderly outpatients with chronic primary insomnia examining the effects of 1.5 mg or 3.0 mg of Org 50081

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Primary • To investigate the safety and tolerability of long-term treatment with 1.5 mg or 3.0 mg of Org 50081 in elderly outpatients with chronic primary insomnia. Secondary • To collect exploratory efficacy data of long-term treatment with Org...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON31525

Source
ToetsingOnline

Brief title
JADE

Condition

- Other condition

Synonym
insomnia, sleeplessness

Health condition

slaapstoornissen

Research involving

Human

Sponsors and support

Primary sponsor: Organon Nederland BV
Source(s) of monetary or material Support: door de opdrachtgever

Intervention

Keyword: efficacy, elderly, insomnia, safety

Outcome measures

Primary outcome

To investigate the safety and tolerability of long-term treatment with 1.5 mg

or 3.0 mg of Org 50081 in elderly outpatients with chronic primary insomnia.

Secondary outcome

To collect exploratory efficacy data of long-term treatment with Org 50081 in

elderly outpatients with chronic primary insomnia.

Study description

Background summary

Org 50081 is the maleate salt of the S-enantiomer (Org 4420) of the racemic mixture mirtazapine. Several preclinical and clinical studies have demonstrated sleep-promoting effects of mirtazapine. Increases in sleep efficiency, increases in total sleep time and slow wave sleep, and shorter sleep latency have been observed in patients with major depressive disorder, primary insomnia and in healthy subjects. A dose-finding trial with Org 50081 has been performed in 60 patients with primary insomnia to demonstrate superiority of treatment with Org 50081 compared to placebo on Total Sleep Time as measured by polysomnography. Secondary objectives were to investigate dose-response, safety and tolerability and hangover effects after two days of treatment with Org 50081. The fact that sleep promoting effects of Org 50081 may be primarily related to deep stages of sleep and are exerted through a different pharmacological action than that of benzodiazepines makes these effects interesting from both a pharmacological and clinical point of view. Worldwide, most sleep promoting medicines used in clinical practice act at the

benzodiazepine receptor site. Adverse drug reactions related to benzodiazepines, such as tolerance, dependence, addiction, withdrawal and rebound phenomena, have led to a steady decline in the prescription of benzodiazepine hypnotics over the last decade6. Consequently, pharmacotherapy has shifted gradually from classical benzodiazepines to new benzodiazepine agonists such as zolpidem or zaleplon. Since the newer hypnotics also exert their mode of action via the GABA system, they are still associated with abuse potential and have been shown to promote the risk of addiction. Unlike other hypnotics currently available, Org 50081 does not exert its action through the GABA receptors. Org 50081 is not expected to have abuse potential. Over the past 10 years, there has been an increasing use of sedating antidepressants for the symptomatic treatment of insomnia, despite the paucity of data on the efficacy of these drugs in treating insomnia. Tricyclic antidepressants, trazodone, nefazodone and mirtazapine are considered to be pharmacotherapeutic candidates for treating insomnia though they are not approved for this indication.

Study objective

Primary • To investigate the safety and tolerability of long-term treatment with 1.5 mg or 3.0 mg of Org 50081 in elderly outpatients with chronic primary insomnia.
Secondary • To collect exploratory efficacy data of long-term treatment with Org 50081 in elderly outpatients with chronic primary insomnia.

Study design

This trial is a 52-week, randomized, parallel group investigation of the dose-related safety and tolerability of Org 50081. Subjects and investigators will be blinded to the dose of Org 50081.
Subjects will be selected on the basis of a screening process (14 days), during which the trial selection criteria should be fulfilled. During this screening period, the subjects will be trained on the LogPad at both Days -14 (Visit 1) and -7 (Visit 2). In the 2 weeks following the Day -14 visit, subjects will practice using the LogPad by daily completing a practice sleep diary on the device. This practice sleep diary, completed daily, is very similar to the once-weekly version, which is used throughout the trial. To be eligible, subjects must have demonstrated capacity to independently complete the LogPad questionnaires in the week preceding Day 1. The practice diary data from the LogPad may be used at a later stage to compare weekly versus daily assessments of sleep parameters.
If eligible, subjects will be randomized in a double-blind manner to 1.5 mg or 3.0 mg of Org 50081 at Day 1 (Visit 3). The treatment duration will be 364 days (52 weeks) and the first dose of trial medication will be administered in the evening of Day 1. During the first month of the trial, subjects will have visits at the end of Weeks 1 (Visit 4), 2 (Visit 5), and 4 (Visit 6).

Following the Week 4 visit, the visit frequency will be every 4 weeks. Patients should adhere to the visit schedule, but deviations of ±1 day are allowed until Visit 6. From Visit 6 onwards, for the event that it is not possible to maintain the visit schedule, a deviation of ±5 days is allowed. The sleep diary will be recorded weekly from Day 1 onwards until Week 52 (Visit 18; see Table 1). The sleep diary will assess subjective sleep parameters, alertness, daytime functioning, energy level and napping in the past 7 days. The ratings on the weekly sleep diary, collected at Day 1, will be used as baseline data. A follow-up visit will take place on Day 372 (Visit 19), 7 days after completion of the active treatment period, or 7 days after premature discontinuation. Unresolved (S)AEs will be followed up until resolved. A telephone call should be scheduled 30 days after the last intake of active treatment (i.e., Day 395 for trial completers) to follow up on any SAE occurring after the follow-up visit.

Study burden and risks

Subjects will be treated during 52 weeks with 1.5 mg or 3.0 mg of Org 50081. The discomfort consists mainly out of 19 visits to the clinic (3 weeks after the 19th visit the subject will be contacted by telephone to follow up on any SAEs occurring after the follow up visit (19th)). Electronic diary, questionnaires, urine- and bloodsamples, physical examinations and ECGs. The subjects will get extensively check ups, a lot of information and a compensation for costs for time, eventual discomforts and traveling.

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

At least 65 years of age at screening.;Have documented diagnosis of chronic primary insomnia with a duration of >_ 1 month.;Are able to speak, read and understand the language of the investigator, study
staff (including raters) and the informed consent form, and possess the ability to respond to questions, follow instructions and complete questionnaires.;Have demonstrated capability to independently complete the LogPad
questionnaires in the week preceding randomization;

Exclusion criteria

have other sleep disorders;have any significant medical or psychiatric illness causing sleepdisturbances;have any significant medical or DSM-IV-TR psychiatric illness causing the sleep
disturbances;;currently meet diagnostic criteria for DSM-IV-TR depression (MDD) or have been
diagnosed and treated for MDD within the last 2 years;;have signs of dementia or other serious cognitive impairment, defined by a score
of less than 26 on the Mini-Mental State Examination (MMSE);;have a history of bipolar disorder, a history of suicide attempt or a family history
of suicide;

Study design

Design

Study phase:	3
Study type:	Observational invasive

Intervention model:	Parallel
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-02-2008
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nog niet bekend
Generic name:	esmirtazapine maleate

Ethics review

Approved WMO Date:	22-10-2007
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-01-2008
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-09-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-09-2008

Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-10-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-11-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-06-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2007-003636-35-NL
CCMO	NL19414.040.07
Other	zie www.organon-trials.com