A 6-month, double-blind, randomized, placebo-controlled, parallel group outpatient trial, investigating the efficacy and safety of Org 50081 in adult patients with chronic primary insomnia.

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Primary: To demonstrate the long-term efficacy of treatment with Org 50081, as compared to placebo, on sleep maintenance in patients with chronic primary insomnia as measured by the subjective Total Sleep Time. Primary efficacy endpoint is the...

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

Summary

ID

NL-OMON33796

Source
ToetsingOnline

Brief title
AQUAMARINE

Condition

- Other condition

Synonym
insomnia, sleeplessness

Health condition

slaapstoornissen

Research involving
Human

Sponsors and support

Primary sponsor: Schering-Plough
Source(s) of monetary or material Support: door de opdrachtgever

Intervention

Keyword: Adult, Efficacy, Insomnia, Safety

Outcome measures

Primary outcome

To demonstrate the long-term efficacy of treatment with Org 50081, as compared to placebo, on sleep maintenance in patients with chronic primary insomnia as measured by the subjective Total Sleep Time. Primary efficacy endpoint is the average of subjective Total Sleep Time (TST) during month 4 to month 6, as recorded daily in the sleep diary.

Secondary outcome

To demonstrate the long-term efficacy of Org 50081 in improving sleep latency (SL)

To investigate the long-term efficacy of Org 50081 on other sleep maintenance parameters WASO, NAW and on sleep quality and satisfaction with sleep duration

To investigate the long-term safety and tolerability of Org 50081, as compared to placebo

To investigate the effects of discontinuation of Org 50081 after long-term treatment

To explore the effect of Org 50081 on functional and quality of life outcomes

as compared to placebo

Study description

Background summary

Org 50081 is the maleate salt of the S-enantiomer (Org 4420) of the racemic mixture mirtazapine. Several preclinical and clinicial 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 beeen 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 form both a pharmacological and clincal 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 decade. Consequently, pharmacotherapy has shifted gradually from classical benzodiazepines to new benzodiazepine agonists such as zolpidem or zaleplon. Since the newer hypnotics als 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 demonstrate the long-term efficacy of treatment with Org 50081, as compared to placebo, on sleep maintenance in patients with chronic primary insomnia as measured by the subjective Total Sleep Time. Primary efficacy endpoint is the average of subjective Total Sleep Time (TST) during month 4 to

month 6, as recorded daily in the sleep diary.

Study design

This trial is a 6-month, double bllind, placebo-controlled, randomized, multi-center, international, parallel group investigation of the efficacy and safety of 4.5 mg Org 50081 with single-blind placebo run-in and a double-blind 7 day discontinuation period after 6 months of treatment in patients with chronic primary insomnia.
Subjects will be selected on the basis of a screening process (7-20 days), during which the trial selection criteria should be fulfilled. During this screening period the subjects receive single-blind placebo. When eligible, subjects will be randomized in a double-blind manner to 4.5 mg of Org 50081 or placebo at a ratio of 3:1 on Day 1.
At the end of the 6-month double-blind treatment period, Org 50081 treated subjects will be re-randomized to receive double-blind treatment of either Org 50081 or placebo at a 1:2 ratio, respectively for additional 7 days. The placebo treated subjects, will continue to receive double-blind placebo for these additional 7 days.

Subjects who have completed Trial 21106 and are willing, will be asked to participate in the long-term open label extension trial 176003. These subjects, provided they meet the entry criteria, will continue with trial 176003 immediately after the 7-day discontinuation period of trial 21106 is complete.

For subjects not participating in the open label extension study 176003, 7 days after the double-blind discontinuation assessment period or after discontinuing prematurely, a follow up visit will be conducted to assesss AEs that had occured after treatment discontinuation. This visit will be followed by a telephone contact 30 days after the discontinuation period to follow-up on any SAEs occruing after the 7 day follow up visit.

Study burden and risks

Subjects will be treated during 6 months with 4.5 mg Org 50081 or placebo. The discomfort consists mainly out of 11 visits to the clinical (30 days after the 11th visit the subject will be contacted by telephone to follow up on any SAEs occuring after the follow up visit (11th). Electronic diary, questionnaires, urine and bloodsamples, physical examiniation 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

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

At least 18 and less than 65 years of age
Have a 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 and have completed the dialy morning questionnaires at least 6 out of 7 days in the week preceding randomisation

Exclusion criteria

Have other sleep disorders
Have any significant medical or DSM-IV-TR psychiatric illness causing the sleepdisturbances
Currently meet diagnostic criteria for DSM-IV-TR depression (MDD) or have been diagnosed

and treated for MDD within the last 2 years
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
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-05-2008
Enrollment:	16
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	30-01-2008
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	07-03-2008
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:	16-09-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-01-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-01-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-03-2009
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	EUCTR2007-005236-92-NL
CCMO	NL21164.040.08
Other	zie www.organon-trials.com