Efficacy of agomelatine 25 mg/day (with possible increase to 50 mg/day after 8 weeks of treatment) given orally during 16 weeks in patients with Obsessive-Compulsive Disorder.A randomised, double-blind, placebo-controlled, parallel groups, international study.

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Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON34855

Source
ToetsingOnline

Brief title
Efficacy of agomelatine in Obsessive-Compulsive Disorder

Condition

- Other condition

Synonym
Obsessive Compulsive Disorder

Health condition

psychiatrische en obsessieve en compulsieve stoornissen

Research involving
Human

Sponsors and support

Primary sponsor: Servier R&D Benelux
Source(s) of monetary or material Support: Institut de Recherches Internationales Servier

Intervention

Keyword: agomelatine, antidepressant, Obsessive-Compulsive Disorder, placebo

Outcome measures

Primary outcome

Y-BOCS total score (expressed as the change from baseline to last post-baseline

value on W0-W16 period) will be used to demonstrate the superiority of

agomelatine compared to placebo on OC symptoms.

Secondary outcome

- National Institute of Mental Health-Obsessive-Compulsive Scale score (NIMH-OC)

- CGI Severity of Illness and Global Improvement scores

- Obsessive Compulsive Visual Aanalogue Scale (OC-VAS)

- Montgomery and Asberg depression rating scale (MADRS) total score

- Hamilton Rating Scale for Anxiety (HAM-A) total score

- Getting off to sleep score, Quality of sleep score, Sleep awakening score and

Integrity of behaviour score obtained from the Leeds Sleep Evaluation

Questionnaire (LSEQ).

- Work, Social life and Family life scores obtained from Sheehan disability

scale

- Adverse events

- Sitting blood pressure (SBP (mmHg) and DBP (mmHg)) and heart rate (bpm).

- Body weight (kg) and BMI (kg/m²).

- Laboratory parameters.

Study description

Background summary

Obsessive-compulsive disorder (OCD) is a severe, chronic and disabling disorder that affects 2 to 4% of the population.
Serotonin reuptake inhibitors (SRIs) are the first line pharmacotherapy for OCD and the only drugs approved by Health Authorities for the treatment of OCD. Approximately 40% to 60% of the OCD patients are improved by a pharmacotherapy with SRI.
The response to these products is only partial with a reduction of 20% to 40% on the Y-BOCS.
The new antidepressant agomelatione has a distinct neurochemical profile. It is a melatoninergic agonist and 5HT2C antagonist. The mechanism of action does not imply 5-HT reuptake inhibition but some properties of agomelatine support its potential interest as an alternative in the treatment of OCD patients.
Pre-clinical and clinical data have shown the involvement of 5-HT2C receptors in the pathophysiology of OCD. Also circadian rhythms and sleep are frequently altered in those patients . Agomelatine directly resets the electrical activity of the suprachiasmatic nucleus and thus resynchronises experimentally disrupted circadian rhythms. Besides its antidepressant activity, agomelatine showed an early improvement of sleep disorders in depressed patients.

Study objective

The primary objective of the study is to evaluate the efficacy of agomelatine (25-50 mg/day) compared to placebo on the reduction of Obsessive and Compulsive symptoms by using the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) after 16 weeks of treatment in patients fulfilling DSM-IV-TR criteria for OCD .

Study design

A 16 week randomized , double blind placebo-controlled international phase II

study with parallel arms. The dose of agomelatine is flexible (25mg/day with possible increase to 50 mg/day after 8 weeks of treatment). 80 patients will be included in the study (40 patients per arm). The expected duration of the study for a patient is maximum 17 weeks + 10 days.
The study will be divided into the following periods:

- A run-in period without treatment (maximum 10 days between Selection and Inclusion visits).
- A double-blind treatment period of 16 weeks (from W0 to W16).
- A follow-up period of 1 week without treatment after the end of the double-blind period or in case of premature withdrawal.

Intervention

4 bloodsamples will be taken during the study for haematology and biochemistry (at selection, W8,W12,W16). The total amount will not exceed 60ml. An ECG needs to be performed during selection or inclusion visit. anyway the results need to be available for inclusion.
Saliva samples need to be taken for pharmacokinetics at W8 and W12, 1, 2 and 3 hours after intake of the study drug.

Study burden and risks

cfr E2 and E9

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

- Out patients, male or female, between 18 and 65 years inclusive with a primary diagnosis of Obsessive Compulsive Disorder (OCD) according to DSM-IV-TR. The diagnosis will be documented by the brief structured interview M.I.N.I.
- Patients previously treated for OCD with a first line pharmacological treatment, i.e, SRI with or without cognitive behavioural therapy .
- Y-BOCS total score * 20 (moderately to severely ill),
- Duration of OCD symptoms of at least one year,
- Requiring a treatment.

Exclusion criteria

cfr p. 25-26
- Episodic OCD, Exclusive hoarders, Early onset OCD
- Refractory patients defined as having not responded to 2 or more adequate treatments (medium or high) dose of a SRI for at least 12 weeks.
- Patients in psychiatric care for more than 5 years for OCD
- Naïve Patients (never received pharmacological treatment for OCD)
- Motor or verbal tic disorder (including Tourette*s),
- Substance or alcohol dependence or abuse
- personality disorders
- Severe or uncontrolled organic diseases, likely to interfere with the conduct of the study (e.g., neurologic, neoplasic, cardiovascular, pulmonary, digestive or metabolic disorders like unstabilized diabetes of type I or II, morbid obesity, untreated or uncontrolled arterial hypertension*),
- Any clinically relevant abnormality detected during the physical examination, ECG or laboratory tests likely to interfere with the study conduct or evaluation,
- Hepatic impairment (i.e. cirrhosis or active liver disease),
- ASAT or ALAT values * 2 times the upper reference value
- Total bilirubin * 2 times the upper reference value or ALAT and total bilirubin >ULN
- Alkaline Phosphatase * 3 times the upper reference value,
- Women of childbearing potential without effective contraception (oral contraceptive pill,

Intra-uterine contraceptive device or condom) as well as
- pregnant or breastfeeding women
- Concomitant psychotropic medications are forbidden during the study.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	15-04-2010
Enrollment:	15
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	valdoxan
Generic name:	agomelatine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	26-03-2010
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-12-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-09-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-05-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-11-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2009-016713-20-NL
CCMO	NL31624.018.10