An eight-week, multinational, multicenter, double-blind, active- and placebo-controlled clinical trial evaluating the efficacy and tolerability of three fixed doses of SSR125543 (20mg daily, 50 mg daily and 100 mg daily) in outpatients with major depressive disorder.

Published: 20-11-2009
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The objective of the study is to evaluate various doses of SSR125543 in first patients (outpatients with a major depressive disorder), evaluate collected information concerning tolerability, efficacy en safety. The same infomation will be evaluated...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Mood disorders and disturbances NEC
Study type	Interventional

Summary

ID

NL-OMON34958

Source
ToetsingOnline

Brief title
AGATE

Condition

- Mood disorders and disturbances NEC

Synonym
depression, depressive disorder

Research involving
Human

Sponsors and support

Primary sponsor: Sanofi-aventis
Source(s) of monetary or material Support: sponsor

Intervention

Keyword: Active- and placebo controlled, Ambulant, Dose ranging, Major depressive disorder

Outcome measures

Primary outcome

The primary objective is to evaluate the efficacy of three fixed doses of

SSR125543 compared to placebo in outpatients with major depressive disorder, as

assessed by the change from baseline (Day -1) to Day 56 in the 17-item HAM-D

t(Hamilton depression) total score.

Secondary outcome

The secondary objectives are to evaluate the tolerability and safety of

SSR125543 in outpatients with major depressive disorder. To evaluate plasma

concentrations of SSR125543.

An optional substudy concerning biomarkers is proposed to evaluate the

influence of genetic and protein biomarkers on the variability of the

therapeutic responses and to evaluate the metabolism of the investigational

product.

Study description

Background summary

CRF (corticotripin releasing factor) is a substance produced in a very specific zone of the brain (the hypothalamus). After CRFbinded at specific receptors (CRF-receptors), it gives various responses in the organism. CRF is excreted in case of stress. The purpose of this excretion is coordinate the total of responses (endrocrine, immune, periferal nervous system, behaviour, ..) to be ready for a good response.
Extensive literature suggests that the "CRF-circuit" (production, activation of the receptors,..) unusually active is at affective and anxiety disorders and that CRF plays a causative role. Additional evidence suggests that particular CRF receptors, the CRF1 receptors, mediate anxiety and depression-like behaviours. These data suggest that a CRF1 antagonist may have efficacy in the treatment of affective and anxiety disorders in man. At the moment, there is no other medicine with this characterics registered in the indication anxiety or depressive disorders, but this research domain is very active because they will expand the therapeutic possibilities for patients.
SSR125543 is in clinical development and is a CRF-type 1 receptor antagonist (=blocking). Numerous preclinical test with this subtance were performed. Because the results were promissing, the clinical development was started. Until this moment only healthy volunteers were admistered with SSR125543 (Fase I) in order to investigate which doses are the most effective.

Study objective

The objective of the study is to evaluate various doses of SSR125543 in first patients (outpatients with a major depressive disorder), evaluate collected information concerning tolerability, efficacy en safety. The same infomation will be evaluated for patients who receive placebo or the active comparator (escitalopram) for which it is proven to be effective in this disorder.

Study design

- 1 week "screening" without treatment
- 8 weeks "dubbel-blind" treatment
- 2 weeks follow-up
In total 11 weeks study per patient.

Intervention

In this study, patients receive one of the following treatments:
- SSR125543 1 capsule at a dose of 20 mg + 1 capsule placebo;
- SSR125543 1 capsule at a dose of 50 mg, + 1 capsule placebo;

- SSR125543 2 capsule at a dose of 50 mg;
- 2 capsules of placebo
- Escitalopram 1 capsule at a dose of 10 mg, + 1 capsule placebo. Escitalopram (= active substance, class: selective serotonin reuptake inhibitor (SSRI)).

Study burden and risks

During this 11 week clinical trial, the patient will visit the research site 8 times. The following procedures will be performed:
- 10 x bloodsampling (1 x hepatitis screen, 2 x pregnancy test, 4 x hormone profile, 6 x monitoring serum cortisol, 6 x standard hematology, biochemistry and coagulation test)
- 8 x measurement heartrate
- 8 x temperature measurement (oral)
- 1 x measurement lenght
- 2 x measurement weight
- 1 x drug screen
- 2 x pregnancy test (for women only, if applicable)
- 4 x ECG

The following questionnaires will be assessed by the investigator:
1 x DSM-IV/MINI
8 x C-SSRS
8 x HAMD
7 x CGI
3 x MADRS

The following questionnaires will be answered by the patient (self-assessment):
- DESS (Discontinuation-emergent signs and symptoms scale) - from visit 7 to visit 8, every two days
- SHEEHAN (SHEEHAN disability scale) - 2 x
- ETISR-SF (Early Trauma Inventory Self Report - Short Form) - 2 x
- PHQ-15 (Patient Health Questionnaire-15) - 2 x

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. Diagnosis of major depressive disorder, as defined by the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR) criteria and confirmed by the Mini International Neuropsychiatric Interview (MINI) criteria.

Exclusion criteria

* Age less than 18 years or greater than 64 years
* Inpatient hospitalization at screening
* Symptoms of depression present for less than 30 days or greater than 2 years prior to screening
* Total score of less than 18 on the 17-item HAM-D at screening
* Total score of less than 24 on the MADRS at screening (visit 1) or baseline (visit 2)
* Depressive episode diagnosed with psychotic or catatonic features, seasonal pattern or post-partum onset
* Significant currect suicide risk at screening or baseline (visit 1, visit 2) using the following scales: HAM-D, MADRS, Mini Module C, C-SSRS
* Patients with antisocial personality disorder, borderline personality disorder, bipolar disorders, psychotic disorders, post-traumatic stress disorder, anorexia nervosa, bulimia nervosa, alcohol dpendence substance dependence
* Pregnancy
* Women not willing to use highly effective contraception
* Seizures
* Cushing's syndrome, adrenal insufficiency

* Diabetes Mellitus requiring treatment with insulin or oral hypoglycemic agents
* Treatment with growth hormone
* ECG abnormalities including QTcB 500 milliseconds or more
* Liverfunction disorders
* Hematologic disorders

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:	Will not start
Start date (anticipated):	01-02-2010
Enrollment:	4
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Lexapro
Generic name:	escitalopram
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	20-11-2009

Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-12-2009
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-02-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-02-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-11-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2009-010339-42-NL
CCMO	NL30310.040.09
Other	Zie sectie J