Long-Term, Open-Label, Safety Study of LY2216684 12 to 18 mg Once Daily as Adjunctive Treatment for Patients with Major Depressive Disorder Who are Partial Responders to Selective Serotonin Reuptake Inhibitor Treatment

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Mood disorders and disturbances NEC
Study type	Interventional

Summary

ID

NL-OMON36315

Source
ToetsingOnline

Brief title
LNBO 219-381

Condition

- Mood disorders and disturbances NEC

Synonym
low spirits, sadness

Research involving

Human

Sponsors and support

Primary sponsor: Eli Lilly
Source(s) of monetary or material Support: Eli Lilly

Intervention

Keyword: LY2216684, Major Depressive Disorder, SSRI

Outcome measures

Primary outcome

The primary objective of this study is to evaluate the long-term safety and tolerability of LY2216684 administered once daily (QD) in the adjunctive treatment with an SSRI for up to approximately 1 year in patients with MDD who are partial responders to their SSRI treatment.

Secondary outcome

Efficacy: The efficacy measures include the MADRS total score and individual items, CGI-S, HADS anxiety and depression subscale scores, response and remission rates derived from MADRS total score, FAsD average score, experience and impact scores.

Safety and Tolerability: Safety and tolerability assessments include reported SAEs, TEAEs, collection and reporting of discontinuation rates, DEAEs, vital signs, weight, ECGs, laboratory analyses, C-SSRS, ASEX, and CPFQ.

Health Outcomes: Health Outcomes (including quality of life and functioning) assessments include SDS global functional impairment, work/school, social life/leisure activities, and familylife /home responsibilities impairment scores, number of days lost, and number of days underproductive, Q-LES-Q-SF, EQ-5D, and RU.

Pharmacokinetic/Pharmacodynamic: Plasma concentrations of LY2216684, dose regimen, patient characteristics

Study description

Background summary

Major depressive disorder (MDD) is defined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision® (DSM-IV-TR) as pervasive depressed mood or loss of interest that occurs for at least 2 weeks along with other core symptoms of fatigue, difficulty concentrating, feelings of worthlessness/guilt, sleep disturbance, appetite disturbance, and thoughts of death/suicide. Current treatment recommendations for MDD focus on selective serotonin reuptake inhibitors (SSRIs) as a first-line treatment (American Psychiatric Association [APA] 2000). While these medications have demonstrated efficacy, response to treatment is varied. In clinical studies, approximately two thirds of patients meet standard criteria for treatment response (*50% improvement in depressive symptomatology from initiation of treatment); however, only one third of patients meet criteria for remission (resolution of depressive symptoms) during acute treatment (8 to 12 weeks). For example, in the Sequential Treatment Alternatives to Relieve Depression multicenter study (STAR*D), patients were initially treated with citalopram. After 8 weeks of treatment, response rate was 47% and remission rate was 28%.

The purpose of this study, H9P-MC-LNBO (LNBO), is to assess the long-term safety and tolerability of LY2216684 administered QD in the adjunctive treatment with an SSRI for up to approximately 1 year in patients with MDD who are partial responders to their SSRI treatment. The secondary objectives of this study will be to evaluate the long-term efficacy of LY2216684 in adjunctive treatment with SSRIs in patients with MDD.

Study objective

The primary objective of this study is to evaluate the long-term safety and tolerability of LY2216684 administered once daily (QD) in the adjunctive treatment with a selective serotonin reuptake inhibitor (SSRI) for up to approximately 1 year in patients with major depressive disorder (MDD) who are partial responders to their SSRI treatment. The safety measures include the collection and reporting of discontinuation rates, treatment-emergent adverse events (TEAEs), vital signs, weight, electrocardiograms (ECGs), and laboratory analysis.

The secondary objectives of the study are:

-To evaluate the safety and tolerability of LY2216684 as an adjunctive treatment for patients with MDD who are partial responders to their SSRI treatment as measured by the following measures:
* Serious adverse events (SAEs)
* Discontinuation-emergent adverse events (DEAEs)
* Columbia-Suicide Severity Rating Scale (C-SSRS)
* Arizona Sexual Experiences (ASEX) scale
* Massachusetts General Hospital Cognitive and Physical Functioning Questionnaire (CPFQ)

-To evaluate the effect of LY2216684 on depressive symptoms as an adjunctive treatment for patients with MDD who are partial responders to their SSRI treatment as measured by the change from baseline using the following measures:
* Montgomery-Asberg Depression Rating Scale (MADRS) total score and individual items.
* Hospital Anxiety and Depression Scale (HADS) depression subscale
* Clinical Global Impression - Severity (CGI-S)

-To evaluate the effect of LY2216684 as an adjunctive treatment for patients with MDD who are partial responders to their SSRI treatment in reducing fatigue symptoms associated with depression, as measured by the change from baseline using the following measure:
* Fatigue Associated with Depression (FAsD) average score, the fatigue experience subscale score, and the
fatigue impact subscale score.

-To evaluate the effect of LY2216684 on depressive symptoms as an adjunctive treatment for patients with MDD who are partial responders to their SSRI treatment as measured by response and remission rates, as well as time to response and remission.

-To evaluate the effect of LY2216684 as an adjunctive treatment for patients with MDD who are partial responders to their SSRI treatment in reducing anxiety

symptoms associated with depression, as measured by the change from baseline using the following measure:
* HADS Anxiety Subscale score.

-To evaluate the effects of LY2216684 as an adjunctive treatment for patients with MDD who are partial responders to their SSRI treatment on quality of life and health outcomes using the following measures:
* Sheehan Disability Scale (SDS) global functional impairment score, work/school subscore, social life subscore, family life/home responsibilities impairment subscores, number of days lost, and number of days unproductive
* EuroQol Questionnaire * 5 Dimension (EQ-5D)
* Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form (Q-LES-Q-SF)
* Resource Utilization (RU)

-To examine the influence of CYP2D6 genetic variation on LY2216684 response in patients with MDD who are partial responders to their SSRI treatment.

-To assess the plasma concentrations of LY2216684 as adjunctive treatment with SSRIs in patients with MDD who are partial responders to their SSRI treatment

Exploratory Objectives:
* To explore the influence of relevant drug metabolizing enzymes and/or transporters on LY2216684 plasma concentrations and LY2216684 response in patients with MDD who are partial responders to their SSRI treatment.
* To examine the effect of genetic variation on response to treatment in patients with MDD who are partial responders to their SSRI treatment.

Study design

An open-label assessment of safety and tolerability over 1 year treatment of LY2216684 as an adjunctive therapy in patients with MDD who are partial responders to their SSRI treatment

Intervention

Questionnaires and a patient diary will be completed

The blood samples will be collected.

A physical exam (including blood pressure, pulse rate, temperature, height and weight) will be completed

Information on the patients caffeine, tobacco and alcohol use will be collected

A urine sample will be collected

An ECG will be completed to check the patient's overall health

Study burden and risks

The most frequently reported events (more than 10%) by healthy people who have received one
or more than one dose of LY2216684 were feeling sleepy, upset stomach, headache, dizziness,
hard or infrequent stools, problems beginning urination, and feeling of irregular or forceful
beating of the heart

Please refer to Appendix 2 of the Patient Information Sheets for more information regarding the risks and possible discomforts patients might experience during the study procedures

Contacts

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US
Scientific
Eli Lilly

Lilly Corporate Center DC 6076
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US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Male and female, adult outpatients aged *18 years who meet DSM-IV-TR diagnostic criteria for MDD as determined by clinical assessment by the Mini-International Neuropsychiatric Interview (MINI) and confirmed by the physician and who have experienced a partial treatment response to a course of SSRI treatment for at least 6 weeks with at least the last 4 consecutive weeks at a stable, optimized dose prior to Visit 2. Patients must have a score *16 on the GRID 17-Item Hamilton Rating Scale for Depression (GRID HAMD17) total score at Visit 1 and Visit 2. Patients will be determined to be partial responders by history, by the opinion of the investigator. Patients will also be required to have a rating indicating *75% improvement for their current SSRI treatment using the Massachusetts General Hospital Antidepressant Treatment Response Questionnaire (MGH-ATRQ) at Visit 1.

Exclusion criteria

Exclusion criteria include any additional DSM-IV-TR Axis I condition other than major depression that was considered the primary diagnosis within 1 year of Visit 1; other primary Axis I anxiety diagnosis within the past year (including panic disorder, obsessive-compulsive disorder [OCD], posttraumatic stress disorder [PTSD], generalized anxiety disorder [GAD], and social phobia, but excluding specific phobias); current or previous diagnosis of bipolar disorder, schizophrenia, or other psychotic disorder; have a serious or unstable medical condition; have any diagnosed medical condition that could be exacerbated by noradrenergic agents, including unstable hypertension, unstable heart disease, tachycardia or tachyarrhythmia, narrow-angle glaucoma, or history of urinary hesitation or retention; use of excluded concomitant medication; serious ideation/risk for harm to self or others; and pregnancy or breastfeeding status.

Study design

Design

Study phase:	3
Study type:	Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-07-2011
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	LY2216684
Generic name:	N/A

Ethics review

Approved WMO

Date:	04-11-2010
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	26-05-2011
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	03-08-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	22-09-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	25-11-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	25-01-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	31-01-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2010-020726-18-NL
CCMO	NL33527.098.10