An exploratory, multicenter, placebo-controlled, randomized, double-blind study to investigate the antidepressant mechanism-of-action of JNJ-42847922 in subjects with major depressive disorder.

Published: 16-11-2017
Last updated: 25-03-2025

To investigate the effect of JNJ-42847922 given as monotherapy as compared to placebo on symptoms of depression in male and female MDD patients

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

Summary

ID

NL-OMON44498

Source
ToetsingOnline

Brief title
how JNJ-42847922 works in the treatment of depression.

Condition

- Mood disorders and disturbances NEC

Synonym
Depression, MDD

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: Industry

Intervention

Keyword: depression, JNJ-42847922, pharmacodynamics

Outcome measures

Primary outcome

Depressive symptoms: the structured interview guide for the Hamilton Depression Scale (SIGH-D) will be completed at baseline and during the visits.

Secondary outcome

Mood Symptoms:

• the MADRS

• the QIDS-SR16, B&L VAS and the POMS

Cognitive function:

• A cognitive test battery that includes tests to evaluate attention, immediate and delayed verbal and visual memory, working memory, and executive function.

Sleep quality:

• the time to sleep onset, total sleep time (TST), time awake during the night and time of awakening will be recorded in a sleep diary.

• For polysomnography (PSG) measurements subjects will be instructed to go to bed between 10:00 pm and 12:00 am (midnight) and remain in bed for 8 hours. TST, wake after sleep onset, latency to persistent sleep, time spent awake, time spent in deep sleep, and sleep efficiency will be registered.

Rumination:

• the Ruminative Response Scale (RRS), a 22 item self-report measure of rumination, the Sleep and worry VAS which asks the subjects in the morning after wake up whether they could not sleep due to worrying and ongoing thoughts.

Hyperarousal:

Heart Rate Variability (HRV) will be derived from Holter recordings overnight and will be evaluated for arousal. Quantitative EEG (qEEG) will be recorded in a quiet environment with the eyes open for 2 minute and the eyes closed for 2 minutes.

Pharmacokinetic endpoints

Venous blood samples of 3 mL will be collected for determination of JNJ-42847922 plasma concentrations and metabolites.

Tolerability / safety endpoints

Adverse events will be reported from screening until follow-up. Because of the mechanism of action, investigators should pay special attention to parasomnias and episodes of cataplexy. Safety parameters like blood pressure, pulse/heart rate measurements, temperature physical examination and ECG will be performed for safety monitoring. An interview (the C-SSRS) to assess the risk of suicidal ideation and behavior will be conducted.

Study description

Background summary

The selectivity of JNJ-42847922 for the OX2R (approximate 2 logs selectivity ratio versus OX1R) confers blunting of the stress response of the HPA axis

(ACTH release). This inhibition of the HPA axis response is only partially attenuated by pre-treatment with DORAs in preclinical psychological stress models. Since the administration of JNJ-42847922 still reduces response of the HPA axis after treatment with DORAs, antagonism of OX1R is thought to counteract the stress inhibition produced by antagonism of the OX2R. MDD is associated with sustained increases in cortisol levels and it is hypothesized that JNJ-42847922 can attenuate this HPA axis activation and subsequently reduce symptoms of depression. This hypothesis was tested in study 42847922MDD1001/CHDR1504 in which a potentially relevant antidepressant effect with early onset (as early as Day 11 of exposure) of 20 mg JNJ-42847922 versus placebo and diphenhydramine was demonstrated in a small number of patients with MDD. Since this was an exploratory study in a small sample, these initial results warranted a study in a larger sample of MDD patients.

Study objective

To investigate the effect of JNJ-42847922 given as monotherapy as compared to placebo on symptoms of depression in male and female MDD patients

Study design

This will be a multi-center, placebo-controlled, randomized, double-blind study in subjects with MDD not currently treated with antidepressant drugs.
For each subject, the study will consist of four phases: a screening phase of up to 3 weeks, a baseline period including a 48-hour in-house baseline visit, a double-blind treatment phase lasting up to 8 weeks, and a 1 week post-treatment (follow up) phase. The double-blind treatment phase of the trial will consist of 3 periods:
o period 1: a double-blind placebo lead-in period of variable duration
o period 2: at the end of the lead-in period subjects will be divided into 2 groups: placebo lead-in responders and placebo lead-in non-responders. Each group will be randomized to receive 20 or 40 mg JNJ 42847922 or continue placebo for 5 weeks during the double-blind treatment period.
o period 3: subjects who complete the treatment period prior to the end of Week 8, will then enter the double-blind withdrawal period and be treated with placebo for the remaining time of the double-blind phase of the study. The withdrawal period will be used to assess whether there are signs of withdrawal. The duration of the withdrawal period will vary depending on the duration of the placebo lead-in period for the specific subject.

The total study duration for each subject will be approximately 13 weeks. There will be 11 scheduled visits to the clinical research center including screening and follow-up during the study period.

Intervention

JNJ-42847922 is a potent and selective antagonist of the human orexin-2 receptor (OX2R) that is being developed for the treatment of major depressive disorder (MDD) and the treatment of insomnia disorder.

Study burden and risks

To date, 11 Phase 1 clinical studies and 1 Phase 2 study have been completed with oral suspension and solid dosage formulations of JNJ-42847922. Overall, an estimated 389 subjects, have been exposed to JNJ-42847922 in the clinical development. All of these subjects were exposed to JNJ-42847922 in either Phase 1 or Phase 2 clinical trials. Subject may not benefit from the study in terms of long term improvement of their symptoms, however they may benefit from the extensive medical review and disease follow-up during the study. Additionally, the safety and tolerability data so far accumulated for JNJ-42847922 in both healthy subjects and subjects with MDD and/or insomnia were generally acceptable based on a thorough review of the safety information from completed clinical studies. No death or SAEs have been reported after subjects received JNJ-42847922. The most commonly reported TEAEs were somnolence, headache, and dizziness with most TEAEs being mild or moderate in intensity. ADRs attributed to JNJ-42847922 were sleep paralysis, somnolence, and abnormal dreams. Few subjects reported these events at doses planned for this study and all were self-limiting and mild or moderate in intensity.

Contacts

Public
Janssen-Cilag

Turnhoutseweg 30
Beerse 2340 Beerse
BE
Scientific
Janssen-Cilag

Turnhoutseweg 30
Beerse 2340 Beerse
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. 18 to 55 years of age (inclusive).
2. Body Mass Index (BMI) between 18 and 35 kg/m2 inclusive
3. Meets DSM (edition IV or 5) diagnostic criteria for MDD (ICD-code F32.x and F33.x), without psychotic features, and confirmed by the MINI. The length of the current depressive episode must be <=2 years.
4. MADRS total score >25 at screening and must not demonstrate a clinically significant change (i.e., an improvement of >20% on their MADRS total score) from the screening to baseline visit, i.e., subjects must have a MADRS total score of at least 20 at the baseline visit.
5. Not currently receive antidepressant drug therapy for >= 2 weeks before screening.

Exclusion criteria

1. Current or past clinically significant disease of the renal, hepatic, musculoskeletal, gastrointestinal, cardiovascular systems, immunological, endocrine, metabolic, or neurological disease.
2. Signs or symptoms of Cushing*s Disease, Addison*s Disease, primary amenorrhea, or other evidence of significant medical disorders of the HPA axis.
3. Primary DSM (4th or 5th edition) diagnosis of general anxiety disorder (GAD), panic disorder, obsessive compulsive disorder (OCD), posttraumatic stress disorder (PTSD).
4. Current or recent history of clinically significant suicidal ideation within the past 6 months.
5. History of drug or alcohol abuse or dependence according to DSM-IV or 5 criteria, except nicotine or caffeine, within 6 months before screening.
6. Prior electroconvulsive therapy (ECT), vagal nerve stimulation (VNS), or a deep brain stimulation (DBS) device.
7. Narcolepsy, severe obstructive sleep apnea/hypopnea, central sleep apnea, sleep-related, hypoventilation, circadian rhythm sleep-wake disorders, diagnosed with severe restless legs syndrome, substance/medication-induced sleep disorder or parasomnias (NREM sleep arousal disorders, nightmare disorder, REM sleep behavior disorder).

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	10-01-2018
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	JNJ-42847922
Generic name:	JNJ-42847922

Ethics review

Approved WMO Date:	16-11-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	23-11-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	16-01-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-05-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-06-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-06-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-07-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2017-002633-28-NL
CCMO	NL63487.056.17

Study results

Date completed: 29-04-2019

Results posted: 19-10-2021

URL result
URL
Type
int
Naam
M2.2 Samenvatting voor de leek
URL

Internal documents
File