A Double-blind, Randomized, placebo-controlled, 3-way crossover study to eValuate the single dose Effects of Intranasal eSketamine on saFety of on-road driving in healthy subjects(DRiVE SaFe)

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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-OMON40941

Source
ToetsingOnline

Brief title
A study to the effect of intranasal esketamine on driving performance

Condition

- Mood disorders and disturbances NEC

Synonym
Treatment resistent depression

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Driving performance, Esketamine, Healthy volunteers

Outcome measures

Primary outcome

Mean difference of standard deviation of lateral position (SDLP) from an onroad

driving test.

Secondary outcome

1. To evaluate the subjective driving performance of the subjects after the

driving test.

2. To evaluate sleepiness using the Karolinska Sleepiness Scale (KSS).

3. To investigate the safety and tolerability of intranasal esketamine in

healthy subjects, with

special attention to:

a. Effects on suicidal ideation/behavior measured by the Columbia Suicide

Severity Rating Scale (C-SSRS);

b. Psychosis-like side effects by using a four-item positive symptom subscale

of the BPRS+ consisting of: suspiciousness/persecution, hallucinations, unusual

thought content, and conceptual disorganization;

c. Effects on dissociative symptoms using the CADSS;

4. To evaluate the potential relationship between changes in driving

performance, other PD and safety parameters and the Cmax of esketamine or

noresketamine.

Study description

Background summary

Janssen Research & Development (JRD) is currently developing intranasal esketamine for the treatment of two important patient populations, those with treatment-resistant depression (TRD), as well as those with Major Depressive Disorder (MDD) who are assessed to be at imminent risk for suicide.

As with many other central acting drugs, esketamine may limit the ability to drive a car or operate machines for some time after drug administration. The USPI for ketamine (March 2012) states that patients should be cautioned that driving an automobile, operating hazardous
machinery or engaging in hazardous activities should not be undertaken for 24 hours or more (depending upon the dosage of ketamine hydrochloride and consideration of other drugs employed) after anesthesia. It is not clear to which extent this 24 hour period is supported by data
or chosen arbitrarily. Moreover, as esketamine will be administered at a sub anesthetic dose, the period during which the subject may not be able to drive a car or operate a machine may be shorter compared to after its use as an anesthetic.

Study objective

The objective of this study is to investigate whether subjects who have taken esketamine, will be able to drive a car as soon as their cognitive function has been restored. The residual effects on driving performance will be compared to placebo. Mirtazapine will be used as a positive control for assay sensitivity.

Study design

This will be a single center, double-blind, double-dummy, randomized, 3-way cross-over study in healthy male and female subjects. Approximately 24 subjects (12 males and 12 females) will be enrolled in this study.

Intervention

84 mg intranasal esketamine, 30 mg mirtazapine or placebo.

Study burden and risks

Healthy subjects will be exposed to a compound that can cause cognitive and psychiatric symptoms. During the study, regular assessments of the safety and tolerability will be made and evaluated. Also, subjects will be resident in the research unit for dose administration and supervised by the medical staff of the clinical unit during the study day(s) and brought home. When a subject decides to terminate his/her participation in the study, he/she will not be allowed to leave the clinic within 2 hours after dosing. Subjects will be advised not to drive a car themselves or operate machines until at least 24 hours after dosing.

The driving study will be executed using a specially equipped car. A licensed driving instructor (having access to dual controls) guards the safety of the subject during the test. The test vehicle and the test execution will be covered by an insurance.

Contacts

Public
Janssen-Cilag

Turnhoutseweg 30
Beerse 2340
BE
Scientific
Janssen-Cilag

Turnhoutseweg 30
Beerse 2340
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Subject must be a man or woman, 21 to 60 years of age, inclusive and in general good health.;2. Body mass index (BMI) (weight [kg]/height[m]2) between 18 and 30 kg/m2(inclusive), and body weight not less than 45 kg;3. Blood pressure (after the subject is supine for 5 minutes) between 90 and 140 mmHg systolic, inclusive, and no higher than 90 mmHg diastolic at Screening and predose on Day 1 of Period 1.;4. A 12-lead ECG consistent with normal cardiac conduction and function at Screening and predose on Day 1 of Period 1.;5. Comfortable with self-administration of intranasal medication and able to follow instructions provided.;6. Before randomization, a woman must be either: ;Not of childbearing potential: postmenopausal (>45 years of age with amenorrhea for at least 12 months, or any age with amenorrhea for at least 6 months and a serum follicle stimulating hormone (FSH) level >40 IU/L); permanently sterilized (e.g., tubal occlusion, hysterectomy, bilateral salpingectomy); or otherwise be incapable of pregnancy. ;Of childbearing potential and practicing a highly effective method of birth control consistent with local regulations regarding the use of birth control methods for subjects participating in clinical studies: e.g., established use of oral, injected or implanted hormonal methods of contraception; placement of an intrauterine device (IUD) or intrauterine system (IUS); barrier methods: condom with spermicidal foam/gel/film/cream/suppository orocclusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/suppository; male partner sterilization (the vasectomized partner should be the sole partner for that subject); true abstinence (when this is in line with the preferred and usual lifestyle of the subject);Note: If the childbearing potential changes after start of the study (e.g., woman who is not heterosexually active becomes active) a woman must begin a highly effective method of birth control, as described above. ;7. A woman of childbearing potential must have a negative urine pregnancy test at Screening and predose on Day 1 of Period 1.;8. A woman must agree not to donate eggs (ova, oocytes) for the purposes of assisted reproduction during the study and for at least 3 months after receiving the last dose of study drug.;9. A man who is sexually active with a woman of childbearing potential and has not had a vasectomy must agree to use a double-barrier method of birth control e.g., either condom with spermicidal foam/gel/film/cream/suppository or partner with occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/suppository, during the study and for 3 months after receiving the last dose of study drug. All men must also not donate sperm during the study and for 3 months after receiving the last dose of study drug.;10. Subject has a valid driving license for more than 3 years, has driven at least 5000 km in the past year and is driving a car regularly.;11. Normal visual acuity (corrected or uncorrected).;12. Subject must be willing and able to adhere to the prohibitions and restrictions specified in this protocol.;13. Each subject must sign an informed consent form (ICF) indicating that he or she understands the purpose of and procedures required for the study and are willing to participate in the study.

Exclusion criteria

1. Subject has clinically significant liver or renal insufficiency; cardiac, vascular, pulmonary, gastrointestinal, endocrine, neurologic(including cataplexy and cognitive impairment), hematologic,rheumatologic, psychiatric, or metabolic disturbances. A significant primary sleep disorder is exclusionary.;2. Clinically significant abnormal values for hematology, clinical chemistry, or urinalysis at screening, as deemed appropriate by the investigator.;3. Clinically significant abnormal physical examination, vital signs, or 12-lead ECG at screening or on Day 1 of Period 1, as deemed appropriate by the investigator;4. Anatomical or medical conditions that may impede delivery or absorption of study medication (e.g., undergone facial reconstruction, rhinoplasty, significant structural or functional abnormalities of the nose or upper airway; obstructions or mucosal lesions of the nostrils or nasal passages; undergone sinus surgery in the previous 2 years; or signs and symptoms of rhinitispredose on Day 1 of Period 1).;5. Has an abnormal or deviated nasal septum with any oneor more of the following symptoms: blockage of one or both nostrils, nasal congestion (especially 1-sided), frequent nosebleeds, frequent sinus infections, and at times has facial pain, headaches, and postnasal drip.;6. Subject has a current or prior diagnosis of psychosis/psychotic disorder.;7. History of drug or alcohol abuse disorder within the past 1 year of Screening, or a reason to believe a subject has such a history.;8. Positive test for alcohol or drugs of abuse (cannabinoids, opiates, cocaine, amphetamines, benzodiazepines, hallucinogens, or barbiturates)at Screening or on Day 1 of Period 1.;9. Current suicidal or homicidal ideation/intent/behavior.;10. Subject has a history of malignancy within 5 years before screening (exceptions are squamous and basal cell carcinomas of the skin and carcinoma in situof the cervix, or malignancy that in the opinion of the investigator, with concurrence with the sponsor's medical monitor, is considered cured with minimal risk of recurrence).;11. Subject has known allergies, hypersensitivity, or intolerance toesketamine or its excipients (refer to IB)or mirtazapine.;12. Subject has contraindications to the use of esketamine or ketamine, per local prescribing information and/or IB.;13. Donated blood or blood products or had substantial loss of blood (more than 500mL) within 3 months before the first administration of study drug or intention to donate blood or blood products during the study.;14. Disallowed therapies: ;- Received a known potent inhibitor of CYP3A or CYP2B6 activity (e.g., erythromycin, clarithromycin, ketoconazole, or itraconazole) within 1 week or a period less than 5 times the drugs half-life; whichever is longer, before the first dose of the study drug is scheduled.;- Received a potent inducer of CYP3A activity (e.g., rifampin) within 1 month before first dose of study drug is scheduled.;- Use of any prescription or nonprescription medication, within 14 days before the first scheduled dose of the study drug (including vitamins and herbal supplements; vasoconstrictors and decongestants that are administered by the ophthalmic or intranasal routes), except paracetamol, ibuprofen and oral contraceptives.;15. Subject has received an investigational drug (including investigational vaccines) or used an invasive investigational medical device within 90 days, or 10 half-lives, whichever is longer, before the planned first dose of study drug or is currently enrolled in an investigational study.;16. Subject is a woman who is pregnant, breast-feeding,or planning to become pregnant while enrolled in this study or within 3 months after the last dose of study drug.;17. Subject is a man who plans to father a child while enrolled in this study or within 3 months after the last dose of study drug.;18. Subject has any condition for which, in the opinion of the investigator, participation would not be in the best interest of the subject (e.g.,

compromise the well-being) or that could prevent, limit, or confound the protocol-specified assessments.;19. Subject has had major surgery, (e.g., requiring general anesthesia) within 2 weeks before screening, or will not have fully recovered from surgery, or has surgery planned during the time the subject is expected to participate in the study.;20. Subject is an employee of the investigator or study site, with direct involvement in the proposed study or other studies under the direction of that investigator or study site, as well as family members of the employees or the investigator.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-09-2014
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Mirtazapine
Generic name:	Mirtazapine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	S-Ketamine Hydrochloride
Generic name:	S-Ketamine Hydrochloride
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	28-08-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-09-2014
Application type:	First submission
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	EUCTR2014-002005-38-NL
CCMO	NL50355.056.14