An open-label, single-dose study to assess the absolute oral bioavailability and pharmacokinetics of JNJ-42847922 (seltorexant) administered as oral tablet and an intravenous microdose of 14C-seltorexant in healthy participants

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Ethical review	Approved WMO
Status	Completed
Health condition type	Sleep disturbances (incl subtypes)
Study type	Interventional

Summary

ID

NL-OMON51594

Source
ToetsingOnline

Brief title
JNJ-42847922 oral and intervenous microdose study

Condition

- Sleep disturbances (incl subtypes)
- Mood disorders and disturbances NEC

Synonym
major depressive disorder (MDD) and insomnia

Research involving
Human

Sponsors and support

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

Intervention

Keyword: 14C, JNJ-42847922

Outcome measures

Primary outcome

To determine the absolute bioavailability of seltorexant in healthy

participants following a single oral dose of seltorexant and an IV infusion

dose of 14C-seltorexant.

endpoint: Absolute bioavailability calculated as the ratio of dose normalized

AUC of oral and IV administration.

Secondary outcome

To evaluate the PK of seltorexant in healthy participants following a single

oral dose of seltorexant and an IV infusion dose

of 14C-seltorexant. endpoint: Pharmacokinetic parameters: AUC, Cmax, Tmax, and

half-life

To assess the safety and tolerability of a single oral dose of seltorexant and

an IV infusion dose of 14C-seltorexant.

endpoint: adverse events

Study description

Background summary

Seltorexant is a new compound that may potentially be used for the treatment of sleeplessness and depression. Seltorexant binds to the orexin-2 receptor and inhibits it. This receptor is present in the brain of humans. From research it is known that the orexin-2 receptor is important in patients with depression and insomnia. So far 23 studies have been done on seltorexant with a total of 1,355 persons. These persons include healthy participants, patients with depression, patients with sleeplessness, patients with both depression and sleeplessness, patients with obstructive sleep apnea and a patient with renal impairment. There are indications that seltorexant can cause a decrease in depressive symptoms, increases sleeping time and makes falling asleep easier.

Study objective

In this study we will investigate how safe the new compound seltorexant is and how well it is tolerated when it is used by healthy participants.

We also investigate how quickly and to what extent seltorexant is absorbed, transported, and eliminated from the body after oral as well as after intravenous administration. For this study, seltorexant is labelled with low levels of radioactive carbon-14 (14C). In this way seltorexant can be traced in blood. The additional radiation the participant will be exposed to in this study is negligible (that is, it is less than the natural background radiation during 1 month).

We also look at the effect of the genetic information on the body*s processing of seltorexant. This part of the study is mandatory.

Seltorexant has been used by humans before. In addition, it has been extensively tested in the laboratory and on animals.

Study design

For the study it is necessary that the participant stays in the research center for 6 days (5 nights). In addition, participant will be called 1 time 2 days after the research center is left. Questions will be asked about concomitant medication and adverse events.
Day 1 is the day when the participant receives the study compound. Participant will leave the research center on Day 5 of the study

Seltorexant will be administered as an oral tablet with 240 milliliter (mL) of water in the evening of Day 1, approximately 3 hours after dinner. Dinner may

be given earlier than one is used to, at about 17:00. Two hours after administration of the oral tablet, 14C-labeled seltorexant will be administered as an intravenous infusion. The infusion takes approximately 15 minutes.

During the first 4 hours after administration of the study compound as an oral tablet it is advised to lie down (except when instructed to do not so by one of the investigators) or to remain seated, as this may influence the uptake of the study compound.

One of the investigators will inspect the hands and mouth of the participant after the study compound intake as an oral tablet. This is to check if the study compound has been taken.

Intervention

Participant will be given seltorexant as an oral tablet with 240 milliliter (mL) of water in the evening of Day 1, approximately 3 hours after dinner. Dinner may be given earlier than one is used to, at about 17:00. Two hours after administration of the oral tablet, participant will receive of 14C-labeled seltorexant as an intravenous infusion. The infusion takes approximately 15 minutes.

During the first 4 hours after administration of the study compound as an oral tablet participant will be advised to lie down (except when instructed to do not so by one of the investigators) or to remain seated, as this may influence the uptake of the study compound.

On Day 1: Seltorexant as a Tablet, once 3 hours after dinner
On Day 1: 14C-labeled seltorexant in 15 mL as an Intravenous infusion, once during 15 minutes, 2 hours after administration of seltorexant tablet

Study burden and risks

General:
During the first night after the evening doses, the sleep will be disturbed due to the group housing and frequent blood draws with necessary lighting.

Blood draw:
Drawing blood may be painful or cause some bruising. The use of the indwelling cannula can sometimes lead to inflammation, swelling, hardening of the vein, blood clotting, and bleeding in the environment of the puncture site. In some individuals, a blood draw can sometimes cause pallor, nausea, seating, low heart rate, or drop in blood pressure with dizziness or fainting.

In total, we will take not more than 300 milliliters (mL) of blood from the participant from screening to leaving the research center. This amount does not

cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken at once each time. If the investigator thinks it is necessary for the safety of a participant, extra samples might be taken for possible additional testing. If this happens, the total amount of blood drawn may be more than the amount indicated above.

Heart tracing:
To make a heart tracing, electrodes will be placed on the arms, chest and legs. Prolonged use of these electrodes can cause skin irritation.

Coronavirus test:
Samples for the coronavirus test will be taken from the back of the nose and throat using swabs. Taking the samples only takes a few seconds, but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of the throat may cause the participant to gag. When the sample is taken from the back of the nose, participant may experience a stinging sensation and the eyes may become watery.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. 18 to 55 years of age, inclusive.
2. Healthy on the basis of medical history at screening and physical examination, vital signs,
and 12-lead ECG performed at screening and at admission to the study site on Day -1.
3. Healthy on the basis of clinical laboratory tests performed at screening and at admission
to the study site on Day -1. If the results of the clinical chemistry panel, hematology, or
urinalysis are outside the normal reference ranges, the participant may be included only
if the investigator judges the abnormalities or deviations from normal to be not clinically
significant. This determination must be recorded in the participant's source documents
and initialed by the investigator. One repeat for out-of-range laboratory values is
permitted.
4. Body weight not less than 50 kg and body mass index (BMI; weight [kg]/height2 [m]2)
within the range 18 kg/m2 and 32 kg/m2 (inclusive).
5. Man or woman

Exclusion criteria

1. History of or current clinically significant medical illness including (but not limited to) cardiac arrhythmias or other cardiac disease, hematologic disease, coagulation disorders (including any abnormal bleeding or blood dyscrasias), lipid abnormalities, significant pulmonary disease, including bronchospastic respiratory disease, diabetes mellitus, hepatic or renal insufficiency (creatinine clearance below 60 mL/min based on Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] equation), thyroid disease, kidney or urinary tract disturbances, neurologic or psychiatric disease like MDD, generalized anxiety disorder (GAD), psychotic disorders, infection, seizure disorder, or any other illness that the investigator considers should exclude the participant or that could interfere with the interpretation of the study results. Significant past gastrointestinal medical history, or any

disease/surgery (NOTE: cholecystectomy and appendectomy are not exclusionary) that would interfere with drug absorption.

2. Clinically significant abnormal values for hematology, clinical chemistry, or urinalysis at screening or at admission to the study site (Day -1) as determined by the investigator. Alanine transaminase (ALT)/aspartate transaminase (AST) concentrations within normal range at screening. One retest for ALT/AST is permitted

3. Clinically significant abnormal physical examination, vital signs, or 12-lead ECG at screening or at admission to the study site on Day -1 as determined by the investigator.

4.1 Participant has a current or recent history of serious suicidal ideation within the past 6 months, corresponding to a positive response on item 4 (active suicidal ideation with some intent to act, without specific plan) or item 5 (active suicidal ideation with specific plan and intent) for ideation on the Columbia-Suicide Severity Rating Scale (C-SSRS), or a lifetime history of suicidal behavior or suicidal attempt as validated by the C-SSRS at screening.

5. Positive test for human immunodeficiency virus (HIV)-1 and HIV-2 antibodies, hepatitis B surface antigen (HBsAg), or hepatitis C antibodies.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	01-02-2022
Enrollment:	10
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	07-12-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-01-2022
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	EUCTR2021-004068-92-NL
CCMO	NL79719.056.21

Study results

Date completed: 01-03-2022

Results posted: 21-02-2023

First publication
03-02-2023

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

Internal documents
File
File