A double-blind, randomized, controlled, 3-way crossover, pilot study to evaluate the duration of effects on simulated car driving and cognitive performance after a single dose of JNJ-42847922, zolpidem and placebo in healthy subjects

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To evaluate the effects of JNJ-42847922, compared to zolpidem and placebo, on driving performance as assessed by the mean difference of standard deviation of lateral position (SDLP) after forced awakening using a validated driving simulator test at...

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

Summary

ID

NL-OMON42615

Source
ToetsingOnline

Brief title
Effects of JNJ42847922 on Simulated car Driving and Cognition.

Condition

- Sleep disorders and disturbances

Synonym
Depression, Insomnia

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Healthy, JNJ42847922, Placebo, zolpidem

Outcome measures

Primary outcome

To evaluate the effects of JNJ-42847922, zolpidem and placebo on driving

performance

as assessed by the Mean Lateral Position (MLP), distance-keeping, mean speed,

SD of

speed, head movement, reaction-time, inhibition, alertness and Drive safety

Score (DSS)

after forced awakening using a validated driving simulator test at 2, 4, 6 and

8 hours

post-evening dose.

Secondary outcome

To evaluate the effects of JNJ-42847922, zolpidem and placebo on the subjective

driving performance of the subjects after the driving simulator test at 2, 4, 6

and 8 hours postevening dose.

To evaluate the effects of JNJ-42847922, zolpidem and placebo on a cognitive

test battery at 2, 4, 6 and 8 hours post-evening dose.

To evaluate the effects of JNJ-42847922, zolpidem and placebo on sleepiness at

2, 4, 6 and 8 hours post-evening dose using the Karolinska Sleepiness Scale (KSS).

To evaluate the effects of JNJ-42847922, zolpidem and placebo on postural stability (body sway) at 2, 4, 6 and 8 hours post-evening dose.

To investigate the safety and tolerability of 40 mg JNJ-42847922 in healthy subjects.

To evaluate the potential relationship between duration of changes in driving ability and plasma concentrations of JNJ-42847922, its metabolites M12 and M16, and zolpidem.

Study description

Background summary

JNJ-42847922 is a potent and selective antagonist of the human orexin-2 receptor (OX2R) that is being developed for the treatment of insomnia and major depressive disorder (MDD). In rats, JNJ-42847922 quickly and reversibly binds to the OX2R in the brain after oral administration and reduces sleep latency and increases total sleep duration whilst not affecting Rapid Eye Movement (REM) sleep. JNJ-42847922 induced dose-related somnolence in healthy subjects after daytime administration and decreased the latency to persistent sleep (LPS) and increased the total sleep time (TST) in MDD patients with insomnia after nighttime administration of a single dose of 10 mg or higher. During the phase 1 program, single dose levels of 10 to 80 mg of JNJ-42847922 have been administered to healthy subjects and single dose levels of 10 to 40 mg have been administered to subjects with MDD and comorbid insomnia. Dose levels of 5 to 60 mg once daily (q.d.) over 10 days were administered to healthy subjects. JNJ-42847922 was well tolerated by both healthy subjects and subjects with MDD with comorbid insomnia.

The results of this study will contribute to a better understanding of the absence or of possible adverse effects of JNJ-42847922 on driving performance and cognition. In addition, effects of JNJ-42847922 on driving performance and cognition will be compared to those elicited by intake of a 10mg dose of zolpidem to investigate potentially differentiating features.

Study objective

To evaluate the effects of JNJ-42847922, compared to zolpidem and placebo, on driving performance as assessed by the mean difference of standard deviation of lateral position (SDLP) after forced awakening using a validated driving simulator test at 2, 4, 6 and 8 hours post-evening dose.

Study design

This will be a single center, double-blind, randomized, 3-way cross-over, pilot study in healthy male and female subjects.

Intervention

On Day 1 of each study period, subjects will take the study medication 15 minutes prior to bedtime, The dose of the study medication is: JNJ-42847922: 2 capsules containing 20 mg JNJ-42847922 each
Zolpidem: 1 capsule containing 10 mg zolpidem + 1 capsule placebo
Placebo: 2 capsules placebo.

Study burden and risks

JNJ-42487922 has been administered to healthy male and female subjects for 10 days in doses up to 60-mg [42847922EDI1003] and was well tolerated.
JNJ-42847922 causes somnolence/sedation when administered at daytime. When administered in the evening, JNJ-42847922 decreases LPS and increases TST [42847922EDI1002] at all doses tested (10, 20, and 40 mg).
A 40-mg JNJ-42847922 dose level is selected for this study because it has been demonstrated to be well tolerated, has shown significant benefit on sleep parameters, and is expected to be in the range of the highest effective dose.
Zolpidem has been selected as a comparator, because it is one of the most commonly prescribed sleep medications in the EU and USA, and has a well-known profile of residual effects as assessed during on-the-road driving tests (Vermeeren 2004, Verster 2004). Zolpidem has been approved in the European Union and the USA for the treatment of
insomnia. According to the product label of zolpidem in the EU, the dose is 10 mg.

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

-Body mass index (BMI) (weight [kg]/height2[m2]) between 18 and 30 kg/m2 (inclusive)
-Men who are sexually active with a woman of childbearing potential must agree to use a condom, and all men must not donate sperm during the study and for 3 months after receiving the last dose of study drug. In addition, for men who have not had a vasectomy, their female partners should also use an appropriate method of birth control for at least the same duration
-A woman of childbearing potential must have a negative serum pregnancy test at screening and a negative urine pregnancy test predose on Day 1 of each period
-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
-Participant has a valid driving license for more than 3 years, has driven at least 5000 kilometer (km) in the past year and is driving a car regularly
- Women of childbearing potential must practice a highly effective method of birth control consistent with local regulations regarding the use of birth control methods for participants participating in clinical studies (that is, one that results in a less than 1 percent per year failure rate when used consistently and correctly)

Exclusion criteria

-Participant 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
-Clinically significant abnormal values for hematology, clinical chemistry, or urinalysis at screening as deemed appropriate by the investigator
- Subject has a history of substance or alcohol use disorder according to Diagnostic and Statistical Manual of Mental Disorders (5th edition) (DSM5) criteria within 6 months before screening or positive test result(s) for alcohol and/or drugs of abuse (opiates [including methadone], cocaine, amphetamines, methamphetamines, cannabinoids, barbiturates, ecstasy and benzodiazepines) at screening or admission on Day 1 of each study period
- Current suicidal or homicidal ideation/intent/behavior
- Serology positive for hepatitis B surface antigen (HBsAg), hepatitis C antibodies (HCV) or Human immunodeficiency virus (HIV) antibodies

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):	11-11-2015
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	JNJ-42847922
Generic name:	JNJ-42847922
Product type:	Medicine
Brand name:	Zolpidem
Generic name:	Zolpidem
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	06-11-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-11-2015
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	EUCTR2015-004203-24-NL
CCMO	NL55279.056.15