A Multi-cohort, Randomized Study in Healthy Subjects to Assess the Pharmacokinetics and Safety of Single and Multiple Ascending Doses of JNJ-61393215 (Suspension), and to Assess the Relative Bioavailability, and the Effect of Food on the Pharmacokinetics, of a New Solid Formulation (Capsules) of JNJ-61393215

Published: 06-07-2018
Last updated: 25-03-2025

This study will be performed in 56 healthy volunteers. The study will be performed in 3 parts, Part 1, Part 2 and Part 3. Part 1 will be performed in 16 healthy volunteers divided over 2 groups of 8 volunteers each. The purpose of Part 1 of the...

Ethical review	Approved WMO
Status	Completed
Health condition type	Anxiety disorders and symptoms
Study type	Interventional

Summary

ID

NL-OMON46054

Source
ToetsingOnline

Brief title
Orexin SAD MAD FE BA

Condition

- Anxiety disorders and symptoms

Synonym
anxiety, mood disorders

Research involving
Human

Sponsors and support

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

Intervention

Keyword: JNJ-61393215, MAD, PK, SAD

Outcome measures

Primary outcome

Part 1

•to investigate the PK, safety, and tolerability of JNJ 61393215 suspension (ascending dose levels) after single oral dose administration in healthy subjects under fasted conditions.

Part 2

•to evaluate the relative bioavailability of a solid JNJ 61393215 capsule formulation compared to a suspension of JNJ 61393215 in healthy subjects under fasted conditions, and

•to assess the effect of food (high fat/high calorie breakfast and standardized breakfast) on the PK of the solid JNJ 61393215 capsule formulation in healthy subjects.

Part 3

•to investigate the PK, safety, and tolerability of JNJ 61393215 suspension

(ascending dose levels) after 7 days of once daily dosing in healthy subjects

under fasted conditions.

Secondary outcome

The secondary objectives (Part 2 only) are to evaluate the safety and

tolerability of single oral dose administration of a solid formulation of JNJ

61393215 under fed and fasted conditions.

Study description

Background summary

JNJ-61393215 is a new drug being investigated for the treatment of people with mood and/or anxiety disorders. It might normalize certain mechanisms in the brain that cause anxiety (for example panic attacks) without causing sleepiness or reduced awareness.

Study objective

This study will be performed in 56 healthy volunteers. The study will be performed in 3 parts, Part 1, Part 2 and Part 3.

Part 1 will be performed in 16 healthy volunteers divided over 2 groups of 8 volunteers each.
The purpose of Part 1 of the study is to investigate how safe the new compound JNJ-61393215 is and how well it is tolerated when it is administered as single doses to healthy volunteers. It will also be investigated how quickly and to what extent JNJ-61393215 is absorbed by and eliminated from the body (pharmacokinetics). JNJ-61393215 will be compared with a placebo.

Part 2 will be performed in 24 healthy volunteers divided over 2 groups of 12 volunteers each.
The purpose of Part 2 of the study is to investigate the pharmacokinetics (how quickly and to what extent JNJ-61393215 is absorbed by and eliminated from the body) of JNJ-61393215 when administered as an oral solution compared to an oral capsule. In addition, the effect of food on the pharmacokinetics of

JNJ-61393215 will be investigated. It will also be investigated how safe the new compound JNJ-61393215 is and how well it is tolerated when it is administered to healthy volunteers.

Part 3 will be performed in 16 healthy volunteers divided over 2 groups of 8 volunteers each.
The purpose of Part 3 of the study is to investigate how safe the new compound JNJ-61393215 is and how well it is tolerated when it is administered as multiple doses to healthy volunteers. It will also be investigated how quickly and to what extent JNJ-61393215 is absorbed by and eliminated from the body (pharmacokinetics). JNJ-61393215 will be compared with a placebo.

Study design

Part 1:
The study will consist of 1 period during which the volunteer will stay in the research center Martini Hospital location for 4 days (3 nights).
Day 1 is the day of administration of the study compound. The volunteer is expected at the research center at 14:00 h in the afternoon prior to the day of administration of the study compound (Day -1). The volunteer will leave the research center on Day 3 of the study.
The follow-up visit is between 7-14 days after administration of the study compound.

Part 2:
The study will consist of 4 periods during which the volunteer will stay in the research center Martini Hospital location for 5 days (4 nights) each period.
The time interval between administrations of the study compound on Day 1 of each period is at least 7 days.
Day 1 is the day of administration of the study compound. Each period, the volunteer is expected at the research center at 14:00 h in the afternoon prior to the day of administration of the study compound (Day -1). Each period, the volunteer will leave the research center on Day 4 of the study.
The follow-up visit is on Day 4 of the last treatment period (Period 4).

Part 3:
The study will consist of 1 period during which the volunteer will stay in the research center Martini Hospital location for 9 days (8 nights). This will be followed by 1 day during which the volunteer will visit the research center for a short visit. This short visit will take place on Day 9.
Day 1 is the first day of administration of the study compound. The volunteer is expected at the research center at 14:00 h in the afternoon prior to the first day of administration of the study compound (Day -1). The volunteer will leave the research center on Day 8 of the study.
The follow-up visit is between 14-21 days after the last administration of the study compound

Intervention

Part 1:
The study will consist of 1 period during which the volunteer will receive JNJ-61393215 or placebo as a single dose. JNJ-61393215 and placebo will be given as an oral solution with 240 milliliters (mL) of tap water.

When JNJ-61393215 or placebo is administered on Day 1, the volunteer should has fasted for at least 10 hours (no eating and drinking). Also, after administration of the study compound, the volunteer will be required to fast for a period of 4 hours. Then the volunteer will receive lunch. During fasting the volunteer is allowed to drink water, except for 1 hour before until 1 hour after administration of the study compound (apart from the water taken with the dose as described above).

Whether the volunteer will receive JNJ-61393215 or placebo will be determined by chance; *a randomized study*. Per group, 6 volunteers will receive JNJ-61393215 and 2 volunteers will receive placebo. Neither the volunteer, nor the responsible doctor knows if JNJ-61393215 or placebo will be administered; *a double-blinded study*. However, if it is important for volunteers health, for example in case of a serious side effect, this information can be looked up during the study.

For safety reasons, in both groups initially 2 volunteers will receive the study compound. One volunteer will receive JNJ-61393215, and 1 will receive placebo. After administration, the safety and tolerability of the study compound in these 2 volunteers will be closely monitored. If there are no concerns about the safety and tolerability 24 hours after administration, then the remaining 6 volunteers (5 will receive JNJ-61393215 and 1 will receive placebo) will receive the study compound.

Please refer to the table below to see the planned dose levels for the groups.

Group: 1
Day: 1
Treatment A: 145 mg JNJ-61393215 or placebo
How often: once

Group: 2
Day: 1
Treatment B: 225 mg JNJ-61393215 or placebo
How often: once

The dose of JNJ-61393215 of Group 2 can be adjusted based on the results of the previous group. The dose for the next group will only be increased if the lower dose of the previous group was found to be well tolerated and in case of no

objection by the Medical Research Ethics Committee. The study will be discontinued if, in the opinion of the responsible doctor, unacceptable side effects appear.

Part 2:
The study will consist of 4 similar treatment periods, separated by a washout period in which no study compound is given. In each treatment period the volunteer will receive JNJ-61393215 once per period. JNJ-61393215 will be given as an oral solution with 240 milliliters (mL) of tap water in 1 period and as an oral capsule with 240 mL of tap water in 3 periods. When JNJ-61393215 is administered as an oral capsule, the volutneer will receive the study compound when he/she has fasted for at least 10 hours in 1 period, with a high-fat and high-calorie breakfast in 1 period, and with a standardized breakfast in 1 period.

Please see below an overview of the planned treatments.

Group: 3
Treatment C: 30 mg JNJ-61393215 as oral solution
Condition: fasted
How often: once

Treatment D: 30 mg JNJ-61393215 as oral capsule
Condition: fasted
How often: once

Treatment E: 30 mg JNJ-61393215 as oral capsule
Condition: high-fat/high calorie breakfast
How often: once

Treatment F: 30 mg JNJ-61393215 as oral capsule
Condition: Standardized breakfast
Hoe vaak: éénmaal

Groep 4:
Treatment G: X* mg JNJ-61393215 as oral solution
Condition: fasted
How often: once

Treatment H: X* mg JNJ-61393215 as oral capsule
Condition: fasted
How often: once

Treatment I: X* mg JNJ-61393215 as oral capsule
Condition: high-fat/high calorie breakfast
How often: once

Treatment J: X* mg JNJ-61393215 as oral capsule
Condition: standardized breakfast
How often: once

*The dose level of JNJ-61393215 for Group 4 is not known yet and will be determined based on the results of Part 1 of the study. The dose level will be the same for all treatments of Group 4. Each treatment will be given once. The order in which the volunteer will receive the treatments will be determined by chance.

Treatments C, D, G and H
Before administration of the study compound on Day 1, the volunteer should has fasted for at least 10 hours (no eating and drinking). Also, after administration of the study compound, the volunteer will be required to fast for a period of 4 hours. Then the volunteer will receive lunch. During fasting the volunteer is allowed to drink water, except for 1 hour before until 1 hour after administration of the study compound (apart from the water taken with the dose as described above).

Treatments E, F, I and J
After the volunteer has fasted for at least 10 hours (no eating and drinking), the will receive a high-fat and high-calorie breakfast (Treatments E and I) or a standardized breakfast (Treatments F and J) in the morning of Day 1. The breakfast will have to be finished within 30 minutes and the entire breakfast must be consumed. Within 10 minutes after completion of the breakfast the volunteer will receive the study compound; this will not be later than 30 minutes after the start of breakfast. During fasting the volunteer is allowed to drink water, except for 1 hour before until 1 hour after administration of the study compound (apart from the water taken with the dose as described above).

Part 3:
The study will consist of 1 period during which the volunteer will receive JNJ-61393215 or placebo once daily for 7 consecutive days (Day 1 to Day 7). JNJ-61393215 and placebo will be given as an oral solution with 240 milliliters (mL) of tap water.

When JNJ-61393215 or placebo is administered on Days 1 to 7, the volunteer should has fasted for at least 10 hours (no eating and drinking). Also, after administration of the study compound, the volunteer will be required to fast for a period of 4 hours on Day 1 and on Day 7. Then the volunteer will receive lunch. On all other dosing days (Days 2 to 6) the volunteer will receive a breakfast 2 hours before or 1 hour after administration of the study compound. During fasting the volunteer is allowed to drink water, except for 1 hour before until 1 hour after administration of the study compound (apart from the water taken with the dose as described above).

Whether the volunteer will receive JNJ-61393215 or placebo will be determined by chance; *a randomized study*. Per group, 6 volunteers will receive JNJ-61393215 and 2 volunteers will receive placebo. Neither the volunteer, nor the responsible doctor knows if JNJ-61393215 or placebo will be administered; *a double-blinded study*. However, if it is important for volunteers health, for example in case of a serious side effect, this information can be looked up during the study.

For safety reasons, in both groups initially 2 volunteers will receive the study compound. One volunteer will receive JNJ-61393215, and 1 will receive placebo. After administration, the safety and tolerability of the study compound in these 2 volunteers will be closely monitored. If there are no concerns about the safety and tolerability 24 hours after administration, then the remaining 6 volunteers (5 will receive JNJ-61393215 and 1 will receive placebo) will receive the study compound.

Please refer to the table below to see the planned dose levels for the groups.

Group 5
Day: 1 to 7
Treatment: 145 mg JNJ-61393215 or placebo
How often: once daily

Group 6
Day: 1 to 7
Treatment: 225 mg JNJ-61393215 or placebo
How often: once daily

The dose of JNJ-61393215 of Group 6 can be adjusted based on the results of the previous group. The dose for the next group will only be increased if the lower dose of the previous group was found to be well tolerated and in case of no objection by the Medical Research Ethics Committee. The study will be discontinued if, in the opinion of the responsible doctor, unacceptable side effects appear.

Study burden and risks

All potential drugs cause side effects; the extent to which this occurs differs.

JNJ-61393215 is a novel drug that is being developed for the treatment of mood and/or anxiety disorders.

This is the fourth study with JNJ-61393215. Preliminary data from the previous studies show no significant side effects. In the first study, 62 healthy subjects have received JNJ-61393215. In the second study, 49 healthy subjects have received JNJ-61393215; the third study is currently on-going. Side effects

most frequently reported by the subjects were headache and sleepiness. Healthy subjects will not benefit from treatment with JNJ 61393215. Therefore, special precautions are taken to limit the risk to the volunteer.

The results from the study on heart in animals suggest that overall, JNJ-61393215 is considered not to pose a cardiovascular safety concern for humans. JNJ-61393215 did not show any adverse effects on genetic material. In rats and dogs, high JNJ-61393215 levels were measured in the blood after oral dose administration. At high JNJ-61393215 doses, changes in coagulation (clotting) parameters in the blood were detected; those effects were dependent on the dose and were considered adverse only for the highest dose tested, which is associated with higher exposure than what is anticipated in this study. At high JNJ-61393215 doses an increase in liver weight was detected. Importantly, all observed changes were reversible and can be monitored in the clinic.

Specifically in rats, a condition characterized by lack of response to external stimuli and by muscular rigidity was observed in 2 animals at a high dose. Rats receiving a high dose of JNJ 61393215 also were less active and less alert than normal.

Coagulation (clotting) and liver parameters in the blood will be monitored during all parts of the study to identify potential risks early. Regarding the brain and behavioral side effects, it is expected that these side effects will not be seen in humans because the exposure in human studies will stay lower than the exposure that resulted in these effects in rats.

In this study, doses of JNJ-61393215 are higher than the range of dose which have been previously administered to other healthy subjects in previous studies. It is possible that those doses may be less tolerable than doses previously administered to human subjects. Throughout the study, the volunteer will be supervised by the responsible doctor.

There may be risks with the use of JNJ-61393215 that are not yet known. Sometimes during a study the Sponsor may learn new facts about the study compound. It is possible that this information might change volunteers mind about being in the study. If new information is discovered, the responsible doctor will tell the volunteer about it right away.

Tests
Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising. In total, we will take about 115 mL Part 1, 391 mL Part 2 and 188 mL Part 3 of blood from you. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time.

To monitor the heart rate, electrodes (small, plastic patches) will be pasted

at specific locations on the chest and arms and legs. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Procedures: pain, minor bleeding, bruising, possible infection.

Contacts

Public
Janssen-Cilag International NV

Turnhoutseweg 30
Beerse 2340
BE
Scientific
Janssen-Cilag International NV

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

-Healthy male or female subjects
-18-55 yrs, inclusive at screening
-BMI: 18.0-30.0 kg/m2, inclusive at screening
-Weight not less than 50 kg at screening
-Non-smoking
-Female of non-childbearing potential

-Blood pressure between 90 and 140 mmHg systolic, inclusive, and no higher than 90 mmHg diastolic.

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study.

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:	Completed
Start date (anticipated):	03-09-2018
Enrollment:	56
Type:	Actual

Ethics review

Approved WMO

Date:	06-07-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	27-07-2018
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	EUCTR2018-001944-80-NL
CCMO	NL66421.056.18

Study results

Date completed:	14-12-2018
Results posted:	11-06-2021

First publication
16-04-2021

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

Internal documents

File