A 2-Part, Randomized, Placebo-controlled, Double-blind, Single Ascending Dose Study to Investigate Safety and Tolerability, Pharmacokinetics and Pharmacodynamics of JNJ-55375515 in Healthy Male Subjects

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The purpose of this study is to investigate how safe the new compound JNJ55375515 is when it is administered to healthy subjects. JNJ-55375515 has been administered to humans before and will be investigated at various dose levels.It will also be...

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

Summary

ID

NL-OMON46723

Source
ToetsingOnline

Brief title
JNJ-55375515 SAD study

Condition

- Mood disorders and disturbances NEC

Synonym
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-55375515, mood disorders

Outcome measures

Primary outcome

The primary objective is to assess safety and tolerability of day-time and

night-time dosing of JNJ-55375515 in healthy male subjects

Secondary outcome

The secondary objectives are to assess:

- the influence of daytime dosing of JNJ-55375515 on pharmacodynamic markers

including electroencephalography (EEG), heart rate variability (HRV), saccadic

eye movement, body sway, sleepiness, mood, neuroendocrinology,

emotional/motivational processing and simple- and complex cognition

- the effect of JNJ-55375515 administered at day-time on an evoked stress

response

- the influence of night-time dosing of JNJ-55375515 on sleep architecture

using polysomnography;

- the influence of night-time dosing of JNJ-55375515 on sleepiness and

performance of complex cognitive tasks;

- the pharmacokinetics of single-dose morning and evening administration of

JNJ-55375515 in healthy male subjects

Study description

Background summary

JNJ-55375515 is a new compound that may eventually be used for the treatment of mood disorders, like major depression.
Besides the changes in mood that occur with major depression, there are also cognitive problems, such as deficits in memory and attention. The effectiveness of current antidepressant treatments leaves a lot to be desired. In addition, they do not improve the deficits in cognitive function found in depressed patients.
Glutamate is the most important neurotransmitter (chemical messenger) in the brain, and disturbances in this glutamatergic system are thought to be related to several mood disorders, like major depression. Medication that targets this system would provide a novel approach for the treatment of mood disorders.
JNJ55375515 targets the so-called metabotropic glutamate 2 receptor. Via this route it is thought to improve glutamate release,and thus strengthening network connectivity in the brain. It is expected that this would result in improved mood and cognition, especially, in depressed patients who are not helped by the currently available treatments.

Study objective

The purpose of this study is to investigate how safe the new compound JNJ55375515 is when it is administered to healthy subjects. JNJ-55375515 has been administered to humans before and will be investigated at various dose levels.
It will also be investigated how quickly and to what extent JNJ-55375515 is absorbed and eliminated from the body (this is called pharmacokinetics). In addition, the effect of JNJ55375515 on the body will be investigated (this is called pharmacodynamics).
The effects of JNJ55375515 will be compared to the effects of a placebo. A placebo is a medicine without any active ingredient. It is a *fake* medicine.

Study design

Part 1.
Participation of the volunteer from the pre-study screening until the last follow-up visit will last about 8 weeks.

Screening
We will first evaluate whether the volunteer may participate. The investigator will do a physical examination, make a heart tracing (ECG), measure weight, height, blood pressure, heartbeat and body temperature and will do tests on the volunteers blood and urine. A neurological examination will also be done,

including testing the motor (muscle) and sensory (senses) functions, and coordination of the volunteer. The investigator will also ask the volunteer about your medical history, ethnic origin and medication use. These factors are important for the study because they can influence the effects of the study drug. The volunteer will also be tested for the use of alcohol and drugs of abuse (hard drugs and soft drugs), and for the diseases HIV, hepatitis B and hepatitis C. If the volunteer has any of these diseases, either we or the volunteers general practitioner will tell them. If the volunteer does not want to know, they cannot participate in this study.
The screening sometimes reveals findings that require further medical examination. We will always tell the volunteer about these findings. Further medical examination will have to be done by the volunteers own GP or specialist. The costs of this will be charged to their own insurance. The volunteer may also be healthy but may still not be eligible for participation, for example when the volunteers body weight is too high or too low according to the requirements of the study.
Just before administration of the study drug it will be decided based on the latest test results whether the volunteer is suitable for participation or not.

Administration of the study drug
JNJ-55375515 and placebo will be given as a liquid (suspension). The volume can range from 0.4 milliliters to 8 milliliters. After administration of the study drug, the pipet will be rinsed with water, which the volunteer will also be required to drink. Thereafter the volunteer is also required to drink the reminder of the 240 mL of water.
The study drug will be administered within 30 minutes after consumption of a standardized breakfast between 07:00 and 11:00 h. The entire breakfast must be consumed.
The study consists of 3 periods. In which period the volunteer will receive JNJ-55375515 or placebo will be determined by chance. All volunteers will receive JNJ-55375515 twice (2 different doses) and placebo once.
In the table below the volunteer can see how much of the study drug they will receive. The doses in Periods 2 and 3 can be adjusted based on the results of the other group and previous period. However, the dose will not be lower than 0.3 mg and not higher than 30 mg. 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 investigation will be discontinued if, in the opinion of the investigators, unacceptable adverse effects appear.
A third group with a maximum of 12 subjects might be added to investigate 3 additional doses. The highest dose will not exceed 80 mg.
Neither the volunteer, nor the responsible doctor knows if JNJ55375515 or placebo will be dosed; we call this *the study is blinded*. However, if it is important for the volunteers health, for example in case of a serious adverse event, this information can be looked up during the study.
General information on this the volunteer will find in the brochure *medical-scientific research*.

Visits and tests
The actual study will consist of 3 periods during which the volunteer will stay in the research center in Groningen Martini Hospital for 4 days (3 nights). Each period will be followed by 2 short visits to the research center. These short visits will take place on Day 4 and 5. Day 1 of each period will be separated by at least 10 days.
Day 1 is the day of administration of the study drug. The volunteer is expected at the research center at 10:00 h in the morning prior to the day of administration of the study drug. The volunteer will leave the research center on Day 3 of the study. This is the case for each of the 3 periods.
During the study, the following will take place
- We ask about side effects
- We will give the volunteer the study drug
- We will do a physical examination
- We will do a neurological examination
- We will make a heart tracing (ECG)
- We will use telemetry to continuously monitor the volunteers ECG
- We will measure the volunteers brain activity (EEG)
- For Part 2 only: We will measure the volunteers sleep pattern
- We will measure blood pressure, heart rate, number of breaths per minute and body temperature of the volunteer. Blood pressure and heart will also be measured while the volunteer is standing.
- We will draw blood. This is to see how well JNJ-55375515 is absorbed in the volunteers blood and how it affects the volunteers body. In total, about 400 milliliter blood will be taken during the study.
- We will measure the volunteers eye movements.
- We will ask the volunteer to do several cognitive tests.
- We will ask the volunteer to complete questionnaires about feelings of anxiety, sleepiness,mood.
- We will give the volunteer a standardized breakfast.
- We will draw one blood sample for genetic tests (DNA tests) to study genes related to drug activity and for research into what the volunteers body does with the drug. For this study genetic tests are obligatory. These genotyping tests do not have the capability to identify the volunteer or the volunteers general state of health. Genes not related to drug activity or what the volunteers body does to the study drug will not be examined. The volunteers samples will be stored usually for 2 years, but no more than 15 years after the completion of the study and will be used
solely for specific genes related to drug activity or the disposition of the study drug as defined for this study.

Follow-up visit
Between Day 7 and 14 after the last study drug administration the volunteers health will be checked for the last time. The appointment for this follow-up visit will be made during the study. During this health check a physical and neurological examination will be done including measurement of blood pressure, heart rate and body temperature, a heart trace, motor and sensory functions.

And a number of blood and urine tests will be done.

Part 2.
The volunteers participation from the pre-study screening until the last follow-up visit will last about 9 weeks.

Screening
We will first evaluate whether the volunteer may participate. The investigator will do a physical examination, make a heart tracing (ECG), measure weight, height, blood pressure, heartbeat and body temperature of the volunteer and will do tests on the volunteers blood and urine. A neurological examination will also be done, including testing the volunteers motor (muscle) and sensory (senses) functions, and coordination. The investigator will also ask the volunteer about your medical history, ethnic origin and medication use. These factors are important for the study because they can influence the effects of the study drug. The volunteer will also be tested for the use of alcohol and drugs of abuse (hard drugs and soft drugs), and for the diseases HIV, hepatitis B and hepatitis C. If the volunteer has any of these diseases, either we or the volunteers general practitioner will tell them. If the volunteer does not want to know, the volunteer cannot participate in this study.
The screening sometimes reveals findings that require further medical examination. We will always tell the volunteer about these findings. Further medical examination will have to be done by their own GP or specialist. The costs of this will be charged to their own insurance. The volunteer may also be healthy but may s

Intervention

Part 1
Administration of the study drug
JNJ-55375515 and placebo will be given as a liquid (suspension). The volume can range from 0.4 milliliters to 8 milliliters. After administration of the study drug, the pipet will be rinsed with water, which the volunteer will also be required to drink. Thereafter the volunteer is also required to drink the reminder of the 240 mL of water.

The study drug will be administered within 30 minutes after consumption of a standardized breakfast between 07:00 and 11:00 h. The entire breakfast must be consumed.

The study consists of 3 periods. In which period the volunteer will receive JNJ-55375515 or placebo will be determined by chance. All volunteers will receive JNJ-55375515 twice (2 different doses) and placebo once.
In the table below the volunteer can see how much of the study drug they will receive. The doses in Periods 2 and 3 can be adjusted based on the results of the other group and previous period. However, the dose will not be lower than

0.3 mg and not higher than 30 mg. 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 investigation will be discontinued if, in the opinion of the investigators, unacceptable adverse effects appear.
A third group with a maximum of 12 subjects might be added to investigate 3 additional doses. The highest dose will not exceed 80 mg.
Neither the volunteer, nor the responsible doctor knows if JNJ55375515 or placebo will be dosed; we call this *the study is blinded*. However, if it is important for the volunteers health, for example in case of a serious adverse event, this information can be looked up during the study.
General information on this the volunteer will find in the brochure *medical-scientific research*.

Part 2
Administration of the study drug
JNJ-55375515 and placebo will be given as a liquid (suspension). The volume can range from 0.4 milliliters to 8 milliliters. After administration of the study drug, the pipet will be rinsed with water, which the volunteer will also be required to drink. Thereafter the volunteer is required to drink the reminder of the 240 mL of water.

The study drug will be administered approximately 4 hours after dinner, between 22.00 and 0.00 h (midnight), and within 15 minutes prior to bedtime.

The study consists of 4 periods. In which period the volunteer will receive the study drug or placebo will receive the study drug or placebo will be determined by chance. The doses that will be used will be determined based on the outcome of Part 1 of this study. In Periods 1 to 3 volunteers will receive JNJ55375515 twice (2 different doses) and placebo once, or the volunteer will receive placebo 3 times (the chance of this occurring is 25%). During Period 4 all volunteers will receive JNJ55375515, either dose x or y, which dose will be determined by chance. Dose x and y in Period 4 will be two of the doses tested in Period 1 to 3.

Neither the volunteer, nor the responsible doctor knows if JNJ55375515 or placebo will be dosed (except for Period 4, when all volunteers will receive JNJ-55375515); we call this *the study is blinded*. However, if it is important for the volunteers health, for example in case of a serious adverse event, this information can be looked up during the study.
General information on this the volunteer will find in the brochure *medical-scientific research*.

Study burden and risks

The study drug may cause some side effects. Overall JNJ-55375515 was well tolerated in the first clinical trial done, where the compound was given both

in a single dose (with doses ranging from 0.5mg to 12mg) and a multiple dose regimen (2, 6 and 9mg per day for 10 days). All side effects were reversible and of mild intensity, except for 1 case of nausea being of moderate intensity. The most frequently reported side effects were dizziness (often described by the subject as lightheadedness), irritability, headache and nausea.
A serious adverse event of aggression was reported in a subject being dosed with the highest dose in the multiple dosing regimen. This event was looked at with special attention and was deemed possibly caused by JNJ-55375515, but resolved while the subject was further dosed with the study drug.
Drawing blood and insertion of the indwelling cannula may be painful or cause some bruising.

Contacts

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Scientific
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BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy male subject between 18 and 54 years of age, inclusive.
Body Mass Index (BMI) between 18 and 30 kg/m2 inclusive
Non-smoker (not smoked for 3 months prior to screening)

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 90 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):	02-01-2018
Enrollment:	52
Type:	Actual

Ethics review

Approved WMO

Date:	13-12-2017

Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-12-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-06-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-07-2018
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	EUCTR2017-002457-11-NL
CCMO	NL64029.056.17

Study results

Date completed: 04-09-2018

Results posted: 24-02-2021

First publication
17-12-2020

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

Internal documents
File