An Open-label, Randomized Study in Healthy Participants to Investigate Effects of Food (high-fat) and Repeated Administration of Itraconazole on the Pharmacokinetics of JNJ-67953964.

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- To assess the effect of food (high-fat) on the bioavailability and pharmacokinetic (PK)-profile of a solid dosage formulation of JNJ-67953964.- To assess the effects of repeated QD administration of 200 mg of itraconazole (steady state) on the...

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

Summary

ID

NL-OMON49179

Source
ToetsingOnline

Brief title
JNJ-67953964 FE and DDI study

Condition

- Mood disorders and disturbances NEC

Synonym
Major Depressive Disorder

Research involving
Human

Sponsors and support

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

Intervention

Keyword: food effect, JNJ-67953964, Open-label

Outcome measures

Primary outcome

The primary endpoint will be the assessment of the PK of JNJ-67953964 under

different conditions. These include but are not limited to:

- Cmax - peak plasma concentration

- tmax - time to reach the Cmax

- AUClast area- under the plasma concentration-time curve from 0 to t hours

postdosing,calculated by trapezoidal summation (time t is the time of the last

quantifiable concentration Clast)

- AUC* - AUCt extrapolated to infinity, calculated as AUCt + Clast/ *z

- *z - elimination rate constant, determined by linear regression of the

terminal points of the ln-linear plasma concentration-time curve

- t* terminal half-life, defined as 0.693/*z

Geometric mean ratio of the AUCs and Cmax in fed vs fasted conditions and in

the presence vs. absence of itraconazole.

Secondary outcome

Main secondary endpoints include:

- AEs and AEs of interest

- Changes in vital signs and ECG

- Changes in clinical laboratory parameters

- Concentration of JNJ-67953964 metabolites in plasma and urine

- Concentration of JNJ-67953964 in urine.

Study description

Background summary

JNJ-67953964 is a compound that may potentially be used for the treatment of depression. Chronic stress, substance abuse and acute withdrawal results in activation of certain proteins (KOR: kappa opioid receptor) in the brain. This puts a break on the activity of dopamine, which is a chemical messenger that is part of the *rewarding system* of the brain and gives a good feeling. Reduced dopamine has therefore been linked to depression. JNJ-67953964 works by blocking the activity of KOR and can keep the dopamine activity normal.

Itraconazole is a medication that is used to treat fungal infections. In this study it is used because it decreases the activity of CYP3A4. CYP3A4 is an enzyme which helps to break down chemicals in the body. Itraconazole can thereby prolong the activity of certain medications.

Study objective

- To assess the effect of food (high-fat) on the bioavailability and pharmacokinetic (PK)- profile of a solid dosage formulation of JNJ-67953964.- To assess the effects of repeated QD administration of 200 mg of itraconazole (steady state) on the single-dose PK of JNJ-67953964 in healthy participants.- To assess the safety and tolerability of JNJ-67953964
- The determination of metabolites of JNJ-67953964 in plasma
- The determination of JNJ-67953964 and its metabolites in urine.

Study design

The study will consist of 3 periods during which the participant will stay in the research center for 4, 4, and 8 days (3, 3, and 7 nights), respectively. In Period 1 and 2, Day 1 is the day of administration of the study compound. The participants are expected at the research center at 14:00h in the afternoon prior to the day of administration of JNJ 67953964, so on Day -1. In Period 3, Day 4 is the day of administration of JNJ-67953964. There will be at least 6 days between each dosing with JNJ 67953964

The volunteers will be tested for the presence of coronavirus upon admission to

the research center. Until the test results are available, they will be separated from other volunteers and only have very limited contact with study staff. This is to avoid virus spread from potentially infected volunteers to other volunteers or to the study staff. Until the results are available, it is not certain whether the volunteers are infected or not and can thus potentially infect others. The test results will be available within a few hours. If the volunteers test positive for coronavirus, they cannot participate in the study.

Intervention

JNJ-67953964 will be given as 2 capsules of 5 mg for a total of 10 mg JNJ 67953964. The capsules will be ingested with 240 milliliters (mL) of water. In Period 1 and 2 all volunteers will receive the study compound once after a high-fat breakfast and once without breakfast. The order in which this will occur will be determined by chance: the subjects will be assigned at random to one of the two sequences. In Period 3 the subject will receive 10 mg JNJ-67953964 with itraconazole after consuming a high fat breakfast.
The dose of itraconazole in Period 3 will be 200 mg once per day from Day 1 up to and including Day 6. Itraconazole will be given as two capsules containing 100 mg itraconazole each. The capsules will be ingested with 240 mL water.

Study burden and risks

In previous studies in humans, single doses between 2 and 60 mg have been given to healthy volunteers. Multiple doses of 2 and 35 mg once daily over 14 days have also been investigated. JNJ 67953964 was well tolerated in these studies. JNJ 67953964 has been tested in a limited number of studies in humans. The possible discomforts, side effects, and risks related to JNJ-67953964 treatment are not all known. All medications may have side effects. Most side effects are mild to moderate, but some may be serious and/or require treatment or additional testing. Not many people have been treated at this time with JNJ-67953964. Only 263 people have received active JNJ 67953964, so less is known about this compound than is known about other medications you may have taken.

There were some side effects reported by volunteers who have been studied with JNJ-67953964. All the effects were temporary, mild to moderate in intensity, and not necessarily related to their taking JNJ-67953964.

Based on reports by volunteers in these studies possible side effects include:
• Itchiness
• Rash
• Feeling anxious
• Constipation
• Diarrhea
• Ringing in the ears

• Blurry vision
• Dizziness upon standing up
• Difficulty concentrating
• Feeling less coordinated
• Pain or discomfort when urinating
• Pain in the chest (not related to the heart)

Itraconazole may also cause side effects. The most important ones (observed in 1 in 10 people or more) are:
• Shortness of breath (dyspnea), cough.
• Fever.
• Headache, dizziness.
• Nausea, vomiting, abdominal pain, diarrhea, dyspepsia.
• Skin rash.
• Confusion.
• Tremor (a rhythmic, shaking, involuntary movement that occurs when muscles repeatedly contract and relax), drowsiness, fatigue.
• Blood pressure change.
• Chest pain.
• Decreased kidney function.
• Deficiency in certain white blood cells (granulocytopenia).
• Increased blood sugar levels.
• Decreased amount of magnesium in the blood.
• Increased blood levels of certain compounds (LDH, urea, γ-GT).
• Abnormal urine analysis.

Allergic reactions are always possible with a drug a subject has not taken before. Unexpected serious allergic reactions can be life-threatening. Some things that may happen during an allergic reaction to any type of medication include rash, breathing difficulty, sudden drop in blood pressure, swelling of mouth/throat/eyes, fast pulse, and/or sweating.

Drawing blood and/or insertion of the indwelling cannula (tube in an arm vein) may be painful or cause some bruising. In total, not more than 450 milliliters (mL) of blood will be taken from the participant.
To make a heart tracing, electrodes (small, plastic patches) will be pasted at specific locations on your arms, chest and legs. Prolonged use of these electrodes can cause skin irritation (rash and itching).
The high-fat breakfast is a big breakfast consisting of 2 fried eggs, fried potatoes and bacon. The entire breakfast must be consumed within 20 minutes, particularly for small eaters this can be difficult.

A sample for the coronavirus test will be taken from the back of the nose and throat using a swab. Taking the sample 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 volunteer to gag. When the sample is taken from the back of the nose, the 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)
Elderly (65 years and older)

Inclusion criteria

1. Healthy male and female participants between 18 and 55 years of age, inclusive.
2. Body Mass Index (BMI) between 18.0 and 29.9 kg/m2 inclusive (BMI=weight/height2)
3. Participant must be healthy on the basis of clinical laboratory tests performed at screening (e.g. serum chemistry panel, hematology, and urinalysis).
4. Participant must be healthy on the basis of physical examination, medical history, vital signs, and 12-lead ECG [QTcF <= 450 msec for males and <= 470 msec

for females] performed at screening and admission to the clinical unit. Minor abnormalities in ECG, which are not considered to be of clinical significance by the investigator, are acceptable.
5. Non-smokers (not smoked for 3 months prior to screening).

Exclusion criteria

1. History of or current significant medical illness including (but not limited to) cardiac arrhythmias or other cardiac disease, hematological disease, lipid abnormalities, bronchospastic respiratory disease, diabetes mellitus, renal or hepatic insufficiency, thyroid disease, Parkinson*s disease, infection, or any other illness that the Investigator considers should exclude the participant.
2. History of any gastric surgery, documented gastric disease (including peptic ulcer disease, gastritis, achlorhydria, upper GI bleeding, esophagitis, or any GI precancerous condition), current clinically evident GI complaints including functional gastrointestinal disorders (FGID).
3. Serology positive for hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV) antibodies or human immunodeficiency virus (HIV) antibodies.
4. Participant has a history of at least mild drug or alcohol use disorder according to Diagnostic and Statistical Manual of Mental Disorders (5th edition) (DSM-V) criteria within 6 months before Screening or positive test result(s) for alcohol, nicotine metabolites and/or drugs of abuse (opiates [including methadone], cocaine, amphetamines, methamphetamines, cannabinoids, barbiturates, ecstasy and benzodiazepines) at screening or admission.
5. History of malignancy within 5 years before screening (exceptions are squamous and basal cell carcinomas of the skin and carcinoma in situ of the cervix, or malignancy, which is considered cured with minimal risk of recurrence).

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	02-03-2020
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	STADA
Generic name:	Itraconazole
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	04-02-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-02-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-08-2020
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	EUCTR2019-004329-26-NL
CCMO	NL72593.056.20

Study results

Date completed: 08-10-2020

Results posted: 18-05-2021

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

Internal documents
File