A single-center, open-label study to evaluate the distribution, metabolism, and excretion (DME) and pharmacokinetics of MIJ821 following a single intravenous (i.v.) infusion of [14C]MIJ821 in healthy male participants.

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

Summary

ID

NL-OMON51743

Source
ToetsingOnline

Brief title
Distribution, metabolism, and excretion study with [14C]MIJ821

Condition

- Mood disorders and disturbances NEC

Synonym
Major depressive disorder, mental disorder

Research involving

Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: 14C, ADME, MIJ821, PK

Outcome measures

Primary outcome

- To determine the routes and rates of excretion of [14C]MIJ821 related radioactivity, including mass balance of total drug-related radioactivity in urine, feces, and elimination of radioactivity via expired air, following a single 0.16 mg/kg 40-minute i.v. infusion of [14C]MIJ821 in healthy male participants.

- To determine the pharmacokinetics (PK) of total radioactivity radiolabeled components in blood and plasma following a single 0.16 mg/kg 40-minute i.v. infusion of [14C]MIJ821 in healthy male participants.

- To characterize the PK of MIJ821 and known key metabolites, if applicable, in plasma following a single 0.16 mg/kg 40-minute i.v. infusion of [14C]MIJ821 in healthy male participants.

Secondary outcome

- To assess the safety and tolerability of a single 0.16 mg/kg i.v. dose of [14C]MIJ821 in healthy male participants.

Study description

Background summary

MIJ821 is a new compound that may potentially be used for the treatment of major depressive disorder. Major depressive disorder is characterized by low mood and often by low self-esteem, low energy, and a loss of interest. It can strongly affect a person*s life and health, including significantly increased risk of suicidality, and is difficult to treat, even with existing antidepressants. If at least two different types of treatment do not help, this is considered a treatment resistant depression.

Ketamine has been shown to produce rapid (within hours) and long lasting (days to weeks) antidepressant effects in patients with treatment resistant depression, but can result in a dissociative state (a feeling of being separated from the body, like a trance). The mechanisms of action of MIJ821 is similar to that of ketamine. However, by acting more specifically than ketamine, MIJ821 aims to reduce the dissociative side effects, while still having an antidepressant effect.

Study objective

In this study, we will investigate how quickly and to what extent the study compound MIJ821 is absorbed, transported, and eliminated from the body. For this study, MIJ821 is radioactively labelled with carbon-14 (14C). In this way, MIJ821 can be traced in blood, urine, feces, and expired air. We also look at the break down products of MIJ821 in urine, feces, and blood.

We will also investigate how safe the new compound MIJ821 is and how well it is tolerated when it is used by healthy male participants.

We also look at the effect of your genetic information on your body*s response to MIJ821 as follows:
1) We will analyze your DNA for the activity of a gene of the enzyme called CYP2D6. Taking part in this DNA test is mandatory.
2) We will do exploratory research to investigate if differences in genetic information relate to differences in how the body handles MIJ821.Taking part in this DNA test is not mandatory.

MIJ821 has been used by humans before. In addition, it has been extensively tested in the laboratory and on animals.

Study design

The research requires the volunteer to stay in the research center for 17 days

(16 nights). Day 1 is the day the study drug is administered.

From Day 1 to Day 16, all urine and faeces are collected and regular blood and exhaled air samples are taken to measure the amount of radioactivity in the urine, faeces, blood and exhaled air. If the amount of radioactivity on Day 16 is still above predefined limits, the volunteer should return to the study center for up to 4 additional 24-hour visits.

For 24 hours prior to entering the research center for the stay and before the 24-hour visits, the volunteer should collect faeces at home and bring them to the research center.

Below is an overview of the days on which the volunteer stays in the research center or on which the volunteer visits the research center:

Screening
1 short visit between Day -35 and Day 2

Arrival
Day 1

Inhouse stay
Day -1 to Day 16

Departure
Day 16

The volunteers may need to come back to the research center after their departure on Day 16. This depends on the amount of radioactivity in the bodily material.

24-hour visits
Day 18 to Day 19*
Day 22 to Day 23*
Day 27 to Day 28*
Day 33 to Day 34*
*Depending on the radioactivity levels in the bodily material, these visits can be cancelled

The volunteer receives MIJ821 as an intravenous infusion (solution of the drug administered directly into a blood vessel). The infusion lasts 40 minutes.

The volunteer will receive the study drug on the morning of Day 1 after a 10 o'clock overnight fast. After administration, the volunteer must fast for another 4 hours. also, the volunteer should not drink any liquids from 1 hour before to 2 hours after dosing.

Intervention

The volunteer will receive a single dose of 0.16 mg/kg of 14C radioactively labeled MIJ821. This means that 0.16 milligram of MIJ821 will be administered per 1 kg of body weight, so the actual dose will depend on the body weight of the volunteer. The dose will contain between 0.98 mSv and 1.52 mSv of radiation, depending on that body weight.

Study burden and risks

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, sweating, low heart rate, or drop in blood pressure with dizziness or fainting.

In total, we will take a maximum of 500 mL of blood from screening to follow-up. 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 arms, chest and legs. Prolonged use of these electrodes can cause skin irritation.

Intravenous infusion of the study compound
The infusion of the study compound in a vein in your arm may result in reactions in the skin around the place where the needle goes in. Furthermore, reactions such as itching, flushing, headache, nausea/vomiting, low blood pressure, urticaria or changes in breathing could occur.

Fasting:
If someone has to fast for a prolonged time during the study, this may lead to symptoms such as dizziness, headache, stomach upset, or fainting.

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 gagging. When the sample is taken from the back of the nose, The volunteer may experience a stinging sensation and eyes may become watery.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Signed informed consent must be obtained prior to participation in the study.
2. Healthy males, aged 18 to 55 years (inclusive) and in good health as determined by past and current medical history, physical and neurological examination, vital signs, electrocardiogram, and laboratory tests at screening and baseline (whenever applicable).
3. At screening and at baseline (Day -1), vital signs after 5 minutes in supine position must be within the ranges defined in protocol inclusion criteria.
4. Participants must weigh at least 60 kg and should not exceed 90 kg to participate in the study and must have a body mass index (BMI) within the range of 18.0 to 29.9 kg/m² (inclusive) at screening.
5. NM or IM for CYP2D6.
6. Participants must be able to communicate well with the Investigator and to

comply with the requirements of the entire study, including adhering to study restrictions and visit schedule.

See protocol for complete details of inclusion criteria.

Exclusion criteria

1. Recent history (<3 months) prior to screening of nicotine product use or a urine cotinine level >500 ng/mL at Screening or Baseline.
2. Positive blood alcohol concentration or drug test at Screening or Baseline.
3. Absence of regular defecation pattern (participants with an average defecation frequency of less than once per 2 days or chronic diarrhea).
4. Any surgical or medical condition that might significantly alter the (A)DME of drugs, or that may jeopardize the participant in case of participation in the study.
5. Exposure to radiation at a level of up to 1.0 mSv over the past year, or up to 3.0 mSv over the past 3 years. (e.g., due to systemic administration of radioactive substances, or to external irradiation [e.g., by X-rays] for diagnostic, therapeutic, job-related, or research purposes).

Further criteria apply, see protocol.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	20-04-2022
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO Date:	11-04-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-04-2022
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	EUCTR2021-006026-51-NL
CCMO	NL80917.056.22

Study results

Date completed:	10-08-2022
Results posted:	28-07-2023

First publication
20-06-2022