# An Open-Label Study to Investigate the Absorption, Metabolism, and Excretion of [14C]-JNJ-67856633, a MALT1 inhibitor, After a Single Oral Dose in Healthy Male Participants

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In this study we will investigate how quickly and to what extent the new compound JNJ-67856633 is absorbed, transported, and eliminated from the body. JNJ-67856633 is radioactively labelled with carbon-14 (14C).We also investigate how safe JNJ-...

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| **Ethical review** | Approved WMO |
| **Status** | Completed |
| **Health condition type** | Other condition |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON50324

**Source**
ToetsingOnline

**Brief title**
Absorption, metabolism, and excretion of 14C-labeled JNJ-67856633

### Condition

- Other condition
- Lymphomas non-Hodgkin's B-cell

**Synonym**
blood cancers, Lymphomas

**Health condition**

chronic lymphocytic leukemia

**Research involving**
Human

## Sponsors and support

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

## Intervention

**Keyword:** [14C]-JNJ-67856633, Healthy Male Participants, Metabolism

## Outcome measures

### Primary outcome

-To determine the routes of excretion for JNJ-67856633 after administration of a single oral dose of 14C-JNJ-67856633 in healthy adult male participants.

- To characterize the metabolic pathways for JNJ-67856633 and the chemical structure of predominant metabolites after a single oral dose of 300 mg 14C-JNJ-67856633 in healthy adult male participants.

- To determine the PK of JNJ-67856633 and total radioactivity in plasma, whole blood (total radioactivity only), urine, feces (total radioactivity only), and duodenal fluid after administration of a single oral dose of 14C-JNJ-67856633 in healthy adult male participants.

### Secondary outcome

- To characterize the safety and tolerability of a single oral dose of 300 mg 14C-JNJ-67856633 in healthy adult male participants.

# Study description

### Background summary

JNJ-67856633 is a new compound that may potentially be used for the treatment of B cell non Hodgkin lymphoma (NHL) and chronic lymphocytic leukemia (CLL). Lymphomas are blood cancers in the lymph nodes. Leukemia is a group of blood cancers that usually begin in the bone marrow and result in high numbers of abnormal blood cells. JNJ-67856633 blocks an enzyme (MALT1) that plays a role in the regulation of the growth and maturation of B cells, the type of white blood cells that become cancerous in the above conditions.

## Study objective

In this study we will investigate how quickly and to what extent the new compound JNJ-67856633 is absorbed, transported, and eliminated from the body. JNJ-67856633 is radioactively labelled with carbon-14 (14C).

We also investigate how safe JNJ-67856633 is and how well it is tolerated when it is used by healthy participants.

## Study design

Part A:
The study will take a maximum of 10 weeks from the screening until the follow-up visit.
For the study it is necessary that the volunteer stays in the research center for 1 period of 16 days (15 nights).
The volunteer will be given a single dose [14C]-JNJ-67856633 as 3 oral capsules with 240 milliliters (mL) of (tap) water.

Part B:
The study will take a maximum of 10 weeks from the screening until the follow-up visit.
For the study it is necessary that the volunteer stays in the research center for 1 period of 16 days (15 nights).
The volunteer will be given a single dose [14C]-JNJ-67856633 as 3 oral capsules with 240 milliliters (mL) of (tap) water.
On Day 1, a nasoduodenal tube will be inserted approximately 2 hours before administration of the study compound to collect bile.

## Intervention

Screening | Arrival | In-house stay | Departure |
Visits*
Day -21 up to Day -2 Day -1 Day -1 up to Day 15 | Day 15 | Day 22 Day 29 Day 36 Day 43
* These visits are only needed if the volunteer did not excrete enough radioactivity yet.

**Study burden and risks**

Possible side effects:
All medicinal products have known or unforeseeable side effects. There may be risks, discomforts, side effects to using JNJ-67856633.

The potential risks based on an ongoing study in healthy participants are outlined below:
As of 6 May 2021, interim safety data are available for 70 healthy participants from this study. They have been administered a single dose of 100 mg (40 participants) and a single dose of 300 mg (30 participants) of JNJ-67856633. Only 4 drug-related side effects were reported. One participant who received the single dose of 100 mg reported dizziness of mild severity. Two participants who received the single dose of 300 mg reported headaches, one of mild and one of moderate severity. One participant who received the single dose of 300 mg reported diarrhea of mild severity.

There were no clinically significant observations for laboratory safety, vital signs and ECGs.

Side effects that occurred in at least 10% of the patients during chronic dosing with JNJ-67856633 are outlined below:
• hyperbilirubinemia (high level of bilirubin in the blood)
• neutropenia (Low numbers of white blood cells)
• anaemia (Low numbers of red blood cells)
• thrombocytopenia (Low numbers of platelets)
• diarrhoea
• fatigue (Feeling tired)
• creatinine increase
• abdominal pain
• nausea
• peripheral oedema
• constipation
• headache
• dyspnoe (difficulty breathing)

Possible discomforts:
ECG.
There is generally no risk with having an ECG. The sticky patches may pull the volunteers skin or cause redness or itching.

Blood draw.
Taking blood may (rarely) cause pain, bleeding, bruising or infection at the place where the needle goes into the skin. Similarly, the volunteer may feel dizzy or even faint during the procedure. The study staff who take the blood will do all they can to keep these discomforts and risks to a minimum. The

amount of blood drawn during the study will be less than 500 milliliters. This is less than the amount of blood that people give during a normal blood donation (which is about 500 milliliters). Sometimes a blood test may need to be repeated.

Exposure to radiation.
This study involves using radioactive markers. The additional amount of radiation the volunteer will be exposed to in this study is 0.24 mSv. We call this radiation exposure. To compare: the background radiation in the Netherlands is ~2.5 mSv per year. Background radiation is the radiation to which you are exposed every day. Sources of background radiation are for example soil, food, and some building materials. There is always radiation from space as well (cosmic radiation). The total radioactivity can be compared with that of about 2/5 of a mammogram testing (approximately 0.7 mSv), 1/20 of a chest CT scan (approximately 5.8 mSv), or approximately 1.5 months of natural background radiation exposure. A flight from Frankfurt to New York and back results in an average effective dose of about 0.1 mSv. If you participate in scientific research involving exposure to radiation more often, you should discuss with the responsible doctor whether participation at this moment would be safe/advisable.

Duodenal sampling (Part B)
For the bile sampling the tube will be placed through the volunteers nose: this may be painful and cause discomfort. Local anesthesia will be used.

Coronavirus test
Samples for the coronavirus test will be taken from the back of the volunteer his 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 volunteers throat may cause him to gag. When the sample is taken from the back of the volunteers nose, he may experience a stinging sensation and his eyes may become watery.

# Contacts

**Public**
Janssen-Cilag

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**Scientific**
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NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)

## Inclusion criteria

1. Participant must 18 to 55 years of age, inclusive.
2. Must be healthy on the basis of physical examination, and medical history, performed at screening and predose.
3. Must be healthy on the basis of clinical laboratory tests performed at screening. If the results of the serum chemistry panel or hematology panel are outside the normal reference ranges, the participant may be included only if the investigator judges the abnormalities or deviations from normal to be not clinically significant. This determination must be recorded in the participant's source documents and initialed by the investigator. Total bilirubin, ALT, AST, and alkaline phosphatase (ALP) must be within normal limits at screening.
4. Participant has estimated glomerular filtration rate (eGFR) >610 mL/min at screening as calculated by MDRD formula (Section 10.9, Appendix 9).
5. Participants must have regular bowel movements (ie, average production of at least one stool every 2 days).

Further criteria apply

## Exclusion criteria

1. History of or current clinically significant medical illness including (but not limited to) cardiac arrhythmias or other cardiac disease, hematologic disease, coagulation disorders (including any abnormal bleeding or blood dyscrasias), lipid abnormalities, significant pulmonary disease, including

bronchospastic respiratory disease, diabetes mellitus, hepatic or renal insufficiency, thyroid disease, neurologic or psychiatric disease, infection, or any other illness that the investigator considers should exclude the participant or that could interfere with the interpretation of the study results.
2. History of suspected or confirmed Coronavirus Disease 2019 (COVID-19) within 4 weeks before intake of study drug, or tests positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) at admission to the study site.
3. History of stomach or intestinal surgery or resection, including cholecystectomy, that would potentially alter absorption or excretion of orally administered drugs (appendectomy and hernia repair will be allowed).
4. Participants with a removed gallbladder, or with a history of upper gastrointestinal (stomach, duodenum) surgery, or with a recent (less than 3 months prior to screening) episode of gallstones.
5. Participant has intolerance to lidocaine (Group B only).

Further criteria apply

# Study design

## Design

**Study type:** Interventional

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

## Recruitment

NL

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|---|---|
| Recruitment status: | Completed |
| Start date (anticipated): | 17-08-2021 |
| Enrollment: | 8 |
| Type: | Actual |

# Ethics review

Approved WMO

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|---|---|
| Date: | 05-07-2021 |

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| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 26-07-2021 |
| 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 | EUCTR2021-001765-20-NL |
| CCMO | NL78095.056.21 |

# Study results

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|---|---|
| Date completed: | 04-10-2021 |
| Results posted: | 03-04-2024 |

**First publication**
03-11-2022

**URL result**
URL
Type
int
Naam

M2.2 Samenvatting voor de leek
URL

**Internal documents**
File