A Phase 1, Randomized, Double-Blind, Placebo-Controlled, Single and Multiple Day Dose Study to Assess the Safety and Tolerability of JNJ-67670187 in Healthy Participants

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON47984

Source
ToetsingOnline

Brief title
67670187IBD1001

Condition

- Gastrointestinal inflammatory conditions

Synonym
IBD, Ulcerative colitis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: JNJ-67670187, Safety, Single/Multiple dose, Tolerability

Outcome measures

Primary outcome

To assess the safety and tolerability of JNJ-67670187 (11-strain Clostridia mix) compared with placebo after administration of:

Single Dose administered orally once in healthy participants (Part 1).

Multiple Dose administered orally once daily over 14 consecutive days with and without bowel preparation pretreatments in healthy participants (Parts 2 and 3).

Secondary outcome

To assess the colonization dynamics of JNJ-67670187 in the stool following single and multiple oral study intervention administrations (Parts 1 and 2).
To assess the colonization dynamics of JNJ-67670187 following multiple oral study intervention administrations with specific pretreatments (Parts 2 and 3).

Study description

Background summary

JNJ-67670187 is a new compound that may eventually be used for the treatment of

inflammatory bowel disease (IBD).

JNJ 67670187 contains 11 viable bacterium (Clostridium) strains which were isolated from the faeces of a single healthy human donor. These bacteria do not cause illnesses and produce no toxins. Similar bacterial strains have been demonstrated to reduce inflammation in laboratory experiments. JNJ 67670187, which is a so-called live biotherapeutic product (LBP), may provide a therapeutic benefit for patients with IBD. JNJ-67670187 is in development and is not yet registered as a drug.

Study objective

The purpose of this study is to investigate how safe the new compound JNJ-67670187 is and how well it is tolerated when it is administered to healthy volunteers. Another purpose is to see how the body responds to JNJ 67670187 by analysing blood, urine, saliva, and feces samples.

This study will be performed in 102 to 144 healthy volunteers, divided over 3 parts. In Part 1 of this study, JNJ 67670187 will be administered to humans for the first time. This part will run in Belgium and has been approved by the IEC and HA. In this part, 18 healthy volunteers will receive JNJ 67670187 as a single dose at 2 different dose levels. In Parts 2 and 3, JNJ 67670187 will be taken multiple days (14 days) at the same dose levels. The remainder of this document concerns Part 2 / Part 3 only.

In Part 2, another purpose is to evaluate the effect of pre-treatment with an antibiotic on the growth of the bacteria from JNJ 67670187 in the bowel. Therefore, volunteers with and without pre-treatment with an antibiotic will be compared.

The results of Part 2 of the study are expected to allow a well-informed decision on whether to continue with the development of JNJ 67670187 for treatment of IBD and whether to include a pre-treatment with antibiotics in future studies with JNJ 67670187 or in future therapy for IBD patients.

Part 2 will consist of 4 groups of 14 volunteers each.

In Part 3, another purpose is to find out if pre-treatment with a laxative, or with an antibiotic together with a laxative, will help the bacteria in JNJ 67670187 to grow in the bowel of the body.

The results of Part 3 of the study are expected to allow a well-informed decision on whether to continue with the development of JNJ 67670187 for treatment of IBD and also whether to include a pre-treatment with laxative with or without antibiotic in future studies with JNJ-67670187 or in future therapy for IBD patients.

Part 3 of study will consist of up to 2 groups and 1 optional group of 14 volunteers each.

Study design

Group 1: 7 days (6 nights) with an amount of ambulatory visits. On day 1 the subjects will receive one oral capsule of study medication or placebo.(This part is performed in Belgium and has been approved by the HA/IEC).

Group 2: 7 days (6 nights) with an amount of ambulatory visits. On day one the subjects will receive 10 oral capsules of study medication or placebo.(This part is performed in Belgium and has been approved by the HA/IEC).

Group 3: 19 days (18 nights). Admission to clinic on day -2. Days 1-14 the subjects will receive an oral capsule with study medication once a day.

Group 4: 24 days (23 nights). Admission to clinic on day -7 for baseline assesments. Pre-treatment will start on day -6. On days -6 to -2 the subjects will receive 1 vancomycine capsule four times a day. On days 1-14 the subjects will receive an oral capsule with study medication once a day.

Group 5: 19 days (18 nights). Admission to clinic on day -2. On days 1-14 the subjects will receive 10 capsules of study medication once a day.

Group 6: 24 days (23 nights). Admission to clinic on day -7 for baseline assessments. Pre-treatment will start on day -6. On days -6 to -2 the subjects will receive 1 vancomycine capsule once a day. On days 1-14 the subjects will receive 10 capsules of study medication once a day.

Group 7: 20 days (19 nights). Admission to clinic on day -3 for baseline assesments. Pre-treatment will start on day -2. On days -6 to -2 the subjects will receive 17g PEG laxative with 240mL of juice or water 4 times a day. On days 1-14 the subjects will receive 10 capsules of study medication once a day.

Group 8: 24 days (23 nights) Admission to clinic on day -7 for baseline assessments. Pre-treatment will start on day -6. On days -6 to -3 the subjects will receive one capsule with vancomycin four times a day. On days -2 they will receive one capsule of vancomycine four times a day and 17mg PEG laxative with 240
mL juice or water once a day. On days 1-14 they will receive 10 capsules of study medication once a day.

Group 9: 19 days (18 nights). Admission to clinic on day -2. On days 1-14 the subjects will receive 10 capsules of study medication once a day. On day 15 a liquid injection will be inserted in the intestine as a preparation for the biopsy.

Intervention

You will receive JNJ-67670187 or placebo once daily for 14 days as oral capsules with 240 milliliters (mL) of water. JNJ-67670187 will be given at 2 different dose levels, which means that you may receive either 1 capsule or 10 capsules.

In Group 1 and 2 the subjects will receive the study medication once. In group 1 one capsule will be administered. In group 2 ten capsules will be administered.

In Groups 3 and 5, volunteers will only receive the study compound without any pre-treatment. In Group 5, the strength of the study compound will be higher than in Group 3. Therefore, Group 5 will only start when it is confirmed that safety results of the first 18 days of Group 3 do not raise any safety issues.

Volunteers in Groups 4 and 6 will receive pre treatment with an antibiotic (i.e., vancomycin) for 5 days, followed by one day without any treatment before administration of the study compound will be started. The antibiotic will be given 4 times a day at an oral dose of 125 mg / dose for 5 consecutive days. In Group 6, the strength of the study compound will be 10 times higher compared to Group 4.

Group 7 is an optional group which will only be conducted if in previous parts/groups no bacteria from JNJ 67670187 were detected in the feces of the volunteers. Volunteers in Group 7 will be pre treated with a laxative (i.e., Movicolon) for 2 days before administration of the study compound. The laxative will be a polyethylene glycol (PEG) laxative given 4 times a day for 2 days at a dose of 17 grams mixed with approximately 240 mL of water or juice.

Volunteers in Group 8 will be pre treated with an antibiotic (i.e., vancomycin) for 5 days in combination with 2 days of pre treatment with a laxative (i.e., Movicolon), before administration of the study compound .
• The antibiotic vancomycin will be given 4 times a day at an oral dose of 125 mg / dose for 5 consecutive days.
• The laxative will be a polyethylene glycol (PEG) laxative given 4 times a day for 2 days at a dose of 17 grams mixed with approximately 30 240 mL of water or juice.
The 2 day pre treatment with the laxative will be started on the last (5th) day of pre treatment with the antibiotic.

Group 9 is an optional group which will only be conducted if in previous parts/groups no bacteria from JNJ 67670187 were detected in the feces of the volunteers. The purpose of Group 9 would then be to find out if bacteria from JNJ 67670187 will populate the mucous wall of the bowel. This will be

investigated by taking small tissue biopsy and mucous samples of the bowel. Depending on results in previous groups in Parts 2 and 3, pre treatments may be added to this group.

Part 3 will begin after safety and tolerability of the higher dose of JNJ 67670187 are assessed in previous groups in Part 2. As the dose of JNJ 67670187 will be the same in Groups 7 and 8 (i.e., 10 capsules), these groups may be dosed simultaneously.

Study burden and risks

Pre-treatment (if applicable)
Symptoms associated with vancomycin use could include: dropping blood pressure, shortness of breath, redness of the upper body and/or face, and decrease in kidney function (in less than 1 out of 10 people) and transient or permanent hearing loss (in less than 1 out of 100 people). The risk of side effects from vancomycin is expected to be very low during the 5-day period of dosing because the duration of use is shorter than prescribed for a true infection so that the amount of drug taken is not likely to remain in the body for a long period of time.

Laxative(group 7 en 8)
Common side effects include: abdominal cramps, bloating, gassiness, flatulence, burping, and nausea. Rare symptoms associated with Movicolon use could include: vomiting, dehydration, allergic reactions. The risk of side effects from Movicolon is expected to be very low at the doses and for the length of treatment prescribed in this study. Although the risk in healthy adults is very low, to prevent dehydration from occurring during the time you take Movicolon the subjects will be encouraged to drink extra fluids during the day.

Procedures
Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising.
In total, we will take no more than 500 milliliters (mL) of blood from you. This amount does not cause any problems in adults.
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).

Biopsy
Serious complications such as a perforation (a hole in the wall of the colon) are rare (less than 1 out of 1000 people) and could require surgery. The procedure may be associated with abdominal pain, diarrhea, bleeding, flatulence, anal pain and bloating but even these occur in just 1-2% of the procedures.

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. Be a male or female.
2. Be 18 (or the legal age of consent in the jurisdiction in which the study is taking place) to 60 years of age, inclusive.
3. Have a body mass index (BMI) between 18 and 30 kilogram per square metre (kg/m^2) inclusive, and a body weight of at least 50 kilogram (kg).
4. Be otherwise healthy on the basis of physical examination, medical history, and vital signs, and 12-lead electrocardiogram (ECG) performed at screening and at admission.
5. Be otherwise healthy on the basis of clinical laboratory tests performed at screening and at admission. If the results of the serum chemistry panel, hematology, or urinalysis 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.

Exclusion criteria

Coexisting Medical Conditions or Past Medical History
1. History of any clinically significant medical illness or medical disorders the investigator considers should exclude the participant, including (but not limited to), neuromuscular, hematological disease, immune deficiency state, respiratory disease, hepatic or gastrointestinal (GI) disease, neurological or psychiatric disease, ophthalmological disorders, neoplastic disease, renal or urinary tract diseases, or dermatological disease.
2. Has any condition for which, in the opinion of the investigator, participation would not be in the best interest of the participant (eg, compromise the well being) or that could prevent, limit, or confound the protocol-specified assessments.
3. Inability to swallow capsules (dysphagia).
4. Has a known intolerance or allergy to vancomycin, polyethylene glycol (PEG) laxatives, or any of the excipients in the study interventions.
5. Has a known intolerance or allergy to 2 or more classes of the antibiotics that may be used to treat infection with the study intervention (tigecycline, metronidazole, ampicillin/sulbactam, amoxicillin/clavulanate, meropenem, imipenem/cilastatin, and/or vancomycin).

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	31-12-2018
Enrollment:	98
Type:	Actual

Ethics review

Approved WMO Date:	20-11-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-01-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-08-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-08-2019
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	EUCTR2018-002287-81-NL
ClinicalTrials.gov	NCT03723746
CCMO	NL67899.056.18