A Phase 1, Open-label, Randomized, 3-way Crossover Study to Assess the Pharmacokinetic Interaction Between JNJ-64417184 and JNJ-53718678 After Single and Multiple Dosing in Healthy Subjects

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract infections
Study type	Interventional

Summary

ID

NL-OMON48293

Source
ToetsingOnline

Brief title
DDI study JNJ-64417184 and JNJ-53718678

Condition

- Respiratory tract infections

Synonym
cold virus, Respiratory syncytial virus

Research involving
Human

Sponsors and support

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

Intervention

Keyword: DDI, JNJ-53718678, JNJ-64417184, Pharmacokinetic

Outcome measures

Primary outcome

To evaluate the effect of single- and multiple-dose (once daily for 7 days) oral JNJ-64417184 on the PK of single- and multiple-dose (once daily for 7 days) oral JNJ-53718678 when coadministered to healthy adult subjects under fed conditions.

To evaluate the effect of single- and multiple-dose (once daily for 7 days) oral JNJ-53718678 on the PK of single- and multiple-dose (once daily for 7 days) oral JNJ-64417184 when coadministered to healthy adult subjects under fed conditions.

Secondary outcome

To evaluate the safety and tolerability of single- and multiple-dose (once daily for 7 days) oral JNJ-64417184 and JNJ-53718678 when administered alone and in combination in healthy adult subjects under fed conditions.

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Study description

Background summary

JNJ-64417184 and JNJ-53718678 are new compounds that may eventually be used for the treatment of infection with respiratory syncytial virus (RS-virus). Both compounds are able to inhibit the RS-virus by different mechanisms of action. JNJ 64417184 is able to inhibit the RS-virus by inhibiting the viral protein production in the virus whereas JNJ-53718678 is able to inhibit the fusion of RS-viruses with certain cells. A combination of the 2 compounds targeting 2 different mechanisms of action might be a more effective approach for treating RS-virus infection than each compound alone.

Study objective

The purpose of this study is to investigate how quickly and to what extent JNJ-64417184 and JNJ-53718678 are absorbed and eliminated from the body (this is called pharmacokinetics) when administered alone and when administered together. It will also be investigated how safe the new compounds JNJ-64417184 and JNJ-53718678 are and how well they are tolerated when they are administered alone or as a combination to healthy volunteers.

Study design

The actual study will consist of 3 treatment periods during which the subjects will stay in the research center for 9 days (8 nights).

In each treatment period, Day 1 is the first day of administration of the study compound. In each treatment period, subjects are expected at the research center at 14:00 h in the afternoon prior to the day of first administration of the study compound. In each treatment period, subjects will leave the research center on Day 8.

Intervention

The study consists of 3 treatment periods. In each treatment period, subjects will receive either JNJ-6441784 or JNJ 53718678 alone, or a combination of JNJ 64417184 and JNJ 53718678, once daily for 7 consecutive days. There will be 6 different treatment orders as explained in the table below. The order in which subjects will receive these treatments will be determined by chance.

JNJ 64417184 will be given as tablets and JNJ 53718678 will be given as an oral suspension (a drink). Thereafter subjects will have to drink approximately 240 milliliter (mL) of water. When JNJ-64417184 and JNJ-53718678 are coadministered, then intake of JNJ-64417184 will be first followed by

JNJ-53718678. There will be a maximum of 5 minutes between both administrations.

Study burden and risks

JNJ-64417184
JNJ-64417184 is being studied in one other ongoing placebo-controlled clinical study, in which this compound or placebo has been administered to 80 healthy adult subjects as single and multiple doses. The highest dose level tested thus far is 900 mg. All doses were well tolerated. The most commonly reported side effects (reported at least 2 times) were headache, dizziness, vomiting, pruritus (itch) and nasopharyngitis that were all mild or moderate. Two side effects were considered related to the study compound, these were somnolence and dyspepsia (stomach upset).

JNJ-53718678
JNJ-53718678 has been studied in 5 completed clinical studies and is being studied in 3 ongoing clinical studies. A total of 234 subject received at least one dose of JNJ-53718678. Also children which were hospitalized due to naturally acquired RS-virus infection, have received JNJ-53718678. Overall, treatment with JNJ-53718678 was generally safe and well tolerated. The most commonly reported side effects were diarrhea and dysgeusia. All side effects were mild or moderate.

The study compounds may also have side effects that are still unknown.

Possible discomforts due to procedures
Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising.

In total, we will take about 500mL of blood. This amount does not cause any problems in adults.

To make a heart tracing, electrodes will be pasted at specific locations on the arms, chest and legs. Prolonged use of these electrodes can cause skin irritation.

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. Male or female, between 18 and 55 years of age, extremes included, at screening.
2. Body mass index (BMI; weight [kg]/height2 [m]2) between 18.0 and 30.0 kg/m2, extremes included, and body weight not less than 50 kg at screening.
3. Healthy on the basis of physical examination (including skin examination), medical and surgical history, and vital signs (systolic blood pressure [SBP], diastolic blood pressure [DBP], and pulse rate [after the subject is supine for at least 5 minutes], respiratory rate, and oral body temperature) performed at screening. If there are abnormalities (not applicable for the parameters listed in inclusion criterion 5 [for blood pressure]), the subject may be included only if the investigator judges the abnormalities to be not clinically significant. This determination must be recorded in the subject's source documents and initialed by the investigator.
4. Healthy on the basis of clinical laboratory tests performed at screening. If the results of the hematology, biochemistry, blood coagulation, or urinalysis are outside the normal reference ranges (not applicable for the parameters listed in exclusion criteria 1 and 2 [for laboratory parameters]), the subject 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 subject's source documents and initialed by the investigator.

5. Blood pressure (after the subject is supine for 5 minutes) between 90 and 140 mmHg systolic, extremes included, and no higher than 90 mmHg diastolic at screening.
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 (calculated creatinine clearance/estimated glomerular filtration rate [eGFR] <60 mL/min at screening, calculated by the Modification of Diet in Renal Disease [MDRD] formula30), thyroid disease, neurologic or psychiatric disease, infection, or any other illness that the investigator considers should exclude the subject or that could interfere with the interpretation of the study results.
2. Any laboratory abnormality >=grade 1 (as defined by the Division of Acquired Immune Deficiency Syndrome [DAIDS] Table for Grading the Severity of Adult and Pediatric Adverse Events)9, considered to be clinically significant by the investigator at screening.
3. Past history of cardiac arrhythmias (eg, extrasystoli, tachycardia at rest), history of risk factors for Torsade de Pointes syndrome (eg, hypokalemia, family history of long QT Syndrome).
4. Any evidence of heart block or bundle branch block at screening.
5. History of human immunodeficiency virus type 1 (HIV-1) or HIV-2 infection, or tests positive for HIV-1 or -2 at screening.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-09-2019
Enrollment:	16
Type:	Actual

Ethics review

Approved WMO Date:	28-08-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-09-2019
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	EUCTR2019-002695-13-NL
CCMO	NL71262.056.19

Study results

Results posted: 27-06-2022

First publication
23-12-2020