An open-label, single-sequence study to investigate the effects of gastric acid suppression by Rabeprazole on the pharmacokinetics of BMS-986165 in healthy participants

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Ethical review	Approved WMO
Status	Completed
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON47975

Source
ToetsingOnline

Brief title
Gastric pH effect on BMS-986165

Condition

- Autoimmune disorders

Synonym
Psoriasis, systemic lupus erythematosus and Crohn's disease.

Research involving
Human

Sponsors and support

Primary sponsor: BritsolMyers Squibb Research and Development
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: BMS-986165, Rabeprazole

Outcome measures

Primary outcome

PK parameters in healthy participants administered BMS-986165 alone (reference)

versus in combination with rabeprazole (test):

- BMS-986165: Cmax, AUC(0-T), AUC(INF)

Secondary outcome

PK of BMS-986165 administered alone (reference) versus in combination with

rabeprazole (test)

- BMS-986165: Tmax, T-Half

- Total active circulating species: Cmax, AUC(0-T), AUC(INF)

Study description

Background summary

BMS-986165 is a new compound that may eventually be used for the treatment of autoimmune diseases like lupus, moderate to severe psoriasis, and inflammatory bowel disease. In autoimmune diseases the immune system does not only react to foreign substances, as it should, but also to parts of the body. This results in inflammatory reactions throughout the body (lupus), in the skin (psoriasis), or in the bowel (inflammatory bowel disease). The study compound blocks an enzyme (tyrosine kinase 2 [TYK2]) which has a role in the immune response and should decrease the immune response to parts of the body.

There are indications that the acidity of the stomach influences the uptake of BMS-986165. To study this, the uptake of the study compound with normal gastric

acidity will be compared with the uptake after the gastric acid production has been reduced by rabeprazole for several days.

Study objective

The purpose of this study is to investigate how quickly and to what extent the new compound BMS-986165 is absorbed and eliminated from the body (this is called pharmacokinetics) when it is administered to healthy volunteers without and with rabeprazole, a drug used to reduce the production of stomach acid (a proton-pump inhibitor). BMS-986165 has been administered to humans before.

It will also be investigated how safe BMS-986165 is and how well it is tolerated when administered without and with rabeprazole.

This study will be performed in 20 healthy male/female volunteers.

Study design

The actual study will consist of 1 period during which the volunteer will stay in the research center for 13 days (12 nights).

Day 1 is the first day of administration of the study compound. The volunteers are expected at the research center at 10:00 h in the morning prior to the day of first administration of the study compound. The volunteers will leave the research center on Day 12 of the study.

BMS-986165 and rabeprazole will be given as oral tablets with 240 milliliters (mL) of water.

During the first 4 hours after administration of the study compound the volunteer will not be allowed to lie down (except when indicated as such by one of the investigators), as this may influence the uptake of the study compound.

One of the investigators will inspect the hands and mouth after the study compound intake.

Please refer to the table below to see the planned dose levels for each group.

Day Treatment How often Fasted or Fed*
1 BMS-986165 12 mg once daily fasted
5-8 rabeprazole 20 mg once daily fed
9 BMS-986165 12 mg and rabeprazole 20 mg once daily fasted
10-11 rabeprazole 20 mg once daily fed

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Study burden and risks

BMS-986165
BMS-986165 is a compound that is being tested in research studies and is not an approved medicine to treat any condition.

Overall, approximately 774 participants, across 14 research studies, have received one dose or multiple doses of the study compound BMS-986165, comparator treatment, or placebo (a medicine without any active ingredient, a *fake* medicine). In these studies, most of the side effects were mild or moderate in intensity. In a few cases, side effects were serious and required hospitalization. This included 2 side effects in healthy volunteers. One volunteer, with a history of skin abscesses developed an abscess on the forearm which required hospital treatment. Another volunteer developed severe pharyngitis, a swollen face and swollen lymph nodes and trismus (lockjaw) also requiring hospital treatment. Both volunteers recovered completely.

In the research study of BMS-986165, the dose level will be 12 mg.

The side effects described below are based on unblinded information (ie, the actual study treatment given is known) about side effects observed in 276 participants who got multiple doses of BMS-986165 alone up to a maximum dose of 12 mg daily.

The following side effects are most frequently observed (in 10% of users or more):
• Headache

For other (important) side effects, or side effects which may occur based on

the mechanism of action of BMS986165.

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

You should immediately contact the responsible doctor if you develop:
- sudden shortness of breath
- problems breathing
- swelling of the eyelids, the face or the lips
- rash or itching (especially when on the whole body)

Rabeprazole
Rabeprazole may also cause side effects. The most important ones (in 1 in 100 people or more) are:
- Infection
- Sleeplessness
- Headache, dizziness
- Cough, sore throat (inflammation of the pharynx), runny nose
- Diarrhea, vomiting, nausea, abdominal pain, constipation, wind (flatulence)
- Non-specific pain, back pain
- Weakness or loss of strength, flu like symptoms.

Possible discomforts due to procedures
Drawing blood and/or insertion of the indwelling cannula (tube in an arm vein) may be painful or cause some bruising.

In total, we will take less than 500 milliliters (mL) of blood from the volunteer. 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).

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

- Healthy male and female subjects
- Age of 18 to 50 years (inclusive)
- BMI of 18.0 to 32.0 kg/m2 (inclusive)

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. Donation of blood to a blood bank or in a clinical study (except a screening visit) within 4 weeks of study drug administration (within 2 weeks for plasma only). Blood transfusion within 4 weeks of study drug administration.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	22-05-2019
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Rabeprazole
Generic name:	N/A
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	24-04-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-05-2019
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	EUCTR2019-001193-28-NL
CCMO	NL69913.056.19

Study results

Date completed: 07-07-2019

Results posted: 09-06-2021

First publication
24-05-2021