Pharmacokinetics and metabolism of [14C] BMS-986195 in healthy male subjects

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Joint disorders
Study type	Interventional

Summary

ID

NL-OMON44627

Source
ToetsingOnline

Brief title
BMS-986195 ADME study

Condition

- Joint disorders

Synonym
Rheumatoid arthritis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: ADME, BMS-986195

Outcome measures

Primary outcome

To assess the PK, metabolism routes and extent of elimination of a single oral dose of 10 mg [14C] BMS-986195 containing approximately 80 µCi (3.0 MBq) total radioactivity (TRA) in healthy male subjects.

Secondary outcome

To assess the safety and tolerability of a single oral dose of 10 mg [14C] BMS-986195 containing approximately 80 µCi (3.0 MBq) TRA.

Study description

Background summary

BMS-986195 is a new investigational compound that may eventually be used for the treatment of rheumatoid arthritis (RA). BMS-986195 blocks an enzyme (Bruton*s tyrosine kinase [BTK]) which is present in certain white blood cells (B-Cells). In patients with autoimmune diseases like RA these B-Cells react against the own body. Lowering the sensitivity of these cells can reduce the reaction against the own body. BMS-986195 is in development and is not registered as a drug but has been given to humans before.

During this study the volunteer will also receive xylocaine (lidocaine), a drug registered for use as a local anesthetic, and milk of magnesia (magnesium hydroxide), a compound registered for use as a laxative.

Study objective

The purpose of the study is to investigate how quickly and to what extent BMS-986195 is absorbed, distributed, metabolized (broken down) and eliminated from the body (this is called pharmacokinetics). BMS-986195 to be administered will be labeled with 14-Carbon (14C) and is thus radioactive (also called radiolabeled). In this way BMS-986195 can be traced in blood, urine, feces, and

bile. It will also be investigated to what extent BMS-986195 is tolerated.

Study design

Part 1:
The actual study will consist of 1 period during which the volunteer will stay in the clinical research center in Groningen (location Martini Hospital) for at least 6 days (5 nights) but no more than 16 days (15 nights).

During the study the volunteer will receive radiolabeled BMS-986195 after an overnight fast (at least 10 hours no eating and drinking) as an oral solution of 1 mL which will be given using a syringe. After this the volunteer is also required to drink 240 mL water. Fasting will continue until 4 hours after administration of the study compound. Then the volunteer will receive a lunch. During fasting the volunteer is allowed to drink water with the exception of 2 hours prior to until 1 hour after administration of the study compound.

During the first 8 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

Part 2:
The actual study will consist of 1 period during which the volunteer will stay in the clinical research center in Groningen (location Martini Hospital) for at least 6 days (5 nights) but no more than 16 days (15 nights).

During the study the volunteer will receive radiolabeled BMS-986195 after an overnight fast (at least 10 hours no eating and drinking) as an oral solution of 1 mL which will be given using a syringe. After this the volunteer is also required to drink 240 milliliters water. Fasting will continue until 6 hours after administration of the study compound. After removal of the nasoduodenal tube the volunteer will receive a meal.

During fasting the volunteer is allowed to drink water until 2 hours prior to administration of the study compound. In the period between 2 hours before and 6 hours after administration of the study compound the consumption of water is limited to 3 moments on which the volunteer will have to drink a measured amount of water. This is related to the placement of a nasoduodenal tube from 2 hours before until 6 hours after administration of the study compound. A nasoduodenal tube is a slim flexible tube that under local anesthesia via the nose, esophagus and stomach will be placed with its tip in the duodenum. Thirty minutes before the tube is placed, as well as 1.5 and 2.5 hours after administration of the study compound the volunteer will have to consume 125 mL tap water. In addition, as described above, the volunteer will have to drink 240 mL tap water during administration of the study compound.
During the first 6 hours after administration of the study compound the volunteer has to remain upright in bed (except when indicated as such by one of

the investigators). From 4 hours after administration of the study compound the volunteer is allowed to recline to an angle of no more than 45 degrees. After removal of the nasoduodenal tube the volunteer is allowed to leave the bed.

Intervention

The volunteer will receive a single dose of 10 mg radiolabeled BMS-986195 as oral solution of 1 milliliter (mL).

Study burden and risks

All potential drugs cause adverse effects; the extent to which this occurs differs. To date BMS 986195 has been administered to healthy volunteers in 2 ongoing studies. The adverse effects observed after a single dose of BMS-986195 in one of these studies were: headache, upper respiratory tract infection, dizziness, nausea, rash, throat irritation, myalgia, dysgeusia, dysmenorrhea, oral herpes, influenza like illness, malaise, hot flush, tongue ulceration, and dry lips. No additional data from the ongoing studies is available yet.

Based on the working mechanism of the study compound it can be expected that the study compound will affect the immune system. Therefore, the volunteers will be checked for any signs of infections and additional laboratory tests are performed to monitor their health throughout the study.

Xylocaine (lidocaine) side effects are hypersensitivity reactions (1 to 10 in 1000 users), severe allergic reactions (with hypotension, paleness, anxiety, weak and fast pulse, sweating, and decreased consciousness as a result of a sudden vasodilation [anaphylactic shock]), loss of voice, hoarseness, sore throat, local irritation on the place of application (incidence cannot be assessed based on the current data).

Milk of magnesia has been used for over 100 years as a treatment for heartburn and a laxative. The most frequently observed adverse effects are diarrhea and gastrointestinal discomfort. In rare cases severe allergic reactions (rash, hives, itching, difficulty breathing, tightness in the chest, swelling of the mouth, face, lips, or tongue), loss of appetite, muscle weakness, nausea, slow reflexes, and vomiting were observed.

The volunteer should be aware that the aforementioned adverse effects and possibly other, still unknown adverse effects, may occur during the study. However, with the dose used in this study no serious adverse effects are expected.

In this study radiolabeled BMS-986195 will be used. The amount of radioactivity in this dose will be approximately 3.0 MBq (MBq = megaBecquerel, this is a unit to express the amount of radioactivity in the study compound). The average

environmental background radiation burden in The Netherlands is approximately 2 mSv per year (mSv = milliSievert, this unit indicates the burden on the human body; thus the effect on the human body of the amount of radioactivity administered). The additional radiation burden in this study due to the administration of approximately 3.0 MBq radiolabeled BMS-986195 is calculated to be 0.66 mSv. This is approximately 33% of the average annual radiation burden.

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 subjects,
- 18 - 55 years, inclusive

- BMI: 18.0 - 32.0 kg/m2, inclusive

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study.

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):	16-08-2017
Enrollment:	9
Type:	Actual

Ethics review

Approved WMO Date:	02-08-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-08-2017
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	EUCTR2017-002706-12-NL
CCMO	NL62730.056.17