Single dose escalation study in a single-center, randomized, single-blind, placebo-controlled, group-comparison design to investigate pharmacokinetics, safety and tolerability of BAY 2586116 after intravenous administration in healthy male participants.

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Ethical review	Approved WMO
Status	Completed
Health condition type	Upper respiratory tract disorders (excl infections)
Study type	Interventional

Summary

ID

NL-OMON49427

Source
ToetsingOnline

Brief title
Intravenous single dose escalation study of BAY 2586116.

Condition

- Upper respiratory tract disorders (excl infections)

Synonym
Obstructive sleep apnea

Research involving
Human

Sponsors and support

Primary sponsor: Bayer AG
Source(s) of monetary or material Support: Pharmaceutical Industry.

Intervention

Keyword: BAY 2586116, Obstructive sleep apnea (OSA), Pharmacokinetics

Outcome measures

Primary outcome

Investigate the pharmacokinetics (PK) of BAY 2586116 after ascending

intravenous doses.

Investigate the safety and tolerability of BAY 2586116 after ascending

intravenous doses.

Secondary outcome

Not applicable.

Study description

Background summary

BAY 2586116 is a compound that may potentially be used for the treatment of obstructive sleep apnea (OSA). OSA belongs to the most common chronic (long-lasting) diseases of the respiratory system. In patients with OSA, soft tissue in the back of the throat relaxes during sleep. Because of this, the airways are narrowed and the flow of oxygen to the lungs is hindered. Symptoms of this disease are daytime sleepiness, snoring, headache, and disrupted sleep, which all negatively affect the quality of life. BAY 2586116 could potentially prevent the relaxation of the soft tissue in the back of the throat. BAY 2586116 has already been tested in humans before in the form of a nasal spray, which is the intended use. In the current study, an intravenous infusion will be used to test doses that are higher than would be used in the actual treatment of a patient. These doses cannot be reached with the nose spray in

healthy volunteers. It is important to know how the body reacts to higher doses, as future patients might get higher levels of the study compound in their blood due to organ impairment, interactions with other drugs they might take, or misuse of the dosage form.

Study objective

The purpose of this study is to investigate how quickly and to what extent the study compound BAY 2586116 is absorbed and eliminated from the body. It will also be investigated how safe the new compound BAY 2586116 is and how well it is tolerated when it is administered to healthy male volunteers. Furthermore, we will investigate if the study compound has an effect on heart activity. This is why the heart activity will be monitored closely by regularly recording the electrical activity of the heart (electrocardiogram, ECG). Furthermore, the effect of the genetic information on the volunteer body*s response to BAY 2586116 might be investigated.

BAY 2586116 is an investigational compound. It is not approved for sale in any country as it is still under development. Therefore, BAY 2586116 can only be used in studies like this one. BAY 2586116 has already been administered to 64 humans before over 2 previous clinical trials. It has also been extensively tested in the laboratory and on animals.

The study will be conducted in up to 35 healthy male volunteers.

The volunteers will be divided into groups called dosing steps. One can participate in one of these groups.

The effects of BAY 2586116 are compared with the effects of a placebo.

Study design

The actual research consists of 1 period during which the volunteers will stay in the research center for 5 days (4 nights).

Day 1 is the day the study drug is administered. The volunteers are expected at 11:00 in the morning 2 days prior to the day of study drug administration in the study center (i.e. on Day -2). The entry time can be adjusted. The research center is left on Day 3 of the examination.

Prior to receiving the study drug on the day of dosing (Day 1), one should fast for at least 10 hours overnight. BAY 2586116 or placebo is then given as an intravenous infusion. The infusion lasts 30 minutes.

The volunteer will not be allowed to leave the bed during the first 4 hours after administration of the study compound. This is a safety precaution, as the

study compound may have side effects that are still unknown as BAY 2586116 is for the first time being administered to humans directly into the vein. Therefore, the volunteer will be closely monitored directly after administration, and he can only leave the bed when accompanied by study personnel.

Whether one gets BAY 2586116 or placebo is determined by drawing lots. Per dosing step, 5 volunteers receive BAY 2586116 and 2 volunteers receive placebo.

Intervention

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Study burden and risks

BAY 2586116 has been administered to 64 humans before in 2 previous clinical trials. In these studies, the study compound was administered as a nose spray. The current study is the first study where the study compound will be administered via an infusion. Knowledge about possible side effects in humans is therefore still limited.

In one clinical trial, a single dose of BAY 2586116 was administered as a nose spray with doses from 12 µg to 160 µg. BAY 2586116 was considered safe and well tolerated.

In the other study, once daily doses of BAY 2586116 as a nose spray were administered at doses of 50 µg, 80 µg, and 160 µg over 5 days. In this study, no side effects were reported that were judged as being possibly related to the study compound.

On the day of administration of the study compound, blood is drawn using an indwelling cannula from a blood vessel in the forearm to determine the course of the concentration of BAY 2586116 in the blood over time. This might

sometimes cause mild pain, inflammation, swelling, hardening of the vein, blood clotting and bleeding into surrounding (bruising) at the insertion site. In rare cases, there may be inflammation and damage to blood vessels and/or damage to neighboring nerves. In sensitive individuals, blood draws may sometimes cause pallor, nausea, sweating, slow pulse, or drop in blood pressure with dizziness or fainting. The use of adhesive bandages to cover blood draw sites may cause mild, temporary redness and itching of the skin.

For the intravenous administration of the study compound, an extra indwelling cannula will be inserted on Day 1 in addition to the indwelling cannula used for blood sampling. Thus, the volunteer will have a cannula inserted in both arms during the 30 minute infusion of the study compound.

In total, we will take about 130 milliliters of blood. Based on the discretion of the responsible doctor, extra samples might be taken to guarantee the safety of the participants.

To make a heart tracing, electrodes will be pasted on their arms, chest and legs. To monitor the heart rate with telemetry, electrodes will be pasted on the chest and abdomen. Prolonged use of these electrodes can cause reddening and/or itching of the skin.

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

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

Participant must be 18 to 45 years of age inclusive, at the time of signing the informed consent.
Participants who are overtly healthy as determined by medical evaluation (including medical and surgical history, physical examination,laboratory tests, ECG, vital signs, and pulse oximetry). Re-screening may be allowed.
Race: White (Note: Clinical Data Interchange Standards Consortium definition of White: Denotes a person with European, Middle Eastern, or North African ancestral origin who identifies, or is identified, as White (Food and Drug Administration).
Male participant.

Exclusion criteria

Medical disorder, condition or history of such that would impair the participant's ability to take part in or complete this study in the opinion of the investigator
A history of relevant diseases of vital organs, of the central nervous system or other organs
Pre-existing diseases for which it can be assumed that the absorption, distribution, metabolism, elimination and effects of the study intervention will not be normal.
Regular use of medicines.
Positive SARS-CoV-2 viral RNA test.

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	08-01-2021
Enrollment:	35
Type:	Actual

Ethics review

Approved WMO Date:	17-11-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-12-2020
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	EUCTR2019-004479-38-NL
CCMO	NL75743.056.20

Study results

Date completed: 03-09-2021

Results posted: 08-06-2022

First publication
21-03-2022