Single dose escalation study in a single center, randomized, single blind, placebo controlled, group comparison design to investigate pharmacokinetics, safety and tolerability of BAY 2253651 after intravenous administration in healthy male subjects.

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Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON45895

Source
ToetsingOnline

Brief title
Single dose escalation study.

Condition

- Other condition

Synonym
Respiratory disorder, sleep apnea

Health condition

obstructieve slaapapneu.

Research involving
Human

Sponsors and support

Primary sponsor: Bayer AG
Source(s) of monetary or material Support: Farmaceutische Industrie.

Intervention

Keyword: BAY 2253651, obstructive sleep apnea (OSA).

Outcome measures

Primary outcome

• Investigate the pharmacokinetics of BAY 2253651 after single ascending

intravenous doses by means of the assessment of Cmax, AUC, Cmax/D and AUC/D.

• Investigate the safety and tolerability of BAY 2253651 after single ascending

intravenous doses by means of the incidence of treatment emergent adverse

events (TEAEs).

Secondary outcome

Not applicable.

Study description

Background summary

BAY 2253651 is a new compound that may eventually be used for the treatment of obstructive sleep apnea. Obstructive sleep apnea is a common respiratory disorder that involves repetitive occlusion of the airway of the pharynx while sleeping. This leads to oxygen deficiency and sleep disruption. Other symptoms include daytime sleepiness, snoring and headache.

BAY 2253651 is a compound which promises to increase the activity of the genioglossus muscle (the major tongue muscle). Normally, inspiration results in a negative pressure in the pharynx. This negative pressure induces a reflex-driven activation of the genioglossus muscle. In obstructive sleep apnea, this reflex is diminished. BAY 2253651 can sensitize the upper airway receptors resulting in an increased reflex activity of the genioglossus muscle, thereby stimulating opening of the airway.

There is currently no drug treatment for obstructive sleep apnea. A non invasive and easy-to-use therapy would represent a benefit for many patients who suffer from this disease. Because BAY 2253651 acts locally, application of a liquid formulation using a pump spray into the nose is the provided route of administration. However, for the further clinical development of BAY 2253651, it is necessary to investigate the pharmacokinetics of BAY 2253651 when administered intravenously, via a tube in an arm vein. BAY 2253651 has been administered, via the nose, in humans before.

Study objective

The main purpose of this study is to investigate how quickly and to what extent BAY 2253651 is absorbed (taken up), distributed, metabolized (broken down) and eliminated from the body (this is called pharmacokinetics). Multiple dose steps of BAY 2253651 will be tested. Furthermore, it will be investigated how safe BAY 2253651 is and how well BAY 2253651 is tolerated.

The effects of BAY 2253651 will be compared to the effects of a placebo. A placebo is a medicine without any active ingredient. It is a *fake* medicine.

Study design

The study consists per volunteer of 1 period in which the volunteer stays for 5 days (4 nights) in the research center.

A single dose of BAY 2253651 or placebo will be given as an intravenous infusion (solution of the compound that will be administered directly in a blood vessel) over 20 minutes. The volunteer will have to remain lying down during 4 hours after administration of the study compound.

Administration of the study compound will be done after an overnight fast of at least 10 hours. During fasting you are allowed to drink non-sparkling water, except from 1 hour before until 1 hour after administration of the study compound. Following administration, you will fast for another 4 hours. A standardized lunch, snack and dinner will be provided 4, 8 and 10 hours after administration of the study compound, respectively. The same schedule of food, drinks and fasting will be followed on the day before administration of the study compound (so on 2 consecutive days).

Whether the volunteer will receive BAY 2253651 or placebo will be determined by chance. Per group, 5 volunteers will receive BAY 2253651 and 2 volunteers will receive placebo. They will not know if BAY 2253651 or placebo is administered whereas the responsible doctor will know this; we call this a single-blinded study.

Intervention

Group 1: BAY 2253651 or placebo; 5 µg Intravenous solution, once
Group 2 to 5: BAY 2253651 or placebo, once by intravenous solution.
Height of dose depends on the results of the previous groups.

Study burden and risks

Blood sampling
During this study, small amounts of blood will be drawn from a vein and used for routine laboratory tests and for pharmacokinetic testing. Drawing blood may cause pain where the needle is inserted, and there is a small risk of bruising or infection at the place where the needle is inserted. Very rarely, a blockage of the vein or a small nerve injury can occur, resulting in numbness and pain. However, this will resolve with time. Some people experience dizziness, upset stomach, or fainting when their blood is drawn.

The use of adhesive bandages to cover the blood draw sites may cause mild, temporary redness and itching of the skin.

On days when several blood samples will be taken, a cannula (small plastic tube) will be inserted in a vein of the arm using a small needle. This cannula may remain in place for a longer period of time. There is a small chance of infection by placing the cannula in the vein, but every medical precaution will be taken to avoid an infection.

In total, we will take about 120 mL of blood from the volunteer. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time and is allowed 5 times per year.

Heart tracing (ECG) and Holter
Electrodes (small, plastic patches) will be placed temporarily on different parts of your body. There is no pain or discomfort during an ECG or Holter measurement (recording heart rhythm). However, the area of the skin where the patches will be stuck may need to be shaved, and the patches may cause a skin reaction such as redness or itching. Taking the patches off may cause localized irritation to the skin and/or hair loss, similar to having a plaster taken off.

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 white male volunteers
18 - 45 years of age
BMI 18.0 - 29.9 kilograms/meter2
non smokers

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 to the start of this study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	18-01-2019
Enrollment:	35
Type:	Anticipated

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:	04-12-2018
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	EUCTR2018-002884-24-NL
CCMO	NL68073.056.18