Single dose escalation study to investigate safety, tolerability, pharmacokinetics and pharmacodynamics of BAY 2413555 after oral dosing in healthy male participants in a randomized, single-blind, placebo-controlled, group-comparison design

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON54965

Source
ToetsingOnline

Brief title
A safety, absorption, elimination & activity study of BAY2413555

Condition

- Heart failures

Synonym
Heart Failure

Research involving
Human

Sponsors and support

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

Intervention

Keyword: BAY 2413555, Pharmacodynamics, Pharmacokinetics, Safety

Outcome measures

Primary outcome

- Investigate the safety and tolerability of BAY 2413555 after single oral

dosing in healthy participants (Number and percentage of participants with

TEAEs)

- Investigate the pharmacokinetics of BAY 2413555 (Cmax, AUC, Cmax/D, AUC/D of

BAY 2413555 (if AUC cannot be determined reliably in all participants,

AUC(0-tlast) will be used instead))

Secondary outcome

Investigate the pharmacodynamics of BAY 2413555 (Heart rate over 1 min over

time (0-6 hours, adjusted for pre-dosing day and placebo)

Study description

Background summary

BAY 2413555 is a new compound that may eventually be used for the treatment of heart failure. Heart failure is a serious disease and after diagnosis 45% to 60% of heart failure patients will die within 5 years after diagnosis. BAY 2413555 can indirectly modulate the so-called muscarinic M2 acetylcholine receptor. The muscarinic M2 acetylcholine receptor is located on heart muscle cells and when activated it will decrease the heart rate and may improve the

heart function.

Study objective

The purpose of this study is to investigate how safe the new compound BAY 2413555 is and how well it is tolerated when it is administered as a single oral dose to healthy volunteers. BAY 2413555 has not been administered to humans before. It has been previously tested in the laboratory and on animals. BAY 2413555 will be tested at various dose levels.

It will also be investigated how quickly and to what extent BAY 2413555 is absorbed and eliminated from the body. In addition, the effect of BAY 2413555 on indicators related to the heart function will be investigated.

Study design

The subjects will stay in the research center for maximal 12 days (11 nights).

Day 1 is the day of administration of the study compound.

Intervention

Depending on the group in which the volunteer will participate, the study compound will be given once either as a tablet or as an oral solution with a maximum of 20 milliliter (mL), depending on the dose. Thereafter the volunteer is also required to drink an additional amount of 240 mL of water.

Day 1 is the day of study compound administration. On the day before (Day -1) and on the day of study compound administration (Day 1) the subjects will need to lie down resting for most of the time (up to noon on Day 2). This is important to collect stable values for blood pressure and heart rate. This means that overall, the subjects have to stay in bed starting from Day -1 up to noon on Day 2 (3 days in total), and have to remain in supine position for most of the time. If there are no assessments during the bed rest phase, subjects may take a semi-supine position. On Day 1 sybjects have to completely stay in bed for the first 6 hours after dosing and the same time on Day -1. Subjects will stand up for your first meal (lunch) and afterwards they may rise during this bed rest phase after asking the study personnel, for example for using the bathroom. The subjects will then be accompanied by personnel.

Per group, 8 volunteers will receive BAY 2413555 and 2 volunteers will receive placebo.

An ambulatory follow-up visit, performed 11 to 14 days after administration of the study drug. Based on the results of prior dose groups, an additional follow-up visit may be performed between 15 and 20 days after administration of

the study drug.

Study burden and risks

Possible discomforts due to procedures
Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising. Inflammation of the vein, nerve injury, and vasovagal reactions (faint due to e.g. blood draw) may occur as well.

In total, about 500 milliliters (mL) of blood will be taken within approximately 6 weeks. This amount does not cause any problems in adults.

To make a heart tracing (ECG) and monitor the heart rate (telemetry and Holter monitoring), electrodes will be pasted at specific locations on the arms, chest, abdomen and legs. Prolonged use of these electrodes can cause skin irritation.

In the standing blood pressure testing subjects might feel dizziness, nausea or might lost consciousness which might occur already before dosing.

Due to the long period that subjects have to remain in bed in a supine or semi-supine position, the many assessments that will be done on certain days and the connection to the telemetry and Holter devices for most of the time, subjects should be aware that this study can be considered an intensive study and they might feel tiredness, headache or have other discomfort. Such as a feeling of hunger due to long-term fasting conditions that have to be strictly followed during the course of the study.

A sample for the coronavirus test will be taken from the back of the nose and throat using 2 swabs. Taking the sample only takes a few seconds but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of your throat may cause the volunteer to gag. When the sample is taken from the back of the nose, the volunteer may experience a stinging sensation and the eyes may become watery.

If the test is positive during the study and you received BAY2413555, the volunteer will be monitored at the research center (in quarantine), as long as was originally planned for him. This is a measure of safety as the study compound might still be in the body.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Healthy male participants
- Age: 18 to 50 years of age (inclusive), at the time of signing the informed consent
- Race: White
- Body mass index (BMI) within the range of 18-29.9 kg/m2 (inclusive) at the time of screening.
- The informed consent must be signed before any study specific tests or procedures are done

Exclusion criteria

1. 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
2. A history of relevant or ongoing diseases such as:
- respiratory tract: e.g. asthma, any airway obstruction
- central nervous system: e.g. seizures, cerebrovascular malformations (e.g. aneurysm), psychiatric or neurological disorders

- gastrointestinal tract: e.g. gallstones, any obstruction of the intestinum/ intestinal glands (e.g. pancreas), peptic ulcer
- urinary tract: e.g. nephrolithiasis, any obstruction of the urinary passage
3. Any condition for which it can be assumed that the absorption, distribution, metabolism, elimination and effects of the study intervention(s) will not be normal
4. Known hypersensitivity to any study intervention (active substances or excipients of the preparations) to be used in the study - including e.g. non-investigational medicinal products, challenge agents, or rescue medication
5. Known severe allergies, e.g. allergies to more than 3 allergens, allergies affecting the lower respiratory tract - allergic asthma, allergies requiring therapy with corticosteroids, urticaria or significant non-allergic drug reactions.

For the complete overview, see the protocol

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:	Recruitment stopped
Start date (anticipated):	29-08-2019
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO

Date:	09-07-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-07-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-12-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-03-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-03-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	06-08-2021
Application type:	Amendment
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	EUCTR2019-001602-26-NL
CCMO	NL70418.056.19