A NON-RANDOMIZED, OPEN-LABEL, CROSS-OVER, DRUG-DRUG INTERACTION STUDY TO EVALUATE THE EFFECTS OF BIA 28-6156 AT STEADY-STATE ON THE PHARMACOKINETICS OF LEVODOPA/CARBIDOPA AND LEVODOPA/BENSERAZIDE IN HEALTHY SUBJECTS.

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This is a medical-scientific research study. The purpose of the study is to investigate the effect of multiple doses of the study compound BIA 28-6156 on the pharmacokinetics of the drugs levodopa-carbidopa (Group 1) and levodopa-benserazide (Group...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Movement disorders (incl parkinsonism)
Study type	Interventional

Summary

ID

NL-OMON50655

Source
ToetsingOnline

Brief title
BIA 28-6156 & L-Dopa plus Carbidopa or Benserazide DDI in healthy subjects

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's, progressive nervous system disorder that affects movement

Research involving
Human

Sponsors and support

Primary sponsor: BIAL R&D INVESTMENTS, S.A.
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: BIA 28-6156, DDI, L-Dopa - Benserazide, L-Dopa - Carbidopa

Outcome measures

Primary outcome

- To investigate the effects of multiple doses of BIA 28-6156 on the

single-dose PK of Sinemet® (100 mg of levodopa and 25 mg of carbidopa) in

healthy male and female subjects.

- To investigate the effects of multiple doses of BIA 28-6156 on the

single-dose PK of Madopar® (levodopa 100 mg and benserazide 25 mg) in healthy

male and female subjects.

Secondary outcome

- To assess the safety and tolerability of co-administration of BIA 28-6156

with single-dose Sinemet® (100 mg of levodopa and 25 mg of carbidopa)

- To assess the safety and tolerability of co-administration of BIA 28-6156

with single-dose Madopar® (levodopa 100 mg and benserazide 25 mg)

- To investigate the effects of multiple doses of BIA 28-6156 on PK of

metabolite, 3-O-M.

Study description

Background summary

BIA 28-6156 is a new compound that may potentially be used for the treatment of Parkinson*s disease. Parkinson*s disease is a brain disorder with symptoms such as arm or leg shaking and/or stiffness, and difficulty with walking, balance, and coordination. It is caused by the death of specific nerve cells in the brain that are important for controlling movement. There is currently no cure for Parkinson*s disease, and treatment is aimed at reducing the symptoms.

Some types of Parkinson*s disease may be caused by a reduction in the activity of the protein betaglucocerebrosidase. This is due to mutations in the gene, called GBA1, which is responsible for the production of beta glucocerebrosidase. BIA 286156 can bind to and activate beta glucocerebrosidase and is therefore thought to be helpful in the treatment of these types of Parkinson*s disease.

In the future, patients may be given both BIA 28-6156 and levodopa-carbidopa or levodopa-benserazide. It is therefore important to know if these compounds can influence each other.

Study objective

This is a medical-scientific research study. The purpose of the study is to investigate the effect of multiple doses of the study compound BIA 28-6156 on the pharmacokinetics of the drugs levodopa-carbidopa (Group 1) and levodopa-benserazide (Group 2) in healthy male and female participants. Pharmacokinetics is how your body absorbs, breaks down, and removes a drug. We will also investigate the pharmacokinetics of BIA 28-6156 itself.

We will also investigate how safe the compound BIA 28-6156 is and how well it is tolerated when healthy participants use it together with levodopa-carbidopa or together with levodopa-benserazide.

BIA 28-6156 has been administered to humans before. In addition, it has been extensively tested in the laboratory and on animals. BIA 28-6156 is investigational and has not been approved for sale in any country.

Group 1: Levodopa-carbidopa is a drug approved in the Netherlands used to treat the symptoms of Parkinson*s disease such as muscle stiffness, tremors, spasms, and poor muscle control.

Group 2: Levodopa-benserazide is a drug approved in the Netherlands for the

treatment of Parkinson*s disease.

Study design

For the study it is necessary that the volunteer stays in the research center for 9 days (8 nights). After that stay the volunteer will come back to the research center once for the follow-up visit.

Day 1 is the first day when the volunteer will receive the study compound. The volunteer will leave the research center on Day 8 of the study.

On days when the volunteer will receive BIA 28-6156 alone (Day 2 to 6), The volunteer will be given a standard breakfast that must be finished within 20 minutes. After that they will be given 1 oral capsule of BIA 28-6156 with 240 mL of water. After intake of the study compound, The volunteer has to fast 4 hours until lunch.

Group 1:
On days when the volunteer only receives levodopa-carbidopa (Day 1), the volunteer will first be given a standard low-protein breakfast, then fast for 2 hours. After that they will be given 1 oral capsule of levodopa-carbidopa containing 100 mg of levodopa and 25 mg of carbidopa with 240 mL of water. After intake of levodopa-carbidopa, the volunteer has to fast 4 hours until lunch.

Group 2:
On days when the volunteer only receives levodopa-benserazide (Day 1), the volunteer will first be given a standard low-protein breakfast, then fast for 2 hours. After that they will be given 1 oral capsule of levodopa-benserazide containing 100 mg of levodopa and 25 mg of benserazide with 240 mL of water. After intake of levodopa-benserazide, the volunteer has to fast 4 hours until lunch.

On days when BIA 28-6156 is given together with levodopa-benserazide or levodopa-carbidopa (Day 7), the volunteer will be given a standard low-protein breakfast, then fast for 2 hours. After that they will be given 1 oral capsule of BIA 28-6156 and 1 oral tablet levodopa-carbidopa or levodopa-benserazide. After intake of BIA 28-6156 and levodopa-carbidopa or levodopa-carbidopa they have to fast 4 hours until lunch.

They will be given a low-protein breakfast on Day 1 and Day 7, because protein in the diet can reduce the absorption of levodopa-carbidopa by the body.

During fasting the volunteer is allowed to drink water; however water is not allowed from 2 hours prior to until 1 hour after dosing on Day 1 and 7 (except for the 240 mL water taken with the dose and fluid given with the breakfast). There are no fluid restrictions on Days 2-6.

The tablet and capsule should not be chewed. One of the investigators will inspect the volunteers hands and mouth after the study compound intake. This it to check if the volunteer has taken the study compound.

Intervention

Group 1:
• On Day 1: a single dose of 100 mg of levodopa and 25 mg of carbidopa
• On Day 2 to 6: a daily single dose of 60 mg BIA 28-6156
• On Day 7: a single dose of 60 mg BIA 28-6156 and a single dose of 100 mg of levodopa and 25 mg of carbidopa

Group 2:
• On Day 1: a single dose of 100 mg of levodopa and 25 mg of benserazide
• On Day 2 to 6: a daily single dose of 60 mg BIA 28-6156
• On Day 7: a single dose of 60 mg BIA 28-6156 and a single dose of 100 mg of levodopa and 25 mg of benserazide

Study burden and risks

Blood draw
Drawing blood may be painful or cause some bruising. The use of the indwelling cannula (a tube in a vein in the arm) can sometimes lead to inflammation, swelling, hardening of the vein, blood clotting, and bleeding in the environment (bruising) of the puncture site. In some individuals, a blood draw can sometimes cause pallor, nausea, seating, low heart rate, or drop in blood pressure with dizziness or fainting.

In total, we will take about 289 milliliters (mL) of blood from screening to follow-up. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time at once. If the investigator thinks it is necessary for the safety of a participant, extra samples might be taken for possible additional testing. If this happens, the total amount of blood drawn may be more than the amount indicated above.

Heart tracing
To make a heart tracing, electrodes (small, plastic patches) will be placed on arms, chest and legs. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Fasting
If subjects have to fast for a prolonged time during the study, this may lead to symptoms such as dizziness, headache, stomach upset, or fainting.

Coronavirus test
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 you 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.

Eye pressure test
A device blows a brief puff of air onto the eye to measure the eye pressure.
This air puff is not painful, and your eye will not be touched.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Sex: Male or female; females must be of nonchildbearing potential or postmenopausal.

2. Age: 18 to 75 years, inclusive, at time of consent.
3. Body mass index: 18.0 to 32.0 kg/m2, inclusive, at screening.
4. Weight: >=50 kg at screening.
5. Status : Healthy subjects.

+ Further criteria apply.

Exclusion criteria

1. Employee of PRA Health Sciences (PRA) or the Sponsor.
2. History of relevant drug and/or food allergies.
3. History of alcohol abuse or drug addiction (including soft drugs like cannabis products) within 2 years prior to the first drug administration in the current study.
4. Using tobacco or nicotine products within 14 days prior to the first drug administration in the current study.
5. History of liver disease, previous bone marrow depression, hypersensitivity to levodopa/carbidopa, or hypersensitivity to levodopa/benserazide.

+ Further criteria apply.

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):	29-11-2021
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	MADOPAR
Generic name:	levodopa/benserazide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	SINEMET
Generic name:	levodopa/carbidopa
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	16-11-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-11-2021
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	EUCTR2021-005896-37-NL
CCMO	NL79626.056.21