A double-blind, randomised, placebo-controlled, combined single and multiple ascending dose study to investigate the safety, tolerability, pharmacokinetic, including food interaction, and pharmacodynamic profile of BIA 5-1058, in healthy male volunteers.

Published: 30-12-2010
Last updated: 04-05-2024

Primary to assess the tolerability of the compound after single and multiple oral dosesSecondaryto measure the plasma and urine concentrations of the compound and its metabolites after single and multiple oral doses and to characterise its...

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

Summary

ID

NL-OMON36800

Source
ToetsingOnline

Brief title
BIA 5-1058 SAD/MAD study.

Condition

- Other condition
- Heart failures

Synonym

Hypertension and Chronic Heart Failure

Health condition

verhoogde bloeddruk

Research involving
Human

Sponsors and support

Primary sponsor: Bial Portela & Ca.
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: BIA 5-1058., Chonic heartfailure., Hypertension.

Outcome measures

Primary outcome

Pharmacokinetics:

plasma and urine BIA 5-1058 & metabolites concentrations; PK parameters in

plasma for SAD and food interaction parts: Cmax, tmax, kel, t*, AUClast,

AUCinf, Fr (food interaction part only), Vz/F, CL/F, CLr; MAD part, Day 1:

Cmax, tmax, AUC0-tau; MAD part, Day 10: Cmax, tmax, AUC0-tau, kel, t*, Vz/F,

Cmin, Rac, Ctrough; in urine (SAD and MAD parts only): Ae, Ae %dose.

Pharmacodynamics:

plasma D*H activity and urine NE, DA, DOPAC and HVA concentrations; PD

parameters of D*H activity inhibition in plasma in SAD and MAD parts: Emax,

tEmax, AUEC.

Safety:

AEs, vital signs, 12-lead ECG; clinical laboratory, physical examination,

telemetry

Secondary outcome

Not applicable.

Study description

Background summary

The drug to be given is a new investigational compound that may eventually be used for the treatment of hypertension and chronic heart failure.
The compound inhibits the action of the enzyme dopamine *-hydroxylase. Dopamine *-hydroxylase is involved in the synthesis of the neurotransmitter norephinprine, a compound that is involved in the function of the autonomic nervous system that regulates certain body functions which include blood pressure (autonomic = can not be controlled by the mind). It has been studied for many decades that inhibition of dopamine *-hydroxylase has a positive effect on hypertension and heart failure. The application of previously investigated agents with the same mechanism was limited because they not only had an effect on the heart, but also on the central nervous system (the brain). This new product, however, cannot reach the brain via the blood and, therefore, would not have the adverse effects as have agents studied in the past.

Study objective

Primary
to assess the tolerability of the compound after single and multiple oral doses

Secondary
to measure the plasma and urine concentrations of the compound and its metabolites after single and multiple oral doses and to characterise its pharmacokinetic (PK) parameters and steady state PK profile

to investigate the effect of the compound on blood pressure, on plasma dopamine * hydroxylase (D*H) activity, and on the urinary levels of norepinephrine (NE), dopamine (DA) and the amine metabolites 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA)

to investigate the effect of food on the PK of a single dose of the compound

Study design

a double blind, randomised, placebo-controlled combined single ascending dose (SAD), including food interaction analysis, and multiple ascending dose (MAD)

study. SAD part consists of 8 groups of 8 healthy young male subjects each receiving a single oral dose of the study compound or placebo (6 verum and 2 placebo): in the first group, 2 subjects (1 verum and 1 placebo) are dosed 24 h before remaining 6 subjects (5 verum and 1 placebo). If the maximum tolerated dose (MTD) is not reached after completing the planned sequential groups, additional groups can be included to a maximum of 12 sequential groups in total. Food interaction part consists of 12 healthy young male subjects each receiving a single dose of the study compound in either the fed or fasted state in an open-label, two-way crossover design. Each treatment will be separated by at least 7 days. MAD part consists of 4 groups of 8 young healthy male subjects each receiving an oral dose of the study compound or placebo (6 verum and 2 placebo) once daily for 10 days. If the MTD is not reached after completing the planned sequential groups, additional groups can be included to a maximum of 8 sequential groups in total.

Intervention

SAD
In each group subjects will receive a single dose of the study compound (n=6) or matching placebo (n=2) on Day 1

FOOD INTERACTION
The subjects will receive a single dose of the study compound on Day 1 under fasted (one period) and fed (one period) conditions

MAD
In each group subjects will receive multiple doses of the study compound or matching placebo once daily on Days 1 to 10

Study burden and risks

Not applicable.

Contacts

Public
Bial Portela & Ca.

A Avenida da Siderurgia Nacional
4745-457 S. Mamede do Coronado
PT
Scientific
Bial Portela & Ca.

A Avenida da Siderurgia Nacional
4745-457 S. Mamede do Coronado
PT

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy male, 18 - 55 years, BMI 18.0 - 30.0 kg/m2.

Exclusion criteria

Suffering from: hepatitis B, cancer or HIV/AIDS. In case of participation in another drug study within 60 days before the start of this study or being a blood donor within 90 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
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-03-2011
Enrollment:	108
Type:	Actual

Ethics review

Approved WMO Date:	30-12-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-01-2011
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	EUCTR2010-023490-19-NL
CCMO	NL34497.056.10