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Study on the effect of three single ascending doses of sildenafil citrate oral film compared with placebo on blood pressure in healthy young and elderly males

Submission date
15/11/2022

Recruitment status
No longer recruiting

Registration date
28/11/2022

Overall study status
Completed

Last Edited
14/02/2023

Condition category
Other

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
This study was designed to assess the effect on blood pressure and pulse rate of three single-ascending doses of sildenafil citrate as compared to placebo when administered in healthy young and elderly men under fasting conditions. It was designed also to evaluate and compare the hemodynamic responses to sildenafil in healthy young (≤45yrs) and elderly (≥65yrs) male volunteers. The secondary objective of the study was to collect safety and tolerability data after a single dose of the formulations under investigation.

Who can participate?
Healthy men aged between 18-45 years old inclusive (young) and ≥65 (elderly) years old.

What does the study involve?
All the subjects enrolled in the study received the four treatments (the investigational medicinal products T1, T2, T3 and placebo) as follows: a single dose of one Sildenafil IBSA 50 mg, 75 mg, 100 mg and placebo oral film were administered under fasting conditions according to a 4-way cross-over randomized study design in four consecutive study periods with wash-out intervals of at least 5 days between consecutive administrations.
For each administration, the oral film was placed on the tongue on Day 1 of each study period at 08:00±1 h without water. The film was allowed to dissolve completely (without chewing). Afterwards, still mineral water was allowed starting from 1 h post-dose.
The formulations to be tested are already available on the market in Switzerland.
Participants had vital signs measured with ambulatory blood pressure monitoring (ABPM) recorded at regular intervals.

What are the possible benefits and risks of participating?
No specific benefits for the participants in the current study were foreseen. On the basis of sildenafil safety profile, no potential risks were foreseen for the subjects enrolled in the present study.

The most common adverse events (AEs) of sildenafil are headache, followed by dizziness, visual disturbance and color distortion, hot flush, nasal congestion, nausea and dyspepsia.

Where is the study run from?
CROSS Research S.A. Phase I Unit Clinical Centre (Switzerland)

When is the study starting and how long is it expected to run for?
November 2020 to December 2021

Who is funding the study?
IBSA Institut Biochimique SA, Switzerland

Who is the main contact?
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Contact information

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Protocol serial number
20CH-SDF09

Study information

Scientific Title
A phase I study to assess the effect of three single ascending doses of sildenafil citrate oral film compared with placebo on blood pressure in healthy young and elderly male volunteers

Acronym
Sildenafil OF safety assessment

Study objectives
The primary objective of the study was to assess the effect on supine blood pressure and pulse rate of three single ascending doses of sildenafil citrate as compared to placebo when administered to healthy young and elderly men under fasting conditions.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 05/03/2021, Canton Ticino Ethics Committee (c/o Ufficio di sanità, Via Orico 5, 6501 Bellinzona, Switzerland; +41(0)91 814 30 57; beatrice.giberti-gai@ti.ch), ref: 2021-00230 CE 3816

Primary study design
Interventional

Study design
Single dose single-center open-label randomized placebo-controlled four-way cross-over safety tolerability and pharmacodynamics phase I study

Study type(s)
Other

Health condition(s) or problem(s) studied
Pharmacodynamic study on blood pressure and pulse rate in healthy volunteers

Interventions
The randomization list was computer-generated by the Biometry Unit of the Clinical Contract Research Organization (CRO), using the PLAN procedure of SAS® version 9.3 (TS1M1). The randomization list was supplied to the Sponsor before the subject's kit preparation. Randomization was stratified by age group (i.e., young and elderly) in order to have the same number of young and elderly men for every sequence of treatments.

Test investigational medicinal products:
Test 1 (T1): Sildenafil IBSA 50 mg oral film, Test 2 (T2): Sildenafil IBSA 75 mg oral film, Test 3 (T3):

Sildenafil IBSA 100 mg oral film, IBSA Institut Biochimique SA, Switzerland
Placebo:
Sildenafil IBSA 100 mg oral film matching placebo, IBSA Institut Biochimique SA, Switzerland

All the subjects enrolled in the study will receive the four treatments (the investigational medicinal products T1, T2, T3 and placebo) as follows: a single dose of one Sildenafil IBSA 50 mg, 75 mg, 100 mg and placebo oral film will be administered under fasting conditions according to a 4-way cross-over randomized study design in four consecutive study periods with wash-out intervals of at least 5 days between consecutive administrations.
For each administration, the oral film will be placed on the tongue on Day 1 of each study period at 08:00±1 h without water. The film will be allowed to dissolve completely (without chewing). Afterwards, still mineral water will be allowed starting from 1 h post-dose.
T3 and matching placebo are undistinguishable, thus allowing their administration under blind conditions. T1 and T2 are distinguishable from each other and from T3 and its matching placebo due to their size. Therefore, the administration of T1 and T2 will be done under open-label conditions.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Sildenafil citrate

Primary outcome(s)
The primary outcome was to evaluate the pharmacodynamic effects on blood pressure and pulse rate in healthy male subjects after a single dose of the 3 investigational medicinal products as compared to placebo in terms of:
1. Maximum change from pre-dose blood pressure and pulse rate expressed as a post-dose maximum decrease in blood pressure or maximum increase in pulse rate
2. Mean change from pre-dose in blood pressure and pulse rate across all post-dose time points
3. Proportion of subjects with a clinically significant decrease in blood pressure
4. Proportion of subjects with a clinically significant increase in heart rate
5. Proportion of subjects with symptomatic hypotension, defined as palpitations, tachycardia, visual disturbances, blurry vision, nausea, vomiting, dizziness, syncope, hypotension and pallor

In addition, hemodynamic responses to sildenafil were evaluated in healthy young (≤45yrs) and elderly (≥65yrs) male volunteers.

Measures of systolic and diastolic blood pressure and pulse rate and their changes from the pre-dose mean were done at rest in a supine position for the first 4 hours after administration with ambulatory blood pressure monitoring (ABPM) at the following times: -15, -10 and -5 min pre-dose and 15, 30, 45 min and 1, 1.25, 1.5, 1.75, 2, 2.25, 2.5, 2.75, 3, 3.25, 3.5, 3.75, 4, 5, 7 and 10 h post-dose (i.e., every 15 min for 4 h post-dose and at 5, 7 and 10 h post-dose).

Key secondary outcome(s)
The secondary outcome was to collect safety and tolerability data after a single dose of T1, T2, T3 and T3 matching placebo and measured using the following assessments: treatment-emergent adverse events collection, manually measured vital signs (blood pressure and heart

rate), body weight, physical examination, ECG, laboratory assays.
Method of measurement:
1. Treatment-emergent adverse events recordings throughout the study duration
2. Vital signs: blood pressure (BP) and heart rate (HR) were measured by the Investigator or their deputy after 5 min at rest (in a sitting position) at screening and ETV, if applicable or final visits.
3. 12-Leads ECGs were performed in a supine position at screening and final visit/ETV
4. Body weight was recorded at screening and final visit/ETV. Subjects were weighed (kg) while lightly clothed without shoes. Height was measured at screening
only and BMI was recorded. BMI was calculated as weight [kg]/(height [m] x height [m]).
5. Laboratory parameters: blood and urine samples were collected at screening and final visits.

Completion date
01/12/2021

Eligibility

Key inclusion criteria
1. Informed consent: signed written informed consent before inclusion in the study
2. Sex and Age: males, 18-45 inclusive (young) versus ≥65 (elderly) years old
3. Body Mass Index: 18.5-30 kg/m2 inclusive
4. Vital signs: systolic blood pressure 100-139 mmHg, diastolic blood pressure 50-89 mmHg, heart rate 50-90 bpm, measured after 5 min at rest in the sitting position
5. Full comprehension: the ability to comprehend the full nature and purpose of the study, including possible risks and side effects; ability to cooperate with the Investigator and to comply with the requirements of the entire study

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
65 Years

Sex
Male

Total final enrolment
26

Key exclusion criteria
1. Electrocardiogram (12-lead ECG in supine position): clinically significant abnormalities
2. Physical findings: clinically significant abnormal physical findings which could interfere with

the objectives of the study; presence or history (within 28 days) of any tongue piercings
3. Laboratory analyses: clinically significant abnormal laboratory values indicative of physical illness
4. Allergy: ascertained or presumptive hypersensitivity to the active principle (PDE5 inhibitors) and/or formulations' ingredients; history of anaphylaxis to drugs or allergic reactions in general, which the Investigator considers may affect the outcome of the study
5. Diseases: significant history of renal, hepatic, gastrointestinal, cardiovascular, respiratory, skin, hematological, endocrine or neurological diseases that may interfere with the aim of the study; history of vision or hearing problems related to drugs of the PDE5 inhibitor pharmacological class; history of priapism; anatomical deformation of the penis (such as angulation, cavernosal fibrosis or Peyronie’s disease); history of ophthalmologic diseases like non-arteritic anterior ischemic optic neuropathy or retinitis pigmentosa
6. Medications: medications, including over-the-counter medications and herbal remedies for 2 weeks before the screening visit
7. Nitrates: treatment with nitrates for 2 weeks before the screening visit
8. Investigative drug studies: participation in the evaluation of any investigational product for 3 months before this study. The 3-month interval is calculated as the time between the first calendar day of the month that follows the last visit of the previous study and the first day of the present study
9. Blood donation: blood donations for 3 months before this study
10. Drug, alcohol, caffeine, tobacco: history of drug, alcohol [>2 drinks/day, defined according to the USDA Dietary Guidelines 2015-2020], caffeine (>5 cups coffee/tea/day) or tobacco abuse (10 cigarettes/day)
11. Drug test: positive result at the drug test at screening or day-1
12. Alcohol test: positive alcohol breath test at day -1
13. Diet: abnormal diets (<1600 or >3500 kcal/day) or substantial changes in eating habits in the 4 weeks before this study; vegetarians

Date of first enrolment
13/04/2021

Date of final enrolment
12/11/2021

Locations

Countries of recruitment
Italy

Switzerland

Study participating centre
CROSS Research SA, Phase I Unit
Via F.A. Giorgioli, 14
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Sponsor information

Organisation
IBSA Institut Biochimique (Switzerland)

ROR
https://ror.org/051tj3a26

Funder(s)

Funder type
Industry

Funder Name
IBSA Institut Biochimique SA - Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository: the IBSA Institut Biochimique S.A. repository.

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		29/11/2022	29/11/2022	No	No