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A study to assess the amount of active ingredient that reaches the blood circulation after administration of a new drug dissolvable in the mouth for treating the erectile dysfunction in comparison to the marketed tablet Cialis®, taken by healthy men under fed and fasting conditions

Submission date
20/12/2022

Recruitment status
No longer recruiting

Registration date
19/01/2023

Overall study status
Completed

Last Edited
30/05/2023

Condition category
Urological and Genital Diseases

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

Plain English summary of protocol

Background and study aims
A new film containing tadalafil, the active ingredient of Cialis®, has been developed to provide an easy-to-take and rapidly dissolvable alternative to the marketed products for erectile dysfunction treatment. As observed in clinical practice, meal intake could affect the pharmacokinetic (i.e., absorption, distribution, metabolism and elimination) of tadalafil. Consequentially, this study is designed to investigate the amount of tadalafil that reaches the blood circulation after administration of the new tadalafil orodispersible film under fed and fasting conditions versus the Cialis® tablet under fed conditions. Fed conditions will be warranted through a high-fat high-caloric breakfast.

Who can participate?
Healthy men aged 18-45 years can participate. They must comprehend the full nature and purpose of the study, including possible risks and side effects and co-operate with the investigator to comply with the requirements of the entire study.

What does the study involve?
The study will be conducted at the CROSS Research S.A. Phase I Unit Clinical Centre, in Arzo, Switzerland. Study participants will receive a single dose of IBSA tadalafil 20 mg orodispersible film under fed conditions, a single dose of IBSA tadalafil 20 mg orodispersible film under fasting conditions and a single dose of Cialis® film-coated tablet under fed conditions in 3 study periods, with a wash-out interval of at least 12 days between the consecutive administrations. Participants will have blood samples taken and vital parameters recorded at regular intervals.

What are the possible benefits and risks of participating?
Participating in this study will not bring any direct benefit to participants, with the exception of the medical tests that will be performed during it. Generally, the administration of IBSA tadalafil 20 mg orodispersible film to healthy subjects in previous clinical studies was safe and well tolerated. Furthermore, no particular risks related to Cialis® administration are expected. However, as with all products, the appearance of allergic reactions or side effects that are known or not yet known cannot be ruled out.

Where is the study run from?
The study will be conducted at the CROSS Research S.A. Phase I Unit Clinical Centre, in Arzo, Switzerland.

When is the study starting and how long is it expected to run for?
September 2021 to April 2022

Who is funding the study?
IBSA Institut Biochimique S.A. (Switzerland)

Who is the main contact?
Dr. Milko Radicioni, clinic@croalliance.com

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
21CH-TAD08

Study information

Scientific Title

Comparative bioavailability study of a new IBSA tadalafil 20 mg orodispersible film vs. Cialis® 20 mg film-coated tablet in healthy men under fed and fasting conditions

Study objectives
To evaluate the bioavailability of tadalafil in healthy male volunteers after a single dose of tadalafil 20 mg orodispersible film administered under fed and fasting conditions versus Cialis® 20 mg tablet administered under fed conditions.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 09/11/2021, 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: 2021-02114 / CE 3970

Primary study design
Interventional

Study design
Single-centre single dose open-label randomized three-way cross-over fed and fasting conditions pilot bioavailability study

Study type(s)
Other

Health condition(s) or problem(s) studied
Tadalafil for erectile dysfunction

Interventions
For each subject, a single dose of IBSA tadalafil 20 mg orodispersible film under fed conditions, a single dose of IBSA tadalafil 20 mg orodispersible film under fasting conditions and a single dose of Cialis® film-coated tablet under fed conditions will be administered in 3 study periods, according to a 3-way cross-over randomised design, with a wash-out interval of at least 12 days between the 3 consecutive administrations. The investigational products will be orally administered to the volunteers on Day 1 of each study period at 08:00±1 h as follows:
- one IBSA tadalafil 20 mg orodispersible film administered under fed conditions
- one IBSA tadalafil 20 mg orodispersible film administered under fasting conditions
- one Cialis® 20 mg film-coated tablet administered under fed conditions.

Before the administration of IBSA tadalafil 20 mg orodispersible film, the subject will wet the mouth with 20 mL of still mineral water. Then, the Investigator or deputy will take the film out of the sachet and place it directly on the subject's tongue. The Investigator will wear gloves during the administration procedure. Subjects will let the orodispersible film completely dissolve in their mouth. The film must not be swallowed whole and must not be chewed or broken. The subject will be allowed to swallow saliva as the film dissolves in the mouth. In detail, once the subject feels that the film has completely dissolved, he will inform the Investigator who will inspect the subject’s mouth and verify the complete dissolution in the mouth. If the subject does not inform the investigator within 2 minutes of the administration, his mouth will be checked by the Investigator at 2 and 3 minutes. If, upon inspection at 2 or 3 minutes, the film is

already dissolved, the time of mouth check will be recorded as the time of dissolution. If the film is not completely dissolved within 3 min, the subjects will be allowed to swallow without water. In this case, the dissolution end time will be considered as not applicable. For IBSA tadalafil 20 mg orodispersible film, the exact date and time of orodispersible film administration (defined as the time at which the orodispersible film is placed on the subject's tongue by the Investigator or deputy) and the time of complete dissolution of the orodispersible film (no residues present at inspection of the oral cavity by the Investigator or deputy) will be recorded. Film dissolution times will be collected in specific source documents and subjects' case report forms. The occurrence of inadvertent chewing and/or breaking and/or swallowing will be recorded.

For the administration of Cialis® 20 mg film-coated tablet product, the subject will swallow the tablet with 150 mL of still mineral water. The tablet must be swallowed whole and must not be chewed or broken. Product administration date and time will be recorded as well.
The subjects receiving the treatments under fed conditions will take the investigational medicinal product 30 min after having started to eat a high-fat and high-caloric breakfast. Breakfast must be completed within 30 minutes from start. The subjects receiving IBSA tadalafil 20 mg orodispersible film under fasting conditions will take it under prolonged fasting conditions (from at least 10 h pre-dose).

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Tadalafil

Primary outcome(s)
Rate (Cmax and tmax) and extent (AUC0-72h) of tadalafil absorption in plasma measured from plasma samples taken at pre-dose (0) and 20 min, 40 min, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 6.5, 7, 8, 10, 12, 24, 48 and 72 h post-dose after administration of IBSA tadalafil 20 mg orodispersible film and Cialis® 20 mg film-coated tablet under fed conditions

Key secondary outcome(s)
1. Rate (Cmax and tmax) and extent (AUC0-72h) of tadalafil absorption in plasma measured from plasma samples taken at pre-dose (0) and 20 min, 40 min, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 6.5, 7, 8, 10, 12, 24, 48 and 72 h post-dose after administration of IBSA tadalafil 20 mg orodispersible film under fed and fasting conditions
2. Relative bioavailability (Frel), area under the concentration-time curve from administration to 8 h post-dose (AUC0-8h) and, if feasible, area under the concentration-time curve extrapolated to infinity (AUC0-inf) and elimination half-life (t1/2) of plasma tadalafil
3. All adverse events occurring after informed consent signature but before the first dose of the investigational medicinal product (PTAEs), all adverse events occurring or worsening after the first dose of the investigational medicinal product (TEAEs), vital signs (blood pressure and heart rate, measured at the screening visit, on Days 1-2 and 4 at pre-dose (0), 4, 5, 24 and 72 h post-dose of each study period and at early termination visit [ETV], if applicable), body weight (measured at screening and final visit/ETV as applicable), physical examinations (performed at screening and final visit/ETV as applicable), clinical laboratory parameters (haematology, blood

chemistry and urine analysis performed at screening and final visit/ETV as applicable; virology performed at screening visit; urine drug test performed at screening and at the entrance of each study period), ECG (performed at screening and final visit/ETV as applicable).

Completion date
16/04/2022

Eligibility

Key inclusion criteria
1. Informed consent: signed written informed consent before inclusion in the study
2. Sex and Age: men, 18-45 years old inclusive
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: ability to comprehend the full nature and purpose of the study, including possible risks and side effects; ability to co-operate with the Investigator and to comply with the requirements of the entire study.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
45 Years

Sex
Male

Total final enrolment
15

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 of mouth lesions or any other oral mucosa alteration; presence or history (within 28 days) of any tongue piercings; presence of any partials, braces or dentures
3. Laboratory analyses: clinically significant abnormal laboratory values indicative of physical illness
4. Allergy: ascertained or presumptive hypersensitivity to the active principle (PDE5 inhibitors) or formulations' ingredients or both; 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, haematological, endocrine, immunological 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 start of the study. Nitrates will not be allowed for 2 weeks before screening.
7. 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
8. Blood donation: blood donations for 3 months before this study
9. Drug, alcohol, caffeine, tobacco: history of drug, alcohol [>2 drinks/day, defined according to the USDA Dietary Guidelines 2020-2025], caffeine (>5 cups coffee/tea/day) or tobacco abuse (10 cigarettes/day)
10. Drug test: positive result at the drug test at screening or Day-1
11. Alcohol test: positive alcohol breath test at Day -1
12. 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
15/03/2022

Date of final enrolment
17/03/2022

Locations

Countries of recruitment
Switzerland

Study participating centre
CROSS Research S.A.
Via F.A. Giorgioli 14
Arzo
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6864

Sponsor information

Organisation
IBSA Institut Biochimique (Switzerland)

ROR

https://ror.org/051tj3a26

Funder(s)

Funder type
Industry

Funder Name
IBSA Institut Biochimique S.A.

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Stored in non-publicly available repository, Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		30/05/2023	30/05/2023	No	No
Protocol file	version 1.0	21/10/2021	10/01/2023	No	No