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Study to assess the distribution in healthy male volunteers' blood and urine of one and two consecutive doses of the antibiotic fosfomycin

Submission date
22/03/2022

Recruitment status
No longer recruiting

Registration date
25/03/2022

Overall study status
Completed

Last Edited
25/03/2022

Condition category
Other

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Fosfomycin is a widely used antibiotic for urinary tract bacterial infections and has been shown to prevent infectious complications in patients after undergoing urological procedures, such as surgical and transurethral diagnostic procedures and transrectal prostate biopsy, which are commonly performed to diagnose prostatic carcinoma (prostate cancer). The sponsor designed the present study to get more information in healthy male volunteers about fosfomycin concentrations in blood, urine and the male genital tract and its safety of use after two doses (one dose of 3 g fosfomycin given 3 hours before surgery and a second dose of 3 g given 24 hours after surgery), which is currently used in the above-mentioned urological procedures.

Who can participate?
Healthy men volunteers aged 40-70 years

What does the study involve?
All participants receive the following treatment: one dose of 3 g of fosfomycin (as fosfomycin trometamol) on Day 1, at 07:00 ± 1 h under fasting conditions and one dose of 3 g of fosfomycin (as fosfomycin trometamol) on Day 3 at 07:00 ± 1 h under fasting conditions followed by a second dose of 3 g of fosfomycin (as fosfomycin trometamol) exactly 27 h later, that is on Day 4, at 10:00 ± 1 h. During the study, blood, urine and seminal plasma samples are collected from participants for the measurement of fosfomycin in the bloodstream, urine and seminal plasma and of fructose and PSA in seminal plasma. Heart rate and blood pressure are measured, ECG is recorded and blood and urine laboratory tests are performed to test the safety of the medication.

What are the possible benefits and risks of participating?
No specific benefits for the study participants are foreseen. Their remuneration is paid after study completion. The remuneration covers loss of time and any inconvenience caused by the participation in the study. No particular risks are expected for the study subjects originating from the scheduled fosfomycin dose regimen, considering that fosfomycin trometamol is a well-known drug which has been used for decades. The safety of the drug is generally good. A few

undesired effects have been commonly (at a frequency ≥1/100 and <1/10) reported: diarrhoea, nausea, dyspepsia, headache and dizziness. Blood sampling with cannula insertion may cause minor discomfort. The risks associated with blood draws include pain, bleeding and bruising.

Where is the study run from?
Zambon S.p.A. (Italy)

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

Who is funding the study?
Zambon S.p.A. (Italy)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CRO-PK-20-349, sponsor code Z7215J01

Study information

Scientific Title
Pharmacokinetic study of one and two consecutive doses of oral fosfomycin trometamol in healthy male volunteers

Study objectives
To evaluate fosfomycin concentrations and pharmacokinetics (PK) in plasma and urine in healthy men after one and two consecutive doses of the investigational medicinal product (IMP).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/02/2021, Cantonal Ethics Committee Canton Ticino (c/o Health Office, Via Orico 5, 6501 Bellinzona, Switzerland; +41 (0)91 8143057; dss-ce@ti.ch), ref: CE 3796, BASEC 2020-03039

Study design
Single- and multiple-dose single-centre open-label one-way pharmacokinetics, safety and tolerability Phase I clinical study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Pharmacokinetic study in healthy male volunteers

Interventions
All the subjects enrolled in the study receive the same treatment with the investigational medicinal product (IMP) as follows:
1. On Day 1, one dose of 3 g of fosfomycin (as fosfomycin trometamol) is administered under fasting conditions at 07:00 ± 1 h.

After a wash-out of exactly 48 h:
2. On Day 3, one dose of 3 g of fosfomycin (as fosfomycin trometamol) is administered under fasting conditions at 07:00 ± 1 h, followed by a second dose of 3 g of fosfomycin (as fosfomycin trometamol) exactly 27 h later, on Day 4, at 10:00 ± 1 h.

At each dosing, the entire content of one sachet of IMP is dispersed until complete dissolution in 75 ml of still mineral water and drunk by the subject. Afterwards, the glass is rinsed with a further 50 ml of still mineral water and the rinse drunk.

This is a non-randomised study. All the subjects receive the same study treatment.

During the interventional phase, blood samples are collected for PK analysis at pre-dose (0), 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 6, 8, 10, 12, 16, 24, 30 and 36 h post-dose. Urine is collected during the following time intervals on Days 1-2, after the single dose, and on Days 4-5, after the second multiple dose: 0-4, 4-8, 8-12, 12-16, 16-24 and 24-36 h post-dose.

Together with blood and urine, also the seminal plasma is collected for PK analysis. In detail, the subjects are instructed to masturbate and ejaculate their semen at about 2.5 h post-dose on Day 1, after the single dose, and Day 4, after the second multiple dose, and in any case, before the 2.5-h post-dose blood sampling. They are instructed to collect their semen into a five-compartment plastic collection tray in a single pass across the long axis of the tray. Each sample is processed for the determination of the concentration of fosfomycin in plasma, urine and seminal plasma. Seminal plasma is analysed also to determine the concentration of fructose and PSA. Safety and general tolerability of the IMP are based on adverse events, ECG, physical examinations including body weight, vital signs and routine haematology, blood chemistry and urinalysis laboratory tests.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Monuril® (fosfomycin trometamol)

Primary outcome measure
Fosfomycin concentrations and pharmacokinetics evaluated in plasma and urine using a fully validated liquid chromatography with tandem mass spectrometry (LC-MS-MS) method after one dose (Day 1) and two consecutive doses (Day 4) of the investigational medicinal product

Secondary outcome measures
1. Fosfomycin concentrations evaluated in prostate and seminal vesicles using a fully validated liquid chromatography with tandem mass spectrometry (LC-MS-MS) method after one dose (Day 1) and two consecutive doses (Day 4) of the investigational medicinal product
2. Safety and tolerability of the treatment evaluated by collecting the adverse events during the whole study and measuring vital signs (blood pressure and heart rate) at screening, on Days 1-2 and Days 4-5 and at the final visit. Safety and tolerability of the treatment are also evaluated by measuring the laboratory parameters, performing physical examinations including body weight and registering the ECG at screening and the final visit.

Overall study start date
01/12/2020

Completion date
08/09/2021

Eligibility

Key inclusion criteria
1. Informed consent: signed written informed consent before inclusion in the study
2. Sex and age: men, 40-70 years old inclusive
3. Body Mass Index (BMI): 18.5-30 kg/m2 inclusive
4. Vital signs: systolic blood pressure (SBP) 100-139 mmHg, diastolic blood pressure (DBP) 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 study

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Male

Target number of participants
24

Total final enrolment
24

Key exclusion criteria
1. Electrocardiogram (ECG) 12-leads (supine position): clinically significant abnormalities
2. Physical findings: clinically significant abnormal physical findings which could interfere with the objectives of the study
3. Laboratory analyses: clinically significant abnormal laboratory values indicative of physical illness
4. Allergy: ascertained or presumptive hypersensitivity to the active principle 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, genitourinary, skin, haematological, endocrine or neurological diseases that may interfere with the aim of the study
6. Medications: medications, including over the counter (OTC) medications and herbal remedies for 2 weeks before the screening visit
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 2015], 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
18/03/2021

Date of final enrolment
12/04/2021

Locations

Countries of recruitment
Switzerland

Study participating centre
CROSS Research S.A. - Phase I Unit
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Sponsor type
Industry

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https://ror.org/04zzq8d03

Funder(s)

Funder type
Industry

Funder Name
Zambon S.p.A.

Results and Publications

Publication and dissemination plan
Neither the clinical study protocol nor any other study document is expected to be made available. To date, there are no plans to publish the study results in scientific journals.

Intention to publish date

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
Data sharing statement to be made available at a later date