ISRCTN46559299 https://doi.org/10.1186/ISRCTN46559299

Bioavailability study of a new testosterone tablet formulation administered as single doses of 1, 2 and 3 mg to healthy postmenopausal women

Submission date
20/09/2017

Recruitment status
No longer recruiting

Registration date
21/09/2017

Overall study status
Completed

Last Edited
21/09/2017

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
Testosterone is a naturally occurring hormone that is responsible for the development of the male external genitalia and secondary sexual characteristics. Testosterone replacement therapy is required to restore the natural hormone levels of men with low levels of testosterone . The aim of this study is to assess the effect of 1, 2 and 3 mg single doses of the new testosterone tablets on the levels of testosterone in the blood. The tablets are tested in healthy postmenopausal women as women have much lower levels of testosterone compared to healthy men.

Who can participate?
Healthy postmenopausal women aged 45 to 65

What does the study involve?
Participants are randomly allocated to take 1, 2 or 3 mg single doses of the new testosterone tablets on three different days with a gap of at least 3 days between each treatment. After each treatment blood samples are taken regularly over 8 hours to measure testosterone levels.

What are the possible benefits and risks of participating?
No specific benefits for the participants are foreseen. The doses of testosterone used are lower than the doses used in previous studies.

Where is the study run from?
CROSS Research Phase I Unit (Switzerland)

When is the study starting and how long is it expected to run for?
February 2016 to October 2016

Who is funding the study?
IBSA Institut Biochimique SA (Switzerland)

Who is the main contact?
Mr Milko Radicioni

Contact information

Type(s)
Scientific

Contact name
Mr Milko Radicioni

ORCID ID
https://orcid.org/0000-0002-3940-8375

Contact details
CROSS Research S.A. – Phase I Unit
Via F.A. Giorgioli 14
Arzo
Switzerland
CH-6864

Additional identifiers

Protocol serial number
Study CRO-PK-16-311 - Sponsor code 15CH-Tes04

Study information

Scientific Title
Bioavailability study of a new testosterone tablet formulation administered as single doses of 1, 2 and 3 mg to healthy postmenopausal women

Study objectives
Testosterone is a naturally occurring steroid hormone. It is responsible for the development of the male external genitalia and secondary sexual characteristics. Testosterone replacement therapy is required to restore the natural androgen levels in men with primary or secondary hypogonadal disorders, and to treat symptoms of partial androgen deficiency in aging men (andropause). Although testosterone can be orally administered, it is rapidly metabolised in the intestinal wall and during its first pass through the liver, whereby approximately the 98% of the amount administered is inactivated. As a consequence, oral administration of pure, crystalline testosterone does not sufficiently increase serum testosterone levels.Testosterone circulates in plasma bound to sex hormone-binding-globulin (SHBG) and, in a small percentage, unbound. The free and non-specifically bound hormone fraction (commonly referred to as the bioavailable fraction) reflects only partially the hormone available at the cellular level. Only a very small fraction of about 1-2% is unbound or free and is biologically active and able to enter a cell and

activate its receptor. The oral formulations available in Europe are Andriol® or Andriol® Testocaps containing 40 mg of testosterone undecanoate dissolved in oleic acid in soft gelatin capsules, as solid dosage form.

Solid dosage forms are popular because of the ease of administration, accurate dosage, self-medication, pain avoidance. Even if tablets and capsules are most popular forms, many people face difficulty in swallowing tablets and hard gelatin capsules. Thus, these conventional dosage forms may result in high incidence of noncompliance and ineffective therapy with respect to swallowing.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Independent Ethics Committee (Comitato Etico Cantonale, Canton Ticino, Switzerland; Appendix 16.1.3), 13/06/2016, ref. nr. CE3069 – Basec 2016-00869
2. The Federal Health Authorities (Swissmedic), 29/06/2016, ref: 2016DR1094

Study design
Single-dose open randomised three-period three-way cross over exploratory bioavailability study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Testosterone hydroxypropyl-β-cyclodextrin (HPBCD), 1 mg and 2 mg tablets

Interventions
The subjects were assigned to one sequence of treatments, e.g. T1/T2/T3 or T1/T3/T2 or T2/T1 /T3 or T2/T3/T1 or T3/T1/T2 or T3/T2/T1 according to the randomisation number. Randomisation number was given to the subjects on study day -1, period 1, and was used to assign the treatment sequence according to the randomisation list. The randomisation list was computer-generated by the Biometry Unit of the Clinical Contract Research Organisation (CRO), using the PLAN procedure of the SAS® version 9.3 (TS1M1). The randomisation list was supplied to the Phase I Unit before study start.

Test 1 (T1): testosterone hydroxypropyl-β-cyclodextrin (HPBCD), 1 mg tablets, IBSA Institut Biochimique S.A., Switzerland. Batch: 006C16-173; expiry: SEP17
Test 2 (T2): testosterone HPBCD, 2 mg tablets, IBSA Institut Biochimique S.A., Switzerland. Batch: 007C16-173; expiry: SEP17
Test 3 (T3): T1+T2, i.e. 1 mg tablets + 2 mg tablets for a total dose of 3 mg

Each test investigational product was administered under fasting conditions. A wash out interval of at least 3 days elapsed between 2 subsequent administrations. The subjects wetted their mouth by drinking 20 mL of still mineral water before each administration. Each tablet was placed on the tongue and allowed to dissolve completely (without chewing). Afterwards, water was allowed starting from 1 h post-dose.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
Total testosterone, free testosterone and DHT rate (Cmax) and extent (AUC0-t) of absorption after single dose administration of the test treatments. The concentration of testosterone, DHT, albumin, SHBG was measured in serum at the following time-points: pre-dose (0), 10, 20, 30, 45 min, 1, 1.5, 2, 3, 4, 5, 6 and 8 h post-dose.

Key secondary outcome(s))
1. Serum pharmacokinetic parameters for total testosterone, free-testosterone and DHT after single dose of the test treatments. The concentration of testosterone, DHT, albumin, SHBG was measured in serum at the following time-points: pre-dose (0), 10, 20, 30, 45 min, 1, 1.5, 2, 3, 4, 5, 6 and 8 h post-dose.
2. Safety of the test treatments, assessed throughout the study

Completion date
01/10/2016

Eligibility

Key inclusion criteria
1. Informed consent: signed written informed consent prior to inclusion in the study
2. Menopause: postmenopausal women for at least one year
3. Age: 45-65 year old inclusive
4. Body Mass Index (BMI) from 18.5 to 30 kg/m2
5. 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
6. Testosterone levels: endogenous testosterone levels <3.5 nmol/L (about 1.00 ng/mL)
7. Pap test: normal or not clinically relevant abnormal cervical smears at Papanicolaou test performed within the last 12 months or during the screening phase
8. Mammography: normal or not clinically relevant abnormal mammograms at mammography performed within the last 24 months or during the screening phase
9. 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

Sex
Female

Key exclusion criteria
1. Electrocardiogram (ECG) 12-leads (supine position): clinically relevant abnormalities
2. Physical findings: clinically relevant abnormal physical findings which could interfere with the objectives of the study
3. Laboratory analyses: clinically relevant 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 considered could affect the outcome of the study
5. Diseases: relevant history of cardiovascular, pulmonary, hepatic, renal, haematological, gastrointestinal, immunological, dermatological, endocrine (e.g. hyper-prolactinemia or uncontrolled thyroid and adrenal dysfunction), genitourinary, neurological or psychiatric diseases that could interfere with the aim of the study; malignant neoplasia
6. Medications: intake of other medications, including over the counter medications and herbal remedies, for 2 weeks before the start of the study. Intake of any drug affecting the cytochrome P450 for 28 days before the start of the study
7. Hormonal replacement therapy: any hormonal replacement therapy (estrogen-progestin formulations) within 4 weeks, any sex hormone depot injection within 6 months and any sex hormone implants within 5 years before the start of the study
8. Investigative drug trials: participation in the evaluation of any drug for 3 months before this study, calculated from the first day of the month following the last visit of the previous study
9. Blood donation: blood donations for 3 months before this study
10. Drug, tobacco, alcohol, caffeine: history of drug, alcohol (>1 drink/day, defined according to USDA Dietary Guidelines 2015-2020), caffeine (>5 cups coffee/tea/day) or tobacco (10 cigarettes per day) abuse
11. Diet: abnormal diets (<1600 or >3500 kcal/day) or substantial changes in eating habits in the 4 weeks before the start of this study; vegetarian
12. Pregnancy test: positive urine pregnancy test at screening
13. Drug test: positive abuse drug test at screening
14. Alcohol breath test: positive alcohol breath test at day -1

Date of first enrolment
01/09/2016

Date of final enrolment
01/10/2016

Locations

Countries of recruitment
Switzerland

Study participating centre
CROSS Research Phase I Unit
Via F. A. Giorgioli 14, CH-6864 Arzo
6864

Sponsor information

Organisation
IBSA Institut Biochimique SA

ROR
https://ror.org/051tj3a26

Funder(s)

Funder type
Industry

Funder Name
IBSA Institut Biochimique SA

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 publically available repository.

IPD sharing plan summary
Stored in repository