A study to investigate the pharmacokinetic profile of 3 doses of sublingual testosterone solution and their effect on physiological and subjective arousal in healthy, sexually functional premenopausal women.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21403

Source
Nationaal Trial Register

Brief title
PK-PD Testosterone

Health condition

Pharmacokinetics of sublingual testosterone, female sexual arousal, Vaginal Pulse Amplitude (VPA)

Farmacokinetiek sublinguale testosteron, seksuele opwinding bij vrouwen, vaginale pulse amplitude (VPA)

Sponsors and support

Primary sponsor: Emotional Brain BV
Source(s) of monetary or material Support: Emotional Brain BV

Intervention

Outcome measures

Primary outcome

1. To establish the lowest effective dose using physiological and subjective measures of sexual arousal;

2. To evaluate and compare the pharmacokinetics of testosterone and its metabolites following administration of three doses of sublingual testosterone.

Secondary outcome

To investigate the effect of three different doses of sublingual testosterone on the duration of increased physiological and subjective measures of sexual arousal.

Study description

Background summary

This is a single-center, single-blind, randomized, cross-over placebo controlled dose-finding study with three doses of testosterone administered sublingually and placebo.
A total of 16 subjects receive each investigational drug dose once in random order. Wash-out between treatments will be at least 48 hours. Baseline pharmacodynamic and pharmacokinetic assessments will be performed each experimental day before each dosing. Pharmacokinetic and pharmacodynamic (physiological and subjective measures of sexual arousal) assessments will be performed at pre-determined time points. Subjects visit the site a total of 6 times: 1 day screening (V0), 4 experimental days and 1 follow up visit. During all visits the subject's health will be monitored.

The main goal is to establish the lowest effective dose of testosterone sublingual in premenopausal sexually healthy women using physiological and subjective measures of sexual arousal. Also, it is directed at evaluating and comparing the pharmacokinetics of testosterone and its metabolites following administration of three single doses of testosterone sublingual.

Pharmacodynamic parameters are: Vaginal Pulse Amplitude (VPA) and SARSAQ questionnaire.

Pharmacokinetic parameters for total and free testosterone:

1. Maximum concentration (Cmax);

2. Area under the curve (AUC0-240);

3. Time to Cmax (Tmax);

4. Terminal elimination halflife (T1/2).

Study objective

In the present study we will investigate the pharmacokinetic profile of three doses of sublingual testosterone, and measure subjective and physiological measures of sexual functioning in healty premenopausal women.

The lowest effective dose of testosterone sublingual will be established through the comparison of the three doses' effect on the pharmacodynamic parameters.

1. It is expected that the lowest dose will not increase Vaginal Pulse Amplitude (VPA) or Sexual Arousal Response Self Assessment Questionnaire (SARSAQ) significantly ($p<0.05$) from baseline (pre-dose) in response to erotic film excerpts, as compared to placebo;

2. It is expected that the middle dose will increase VPA and SARSAQ significantly ($p<0.05$) from baseline (pre-dose) in response to erotic film excerpts, as compared to placebo;

3. It is expected that the highest dose will increase VPA and SARSAQ significantly ($p<0.05$) from baseline (pre-dose) in response to erotic film excerpts, as compared to placebo, but not as compared to the middle dose;

4. A linear dose relationship is expected for Cmax of total testosterone;

5. A linear dose relationship is expected for AUC0-240 of total testosterone;

6. Tmax of total testosterone is expected to be the same for the three doses of testosterone sublingual;

7. A nonlinear dose relationship is expected for Cmax of free testosterone;

8. A nonlinear dose relationship is expected for AUC0-240 of free testosterone;

9. Tmax of free testosterone is expected to be the same for the three doses of testosterone sublingual.

Study design

The trial duration is 7 weeks, with 4 experimental days where medication is administered.

Intervention

Three doses of sublingual testosterone and onde dose of placebo. Medication administration is separated by a 48 hour washout period.

Contacts

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Eligibility criteria

Inclusion criteria

1. Provision of written informed consent;

2. Female 21-40 years of age;

3. Healthy according to normal results of medical history, physical examination, laboratory values and vital signs, unless the investigator considers an abnormality to be clinically relevant;

4. Subject must be heterosexually oriented;

5. BMI ≥ 18 and ≤ 30 kg/m2;

6. Venous access sufficient to allow blood sampling as per protocol.

Exclusion criteria

1. Sexual dysfunction as determined by Sexual Function Questionnaire (SFQ) diagnostic scores (within ‘high probability of dysfunction’ or ‘possibility of dysfunction’ ranges) for all functional domains (desire, arousal-lubrication, arousal-sensation, orgasm and pain) as described by Quirk et al. 2005;

2. Subjects who had used testosterone therapy within 6 months before study entry;

3. (A history of) hormone-dependant malignancy;

4. Use of oral contraception containing anti-androgens (e.g. Diane 35; Minerva);

5. Use of oral contraception containing 50 µg estrogen or more;

6. Pregnancy, or intention to become pregnant during this study (Note: a serum or urine pregnancy test will be performed in all women prior to the administration of study medications);

7. A pelvic inflammatory disease or an untreated vaginal infection at screening;

8. Lactating, or subjects who have given birth in the previous 6 months;

9. Previous prolapse and incontinence surgery affecting the vaginal wall, which in the opinion of investigator would interfere with the VPA measurement;

10. Women with other unexplained gynecological complaints, such as abnormal uterine bleeding patterns;

11. (History of) endocrine disease;

12. (History of) severe neurological problems, current severe neurological problems, or other mild or moderate neurological problems which in the opinion of investigator would interfere with the participant’s ability to provide informed consent, comply with study instructions, confound interpretation of study results, or endanger the participant if she took part in the trial;

13. Treatment for a current serious psychiatric disorder (e.g., schizophrenia, psychosis) or treatment for obsessive compulsive disorder, anorexia nervosa, bulimia nervosa and/or social anxiety neurosis;

14. Any underlying cardiovascular condition including unstable angina pectoris, that would preclude sexual activity;

15. (History of) myocardial infarction, stroke or life-threatening arrhythmia within the prior 6 months;

16. Uncontrolled atrial fibrillation/flutter at screening (ventricular response rate > 60-80 bpm in rest, > 90-115 bpm in moderate exercise), or other significant abnormality observed on

ECG;

17. Systolic blood pressure ≥ 130 mmHg and/or diastolic blood pressure ≥ 80 mmHg;

18. Subjects who are taking CYP3A4-inhibitors: ritonavir (HIV-proteaseremmer), ketoconazol en itraconazol claritromycine, erytromycine and saquinavir;

19. Subjects who are taking CYP3A4-inducers: carbamazepine, fenytoïne, fenobarbital, st Johns Wort, rifampicine;

20. Acute/chronic liver disease: ASAT and ALAT > 3x the upper limit of normal;

21. Renal insufficiency (< 29 ml/min): based on the Cockcroft and Gault formula;

22. A substance abuse disorder that in the opinion of the investigator is likely to affect the subject's ability to complete the study or precludes the subject’s participation in the study; mild or moderately alcohol drinking behavior is allowed, only 12 hours before the experimental days is alcohol drinking not allowed. Three weeks before the start of the experimental day is the taking of any recreational drug not allowed. Smoking is allowed;

23. Subjects who are illiterate, unwilling or unable to understand and complete the questionnaires;

24. Any other clinically significant abnormality or condition which in the opinion of investigator would interfere with the participant’s ability to provide informed consent, comply with study instructions, possibly confound interpretation of study results, or endanger the participant if she took part in the trial;

25. Subjects with a peri menopausal hormonal status (FSH > 30).

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	25-05-2010
Enrollment:	16
Type:	Anticipated

Ethics review

Positive opinion

Date:	14-05-2010
Application type:	First submission

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
NTR-new	NL2202
NTR-old	NTR2326
Other	Emotional Brain : EB79
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results

N/A