A double blind, randomized, placebo controlled, cross-over study to validate the predictive power of the demarcation formula for Lybrido and Lybridos efficacy in women with female sexual interest/arousal disorder, in the domestic situation.

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Primary Objective• To validate the existing demarcation formula (consisting of psychometric and biological markers) which predicts the sensitivity to Lybrido or Lybridos in women with female sexual interest/arousal disorder (FSIAD with or without...

Ethical review	Approved WMO
Status	Completed
Health condition type	Sexual dysfunctions, disturbances and gender identity disorders
Study type	Observational invasive

Summary

ID

NL-OMON40620

Source
ToetsingOnline

Brief title
A study to validate the demarcation formula for Lybrido and Lybridos.

Condition

- Sexual dysfunctions, disturbances and gender identity disorders

Synonym
problems with sexual functioning, sexual dysfunction

Research involving
Human

Sponsors and support

Primary sponsor: Companion Diagnostics BV
Source(s) of monetary or material Support: Companion Diagnostics BV sponsor

Intervention

Keyword: Androgen sensitivity, Female sexual dysfunction, Serotonergic sensitivity

Outcome measures

Primary outcome

Change from placebo in frequency of satisfactory sexual events, following study medication intake, measured by the Sexual Event Diary (SED), item 4

Secondary outcome

• Change from placebo in experienced sexually-related personal distress, measured by the Female Sexual Distress Scale-Revised (FSDS-R), specifically item 13.

• Evaluation of meaningful improvement during treatment period, measured by the single item Patient*s Global Impression of Improvement (PGI-I)

• Evaluation of meaningful benefit of study medication during treatment period, measured by the single item Patient Benefit Evaluation (PBE)

• Change from placebo in frequency of orgasms, following medication intake, measured by the SED

• Change from placebo in sexual desire, following medication intake, measured by the SED

• Change from placebo in physical arousal, following medication intake, measured by the SED

• Change from placebo inmental arousal, following medication intake, measured

by the SED

• Change from placebo in sexual pleasure, following medication intake, measured

by the SED

Study description

Background summary

Female sexual dysfunction is a common problem, with ow sexual desire (22% prevalence) and sexual arousal problems (14% prevalence) belong to the most common categories. In previous studies is shown that the medications Lybrido (a combination of sublingual testosterone and sildenafil) and Lybridos (a combination of sublingual testosterone and buspirone) could help for these problems.

The sensitivity of the brain for sexual cues is determined by androgen sensitivity. In previous studies, different variables were examined, which are related to this, like the CAG repeat length of the androgen receptor gene and the 2D4D ratio, which could be a marker for prenatal androgen exposure. Based on this research, a demarcation formula with different biological and psychometric makers which could predict if a women with FSIAD will better respond to Lybrido or Lybridos was developed, as well as successfully tested in Phase 2b studies in the US.

The current study is designed to validate that formula for women with FSIAD. Furthermore, additional biological and psychometrich markers are explored which could increase the predictive power as well as of the clinical usefulness of the demarcation formula.

Study objective

Primary Objective
• To validate the existing demarcation formula (consisting of psychometric and biological markers) which predicts the sensitivity to Lybrido or Lybridos in women with female sexual interest/arousal disorder (FSIAD with or without FOD as secondary diagnosis), measured by the number of satisfactory sexual events (in 150 subjects).

Secondary Objectives
• To identify in an iterative process additional psychometric and biological

markers for the demarcation formula in order to increase predictive power for sensitivity to Lybrido or Lybridos in women with female sexual interest/arousal disorder (FSIAD with or without FOD as secondary diagnosis), measured by the number of satisfactory sexual events (in a first set of 75 subjects of the total amount of 150 subjects).

• To evaluate the altered demarcation formula in women with female sexual interest/arousal disorder (FSIAD with or without FOD as secondary diagnosis), measured by the number of satisfactory sexual events (in a second set of 75 subjects).

Study design

This is a double blind, randomized, cross-over, placebo controlled study with a 2-week single-blind placebo run in period, a 6 week double-blind treatment period, and a 1 week follow up period. The double-blind treatment period consists of a Lybrido (0,50 mg testosterone + 50 mg sildenafil) regime (duration 2 weeks), a Lybridos (0,50 mg testosterone + 10 mg buspirone) regime (duration 2 weeks), and a placebo regime (duration 2 weeks). Each regimen will be separated by at least a 2-day wash out period. Each subject completes the 2-week treatment periods in randomized order. Study medication is taken at least twice a week and once a day at most and should be taken 3 to 6 hours prior to sexual activity.
Subjects will visit the study site a total of 7 times: 1 screening visit, 1 start up visit, 4 study regimen follow up visits, and 1 final follow up visit. During the start-up visit and study regimen follow up visits, the subject*s sexual functioning will be evaluated, subject*s health will be monitored and study medication will be dispensed (no medication will be dispensed on the last study regimen follow-up visit, V6). Sexual satisfaction will be measured using several questionnaires, some of which will be completed at home following a sexual event. At the start-up visit, the subject will see a psycho-educational DVD with theoretical background information about sexual functioning and fantasizing exercises, to keep the basic knowledge of the subjects about sexuality on an approximately equal level. After watching the DVD the information will be discussed with a psychologist or similar healthcare provider.
The study is divided into a validation part and an exploratory part using two populations. In the validation part, the existing demarcation formula, described elsewhere, is validated in 150 subjects with FSIAD. In the exploratory part, the possibility of improving the demarcation formula is examined using the first 75 of these 150 patients, and then validated in the last 75 patients.

Study burden and risks

A total amount of 47ml blood will be drawn.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Provision of written informed consent
2. Females between 18 and 70 years of age, inclusive, pre or postmenopausal, with FSIAD (comorbidity with female orgasmic disorder [FOD]; only as secondary diagnosis) is allowed. The diagnosis of FSIAD will be established by a trained health care professional
3. Be involved in a stable, communicative, monogamous relationship and have a sexually functional partner who will be at home for a large part of the study duration
4. Healthy with normal medical history, physical examination, laboratory values, and vital signs; exceptions may be made if the investigator considers an abnormality to be clinically irrelevant
5. Use of highly effective contraception

Exclusion criteria

1. Any underlying cardiovascular condition, including unstable angina pectoris, that would preclude sexual activity;
2. Systolic blood pressure >= 140 mmHg and/or diastolic blood pressure >= 90 mmHg (supine blood pressure). For subjects >= 60 years old and without diabetes mellitus, familial hypercholesterolemia, or cardiovascular disease: systolic blood pressure >= 160 mmHg and/or diastolic blood pressure >= 90 mmHg;
3. Systolic blood pressure <= 90 mmHg and/or diastolic blood pressure <= 50 mmHg (supine blood pressure);
4. Use of any contraceptive containing anti-androgens (e.g. Cyproteron acetate) or (anti)androgenic progestogens (drospirenone, dienogest, chlormadinone acetate and norgestrel);
5. Use of any contraceptive or hormone replacement therapy (HRT) containing more than 50 µg/day of estrogen;
6. Pregnancy or intention to become pregnant during this study (Note: A urine pregnancy test will be performed in all women of child bearing potential prior to the administration of study medications);
7. Lactating or delivery in the previous 6 months prior to signing Informed Consent Form;
8. History of bilateral oophorectomy;
9. Other unexplained gynecological complaints, such as clinically relevant abnormal uterine bleeding patterns;
10. Perimenopausal status (cycle shortening/irregular menstrual bleeding in the last 12 consecutive months and/or occurrence of vasomotor symptoms (e.g. hot flashes, night sweating) and/or FSH levels (>40 IU/L) for women from age 40 onwards; in women with a history of hysterectomy perimenopausality can be assessed by FSH levels (> 40 IU/L) and/or vasomotor symptoms);
11. Liver and/or renal insufficiency (aspartate aminotransferase, alanine aminotransferase and gamma glutamyltransferase > 3 times the upper limit of normal and/or estimated glomerular filtration rate (eGFR) < 60.00 mL/min based on the Cockcroft Gault formula)
12. Any current endocrine disease or endocrinopathy (e.g. uncontrolled thyroid function) as determined by medical history, basic physical examination and/or laboratory values significantly outside normal range of the central laboratory; or uncontrolled diabetes mellitus (HbA1c > 7.5%)
13. Free- and/or total testosterone levels outside the upper limit of the reference range of the central laboratory;
14. Any current clinically relevant neurological disease which, in the opinion of the investigator, would compromise the validity of study results or which exclude from use of sildenafil, buspirone and/or testosterone;
15. History of hormone dependent malignancy (including all types of breast cancer);
16. Positive test result for immunodeficiency virus, hepatitis B, or hepatitis C (acute and chronic hepatitis infection);
17. History of (childhood) sexual abuse that, in the opinion of the investigator, could result in negative psychological effects when testosterone is administered;
18. (Psychotherapeutic and/or pharmacological treatment for) a psychiatric disorder (other than those under inclusion criterion 6) that, in the opinion of the investigator, would

compromise the validity of study results or which could be a contraindication for sildenafil, buspirone and/or testosterone use;
19. Current psychotherapeutic treatment for female sexual dysfunction;
20. Current genito-pelvic pain/penetration disorder according to the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM 5).
21. 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;
Concomitant Medications
22. Use of potent CYP3A4 inhibitors (eg, ritonavir, ketoconazole, itraconazole clarithromycin, erythromycin and saquinavir);
23. Use of potent CYP3A4 inducers (eg, carbamazepine, phenytoin, phenobarbital, St John*s wort, rifampin);
24. Use of aspirin, nonsteroidal anti-inflammatory drugs, warfarin, or other anticoagulants;
25. Use of antidepressants including SSRIs, tricyclic and other;
26. Use of any other medication that interferes with study medication (eg, triptans, monoamine oxidase [MAO] inhibitors [includes classic MAO inhibitors and linezolid] and spironolactone);
27. Use of medication (including herbs) that would compromise the validity of study results;
28. Use of testosterone therapy within 6 months before study entry prior to signing the Informed Consent Form;
29. Use of any kind of benzodiazepines.
General
30. Illiteracy, unwillingness, or inability to follow study procedures;
31. Participation in other clinical trials within the last 30 days;
32. Any other clinically significant abnormality or condition which, in the opinion of the investigator, might interfere with the participant*s ability to provide informed consent or comply with study instructions, compromise the validity of study results, or be a contraindication for buspirone, and/or sildenafil and/or testosterone use.

Study design

Design

Study phase:	2
Study type:	Observational invasive
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	27-01-2014
Enrollment:	150
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Buspar
Generic name:	Buspirone
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	testosterone
Generic name:	testosterone
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Viagra
Generic name:	Sildenafil
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	28-06-2013
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 28721
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2013-001966-40-NL
CCMO	NL44803.056.13
OMON	NL-OMON28721