Single-Center, Randomized Single-Blind Placebo-Controlled Five-Arm Parallel Group Study to Assess Efficacy of a Single Dose of TBS-2 Intranasal Gel at Four Time Points Post-Dose using Vibrotactile Stimulation combined with Visual Sexual Stimulation in Female Subjects with Primary and Secondary Anorgasmia

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This clinical trial is being performed to evaluate the efficacy of a single dose of TBS-2 on the occurence of orgasm. This study will explore the effect of TBS-2 on inducing an orgasm following sexual stimuli in anorgasmic female subjects at four...

Ethical review	Approved WMO
Status	Pending
Health condition type	Sexual dysfunctions, disturbances and gender identity disorders
Study type	Interventional

Summary

ID

NL-OMON36429

Source
ToetsingOnline

Brief title
Evaluation of TBS-2 in females with anorgasmia

Condition

- Sexual dysfunctions, disturbances and gender identity disorders

Synonym
Anorgasmia and inability to achieve orgasm

Research involving
Human

Sponsors and support

Primary sponsor: Trimel Biopharma SRL
Source(s) of monetary or material Support: Trimel Biopharma SRL

Intervention

Keyword: anorgasmia, Evaluation, Female subjects, TBS-2 Intranasal gel

Outcome measures

Primary outcome

Primary end-point:

- To evaluate the effect of a single dose of TBS-2 (1.2 mg) on the occurrence of orgasm at 0.5, 2.0, 4.0 and 8.0 hours post-dose in females suffering from primary or secondary anorgasmia .

The study will evaluate the occurrence of orgasm following vibrotactile stimulation and visual sexual stimulation (VTS/VSS). The occurrence of orgasm will be evaluated based on subject self-report. The subject is required to press a button to indicate orgasm start.

Secondary outcome

Secondary end-points:

a) To evaluate the effect of a single dose of TBS-2 (1.2 mg) on time to orgasm (TTO) at 0.5, 2.0, 4.0 and 8.0 hours post-dose in female subjects with primary or secondary anorgasmia .

TTO will be recorded as the time from onset of VTS/VSS stimulation until the start of orgasm at which time the subject will press a button so that TTO will be automatically recorded by the computer program.

b) To evaluate the effect of a single dose of TBS-2 (1.2 mg) on quality of orgasm at 0.5, 2.0, 4.0 and 8.0 hours post-dose in female subjects with primary or secondary anorgasmia .

Quality of orgasm will be assessed by Quality of Orgasm
Questionnaire

c) To assess the safety of TBS-2.

The following close-out parameters will be compared to the baseline results:
- Vital Signs: blood pressure, body temperature, respiratory rate, heart rate.
- Hematology: CBC, hemoglobin and hematocrit values.
- Clinical Chemistry Profile - Na/K, glucose, urea, creatinine, calcium, phosphate, uric acid, total bilirubin, albumin, AST, ALT, ALP, GGT, CK, LDL, HDL, triglycerides.
- Thyroid panel - TSH, total and free tri-iodothyronine, total and free

thyroxine.

- Hormone Profile - Estradiol, Free Testosterone, Free Testosterone (percent),

Follicle Stimulating Hormone, Luteinizing Hormone, Prolactin, Progesterone, Sex

Hormone Binding Globulin, Total Testosterone, Dehydroepiandrosterone Sulfate

- Urinalysis - Urine specific gravity, glucose, protein, ketone, pH, bilirubin,

urobilinogen, nitrite, erythrocytes and leukocytes.

- Adverse events

Study description

Background summary

Anorgasmia is the second most frequently reported women*s sexual problem after hypoactive sexual desire disorder. The Global Survey of Sexual Attitudes and Behaviours (Laumann et al., 2005) assessed sexual problems in 9,000 women aged 40-80 years in 29 countries. The prevalence of *inability to reach orgasm* ranged from 17.7% (in Northern Europe) to 41.2% (in Southeast Asia).

Anorgasmia is considered to be the persistent or recurrent delay in, or absence of, orgasm following a normal sexual excitement phase, causing marked distress or interpersonal difficulty (DSM IV). When a woman has sexual activity that is not accompanied by good quality orgasmic release, sexual activity may become a chore or a duty rather than a mutually satisfying, intimate experience. This may also lead to secondary loss of sexual interest and/or interpersonal difficulties.

It is hypothesized that testosterone has central and peripheral effects on sexual function. Testosterone, the primary circulation androgen in women, is a naturally occurring steroid secreted by the ovaries and the adrenal glands. Contrary to the sudden drop in oestrogen during menopause, serum levels of androgens fall gradually as women age primarily due to a decrease in the production of adrenal androgen precursors (Goldstat, 2003). Testosterone plays a role in mood, body composition, bone mineral density and has central and peripheral effects on sexual function (Davis 1999, Goldstat 2003). In the periphery, testosterone is required for nitric oxide to stimulate vasocongestion for the engorgement of clitoral tissue and vaginal lubrication during sexual arousal.

Central effects are less well characterized. Testosterone stimulates dopamine release in various brain structures implicated in motivation and reward systems, including sexual desire. Testosterone was found to stimulate dopamine release in the medial preoptic area of the anterior hypothalamus under basal conditions and with sexual stimulation in rats (Halaris 2003). An fMRI study in healthy women of different ages showed a testosterone level dependent modulation of amygdala activity, suggesting that an age-related decline in androgen levels contribute to the decrease in amygdala reactivity. Decreased amygdala reactivity in older women could be restored to levels of young women with intranasal exogenous testosterone (van Wingen et al, 2009). Exogenous intranasal testosterone thus may enhance healthy sexual functioning through complex brain mechanisms.

Over the two past decades, over 80 studies have been conducted in women showing benificial effects of testosterone on sexual desire, arousal, frequency of satisfactory sexual activity, pleasure and responsiveness (Traish (review 2009)).

The product under investigation in this study, TBS-2, is a testosterone intranasal gel. Contrary to the other routes of administration, administration of the bioadhesive TBS-2 through the nasal route allows for direct uptake of testosterone into the brain and rapid absorption into systemic circulation (Banks et al. 2009). The delivery of testosterone to the brain and systemic absorption is hypothesized to be effective in enhancing sexual desire and orgasm. In addition, TBS-2 may prove effective in alleviating anorgasmia in an "as needed" way, thus avoiding chronic exposure to testosterone.

Study objective

This clinical trial is being performed to evaluate the efficacy of a single dose of TBS-2 on the occurence of orgasm.

This study will explore the effect of TBS-2 on inducing an orgasm following sexual stimuli in anorgasmic female subjects at four different time points post-dose. Pharmacodynamic efficacy will be evaluated using vibrotactile stimulation (VTS) in combination with visual sexual stimulation (VSS). The VTS/VSS procedure was tested in a pilot study in women (Laan & van Lunsen, 2002) and showed that VTS in combination with visual sexual stimulation (VSS) reliably could trigger orgasm in healthy female volunteers with no self-reported difficulties in achieving orgasm. Time to orgasm (TTO) showed an acceptable intra-subject variability. In the present study, a similar clitoral vibrator will be used.

Study design

Single-center randomized, single-blind placebo-controlled five-arm parallel

group study.

This study consists of two parts: Part I - sexual stimulation without medication and Part II - sexual stimulation with TBS2/Placebo single-dose treatment. In case subjects did not reach orgasm during the sexual stimulation in Part I they may continue with Part II. In Part II, subjects will be randomized to receive a single dose of TBS-2 or Placebo and be subjected to VTS/VSS 0.5 hour post-dose in placebo arm or 0.5, 2.0, 4.0 or 8.0 hours post-dose in TBS-2 treatment arms. There will be at least 5-7 days between Part I and Part II.

Intervention

Subjects receive one dose (1.2 mg) of TBS-2 at visit 3

Study burden and risks

Risks
The risks to female subjects in this study are minimal. Subjects will be recieving a single dose 0.9 mg of TBS-2.
Testosterone in approved for women in the form of a patch, Intrinsa. Following 48 weeks of administration, common side effects included hirsutism and reactions at the site of application of the patch (which is not applicable for our product).

Benefits
The product under investigation in this study, TBS-2, is a testosterone intranasal gel. Contrary to the other routes of administration, administration of the bioadhesive TBS-2 through the nasal route allows for direct uptake of testosterone into the brain and rapid absorption into systemic circulation (Banks et al. 2009). TBS-2 has been shown to influence the amygdale. The delivery of testosterone to the brain and systemic absorption is hypothesized to be effective in enhancing sexual desire and orgasm. In addition, TBS-2 may prove effective in alleviating anorgasmia in an "as needed" way, thus avoiding chronic exposure to testosterone.

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

Females aged 18 - 50 years
Anorgasmia
Premenopausal
BMI equal or less than 35

Exclusion criteria

History of any clinically relevant other psychiatric disorder that could impact sexual function
History of Major Depressive Disorder within six (6) months prior to study
Subjects who meet DSM-IV criteria (APA) for Sexual Aversion Disorder, Substance-Induced Sexual Dysfunction, Dyspareunia (not caused by inadequate foreplay stimulation or alleviated by lubricants), Vaginismus, Gender Identity Disorder, Paraphilia, or for Sexual Dysfunction Due to a General Medical Condition.
Patients with pelvic inflammatory disease, urinary tract or vaginal infection

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	28-02-2011
Enrollment:	60
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Intranasal Testosterone Gel
Generic name:	Intranasal Testosterone Gel

Ethics review

Approved WMO Date:	21-12-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-03-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-05-2011
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-06-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
EudraCT	EUCTR2010-023559-27-NL
CCMO	NL34768.018.10