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Trial to evaluate the effect of low-dose hormone therapy on menopausal symptoms and markers of bone turnover in postmenopausal women

Submission date
06/12/2011

Recruitment status
No longer recruiting

Registration date
11/01/2012

Overall study status
Completed

Last Edited
14/07/2015

Condition category
Urological and Genital Diseases

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

Plain English summary of protocol

Background and study aims
In recent decades, hormonal therapy has been used to treat postmenopausal women to control the effects of estrogen deprivation (lack of estrogen) and improve quality of life. Currently, the global trend is to reduce the doses of hormones in order to reduce the side effects. Therefore, the aim of this study is to evaluate the clinical effectiveness and safety of ultra low dose hormone therapy in postmenopausal women, assessing the improvement of menopausal symptoms (vasomotor symptoms [night sweats, hot flashes, and flushes], bleeding and vaginal maturation), bone remodeling and quality of life.

Who can participate?
120 female patients (60 per treatment group) in post natural menopause having at least seven hot flashes per day or 50 hot flashes within one week will be enrolled in this study.

What does the study involve?
Patients will be randomly allocated to receive either the study drug or a placebo (dummy) drug for 24 weeks. Regardless of the treatment group, patients will also receive calcium and vitamin D supplementation.

What are the possible benefits and risks of participating?
In previous studies, the following adverse reactions were observed in less than 5% of women who used the study drug: body ache, headache, pain in extremity, nausea, diarrhea, nasopharyngitis, endometrial thickening and vaginal bleeding. The following adverse reactions were observed in less than 5% of women taking a placebo: headache, diarrhea, nasopharyngitis, and vaginal bleeding.
Regarding benefits, the study medication may help treat symptoms of menopause.

Where is the study run from?
This study will run only in Brazil and around 120 patients will be recruited in eight study centers. The coordinator center is Vox Femina, located in Jundiai city, state of Sao Paulo.

When is the study starting and how long is it expected to run for?
The first visit of the first patient is planned to start in May 2012 and the study will enrol patients until August 2012. As the maximum study period for each participant is 28 weeks, the last visit of the last patient is expected in March 2013.

Who is funding the study?
This study is sponsored by Libbs Pharmaceutical Ltda (Brazil).

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
LB1105

Study information

Scientific Title
A prospective, comparative, double-blind, parallel, multicenter, randomized, placebo-controlled trial to evaluate the effect of ultra-low dose hormone therapy (17beta-estradiol + norethisterone acetate) on climacteric symptoms and markers of bone turnover in postmenopausal women

Study objectives
This study aims to show the superiority of the ultra-low dose therapy compared to placebo in the treatment of climacteric symptoms.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee, Faculty of Medicine of Jundiai, Brazil, 14/12/2011

Study design
Randomized double-blind multicenter comparative prospective parallel placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Climateric symptoms

Interventions
Subjects will be randomized to receive either the test drug or placebo for 24 weeks
1. Test drug = 17beta-estradiol (0.5 mg) + norethisterone acetate (0.1 mg)
2. Placebo

Frequency of administration for both arms: one tablet, once a day during 24 weeks. The total period of follow-up is 28 weeks for both arms.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
17beta-estradiol, norethisterone acetate

Primary outcome(s)
Mean change from baseline to 24 weeks in frequency of hot flushes as recorded by patient in a daily diary

Key secondary outcome(s))
1. Changes in bone marker levels (P1NP, CTX-1, NTX and BSAP) from baseline to 12 and 24 weeks
2. Change in Vaginal Maturation Index (VMI) from baseline to 12 and 24 weeks
3. Mean change from baseline to 4, 8, 12 and 24 weeks in severity of hot flushes
4. Mean change from baseline to 4, 8 and 12 weeks in frequency of hot flushes
5. Quality of life measured by Women's Health Questionnaire
6. Change in lab test results and clinical parameters

Completion date
30/03/2013

Eligibility

Key inclusion criteria

1. Postmenopausal women aged 40 to 65 years
2. Intact uterus
3. Natural menopause, defined as (amenorrhea for at least 12 months and menopausal status must be confirmed by demonstrating levels of follicle stimulating hormone (FSH) > 30 mIU/mL and estradiol < 30 pg/ml)
4. Body mass index (BMI) between 19 and 35.0 kg/m2
5. A minimum average frequency of 50 moderate to severe hot flushes or night sweats episodes per week, as recorded by patient in the screening phase

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Key exclusion criteria
1. Known hypersensitivity to products containing estrogen and/or progestin
2. Surgical menopause
3. Endometrial thickness (bi-laminar) > 5 mm, measured by transvaginal ultrasound
4. Evidence of endometrial polyp by transvaginal ultrasound
5. Abnormal Pap smear, including cervical intraepithelial neoplasia (CIN) or cervical cancer
6. Prior exposure to hormone therapy with estrogen alone or combined therapy with estrogen /progestin, considering the following period before pre-selection (V0):
6.1 Vaginal therapy (cream, gel, vaginal capsule) - <4 weeks
6.2. Transdermal therapy (gel, patch), nasal spray - <4 weeks
6.3. Estrogen therapy/estrogen-progestogen oral SERM (Raloxifene), Tibolone, Androgens - <8 weeks
6.4. Intra-uterine therapy (Mirena) - <8 weeks
6.5. Combined injectable therapy, progestin implant (Implanon) - <3 months
6.6. Estrogenic implant (Riselle) or progestin injection (Depo-Provera) - <6 months
7. Use of medications with known effects on vasomotor symptoms such as selective serotonin-norepinephrine reuptake inhibitor (SSRIs), clonidine, gabapentin, tibolone, methyldopa and phytoestrogens in the last 30 days
8. Use of medications with known effects on bone metabolism such as glucocorticoids, gonadotropin-releasing hormone (GnRH) analogues, anticonvulsants, anticoagulants, immunosuppressive drugs, lithium, thyroxine, calcitonin and bisphosphonates within the last year
9. History or suspected uterine cancer, including endometrial hyperplasia and cancer
10. Abnormal genital bleeding unknown cause in the last 6 months
11. History or suspected breast cancer, ovarian cancer or estrogen-dependent neoplasia
12. Suspected mammography changes for breast cancer that require further investigation (simple cysts confirmed by breast ultrasound are be allowed)
13. History of conditions that affect bone metabolism, such as hypogonadism, gastrointestinal disturbances and hyperparathyroidism
14. History of diabetes mellitus (inclusion of patients with controlled diabetes - glycated hemoglobin <8% at screening ¨C is allowed)

15. History of thyroid disease with abnormal thyroid function (except for subclinical hypothyroidism)
16. History of hypertension with systolic blood pressure > 150 mmHg and/or diastolic pressure > 90 mm Hg (patients with hypertension controlled with antihypertensive drugs may be admitted in the study)
17. History of arterial or venous thromboembolic disease, including myocardial infarction, stroke, deep vein thrombosis and pulmonary embolism
18. History of hepatobiliary disease with hepatic enzymes elevation
19. Women smoking more than 20 cigarettes/day
20. History of alcohol or substance abuse
21. Any condition evaluated by medical history, physical examination or screening test (including but not limited to cardiovascular disease, neoplasias, complex ovarian disease, liver disease, kidney disease, blood disease, neurological or endocrine-metabolic disease) which as judged by the investigator, may be inappropriate for inclusion of patients in the study

Date of first enrolment
25/05/2012

Date of final enrolment
01/08/2012

Locations

Countries of recruitment
Brazil

Study participating centre
Rua Josef Kryss, 250
Sao Paulo
Brazil
13209-000

Sponsor information

Organisation
LIBBS Farmaceutica Ltd (Brazil)

ROR
https://ror.org/055kp8612

Funder(s)

Funder type

Industry

Funder Name
Libbs Pharmaceutical Ltd (Brazil)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration