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Sublingual estradiol alone versus oral estradiol with cyproterone acetate for the initial treatment of transgender women seeking gender-affirming-hormonal-therapy

Submission date
12/09/2024

Recruitment status
No longer recruiting

Registration date
16/09/2024

Overall study status
Completed

Last Edited
16/09/2024

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[X] Individual participant data

Plain English summary of protocol

Background and study aims
Gender dysphoria is when a person feels their gender doesn't match the sex they were given at birth. This can cause distress and mental health issues. Treatment helps people live as the gender they identify with, using therapy, hormones, and sometimes surgery. For transgender women (born male), treatment usually combines estradiol (a female hormone) with a drug to block testosterone (a male hormone). The blocking drug can affect sex drive and function, which some patients want to keep. A new method using estradiol under the tongue without a testosterone blocker has become popular online. It claims to give the desired physical changes with less impact on sexual function, but it is unknown if it's safe or effective.

Who can participate?
Transgender women aged between 18 and 45 years old who have not yet received any hormone treatment

What does the study involve?
This 6-month study compares two treatments, with participants choosing their preferred treatment, either the intervention of estradiol 0.5 mg under the tongue four times daily without a testosterone blocker, or the standard treatment of oral estradiol 2 mg once daily with the testosterone blocker, cyproterone acetate 10 mg. The daily estradiol dose is identical in both groups. The participants will undergo regular check-ups and tests to see which method works better for physical changes while maintaining sexual function.

What are the possible benefits and risks of participating?
The new method might help keep sex drive and function while inducing the desired physical changes. In addition, the study will provide participants in both groups with information about the changes in their body composition. The drawback for the new method group is having to take the medication four times daily. No significant risks are expected, but there is a very small chance of blood clots.

Where is the study run from?
Tel Aviv Sourasky Medical Center

When is the study starting and how long is it expected to run for?
August 2021 to August 2023

Who is funding the study?
Tel Aviv Sourasky Medical Center

Who is the main contact?
Prof. Karen Tordjman, karent@tlvmc.gov.il

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Sublingual estradiol alone versus oral estradiol with cyproterone acetate (CPA) for the initial treatment of transgender women seeking gender-affirming-hormonal-therapy (GAHT)- A

prospective pilot study at the Transgender Health Clinic of the Institute of Endocrinology at Tel Aviv Sourasky Medical Center

Study objectives
The hypothesis is that in sublingual estradiol treatment serum concentrations of estradiol will be higher than those in women receiving the same dose of oral estradiol, while testosterone and gonadotropins concentrations will remain higher. It is also anticipated that libido and erectile function will be preserved more often in women treated with sublingual estradiol, while breast development is expected to be comparable in both groups.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 01/08/2021, Helsinki Committee of Tel Aviv Sourasky Medical Center (6 Weizmann Street, Tel Aviv, 6423906, Israel; +972- 052 4262350; anetad@tlvmc.gov.il), ref: 0325-21-TLV

Study design
Single-center open-label non-randomized prospective interventional study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
University/medical school/dental school

Study type(s)
Treatment

Participant information sheet
Not available in web format

Health condition(s) or problem(s) studied
Gender-affirming-hormone therapy in treatment-naive transgender women

Interventions
Self-allocation to the protocol arm by participants to either oral estradiol 2 mg once daily combined with 10 mg of the antiandrogen cyproterone acetate, or 2 mg daily estradiol divided into 4 doses, administered sublingually every 6 hours without the anti-androgen, both for 6 months

Intervention Type
Drug

Pharmaceutical study type(s)
Alternate route of administration

Phase

Not Applicable

Drug/device/biological/vaccine name(s)
Beta-estradiol, cyproterone acetate

Primary outcome measure
Testosterone concentration measured using an electro-chemiluminescence assay (COBAS 6000, e 691 modules,113 Roche, Switzerland), at baseline before treatment, and at the end of the study after 6 months of treatment

Secondary outcome measures
The following secondary outcome measures were assessed at baseline and after 6 months unless stated:
1. Gender dysphoria measured using the Gender Dysphoria and Life Satisfaction (GCLS) questionnaire
2. Libido measured using the Sexual Desire Inventory (SDI) questionnaire
3. Sexual function measured using the International Index of Erectile Function (IIEF) questionnaire
4. Safety measures consisted of an array of biochemical (on an Advia Centaur XP autoanalyzer, Siemens, 110 Germany), hematological (on a Beckman Coulter Counter, IN, USA), and hormonal laboratory (on the Immulite® 2000, Siemens, Germany) variables, drawn at baseline, 3 months, and 6 months
5. Body composition measured using DXA (Lunar Prodigy system, GE Healthcare, Chicago, IL), and by BIA (InBody 770 body composition analyzer, InBody Co., Ltd, Seoul, Korea) at baseline and 6 months

Overall study start date
01/08/2021

Completion date
01/08/2023

Eligibility

Key inclusion criteria
1. Treatment-naive transgender women aged 18 years and older seeking gender-affirming therapy (GAHT), at the Transgender Health Center Clinic within the Institute of Endocrinology and Metabolism at Tel Aviv-Sourasky Medical Center
2. Willing to participate in the study
3. Mentally capable of giving informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
45 Years

Sex
Male

Target number of participants
22

Total final enrolment
22

Key exclusion criteria
1. A history of chronic liver or kidney disease, GFR≤60 ml/min
2. Hypertriglyceridemia>300 mg/dl
3. Primary hypogonadism as evidenced by below-normal serum testosterone and elevated gonadotropins
4. A history of malignancy in the preceding 5 years
5. Use of CYP3A4 inducers (phenytoin, rifampin) or inhibitors (ketoconazole, clotrimazole or retroviral drugs such as ritonavir)
6. Smoking
7. Drug or alcohol abuse
8. Previous history of suicide attempt

Date of first enrolment
07/11/2021

Date of final enrolment
08/06/2022

Locations

Countries of recruitment
Israel

Study participating centre
Tel Aviv Sourasky Medical Center
6 Weizmann Street
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Sponsor information

Organisation

Tel Aviv Sourasky Medical Center

Sponsor details
Institute of Endocrinology and Metabolism, 6 Weizmann Street
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Sponsor type
Hospital/treatment centre

Website
https://www.tasmc.org.il/Internalmed/Endocrinology/Pages/Endocrinology.aspx

ROR
https://ror.org/04nd58p63

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Tel Aviv Sourasky Medical Center

Alternative Name(s)
Ichilov

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Israel

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal

Intention to publish date

13/12/2023

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be published as a supplement to the results publication

IPD sharing plan summary

Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		13/12/2023	13/09/2024	Yes	No
Dataset		13/09/2024	16/09/2024	No	No
Participant information sheet	AI-generated translation from Hebrew		16/09/2024	No	Yes