Subject information for participation to medical scientific research

Progesterone in trans women

Progesterone for Breast Development in Transwomen; analysis of effectiveness and side effects
A pilot study

Introduction

Dear Ms,

We ask you to participate in a medical scientific study. You are receiving this information because you have indicated that you are interested in participating in this survey.

Participation is voluntary. Your written permission is required to participate.
Before you decide whether you want to participate in this study, you will receive an explanation of what the study entails. Read this information carefully and ask the researcher for an explanation if you have any questions.
You can also ask the independent expert named at the end of this letter for additional information.
You can also talk about it with your partner, friends or family.
You will be given 10 working days to decide whether to participate in this study.
Further information about participating in such a survey can be found on the website of the national government: www.rijkdsoverheid.nl/mensenonderzoek.

1. General information

This research is being done by Amsterdam UMC, location VUmc, and supported by Besins Healthcare, the producer of progesterone. 90 subjects were used for this study required.

The medical-ethical review committee of Amsterdam UMC, location VUmc, has approved this research. General information about the assessment of research can be found in the brochure 'Medical scientific research'.

2. Purpose of the study

The aim of this study is to find out what the effect of the hormone progesterone is when it is added to the treatment with estradiol in trans women. We want to measure whether breast size changes with the use of progesterone and we also want to investigate the safety of progesterone. We compare the effect and safety of progesterone with the effect and safety of treatment with estradiol alone. The combination of

estradiol and progesterone is already used by women with menopausal symptoms. The results of this research will be used for follow-up research.

3. Background of the study

Trans women (born male, female gender identity) are treated with gender-affirming hormone treatment. The purpose of this is to induce female sexual characteristics such as breast formation. After the gender-confirming surgery (vaginaplasty or orchiectomy (testicular removal)), hormone treatment with estradiol also serves to prevent menopausal symptoms. Many trans women find the degree of breast development from the use of estradiol disappointing. In cis women, the hormone progesterone also plays a role in breast development. To date, no scientific research has been conducted into the possible effect of progesterone and estradiol on breast formation, nor into the possible side effects of this treatment. In this study, we want to

to investigate the expected effects of a combination hormone treatment in persons after the gender confirmation surgery.

4. What it means to participate

If you join, it will take you about 12 months in total.

Eligibility Survey

During the first visit we determine whether you can participate. The examiner will measure your weight, height, blood pressure and heart rate, and blood tests will be performed. The examiner will also ask about your medical history.

Therapy

You will be using the study treatment for 12 months. The participants are divided into six groups, which receive different treatment. Four groups receive estradiol and progesterone in different doses, two groups are treated with estradiol and no progesterone. In the subjects in one of these groups, the dose of the estradiol is increased. So there is a group in which the hormone treatment is not adjusted, this is called a control group. The draw determines which treatment you will receive.
General information about this can be found in the brochure 'Medical scientific research'.

Visits and measurements

For the examination it is necessary that you come to the outpatient clinic four times in 12 months: at the start of the study treatment, after approximately 3 months, 6 months and after 12 months. A visit takes about one to one and a half hours. Treatments will then take place according to standard care and additional actions within the framework of this investigation.

Standard care:
- We discuss how you are doing and whether you have any health problems.
- We measure your weight, height, blood pressure and heart rate.

- We take blood on three visits, two tubes at a time. This is, among other things, to see if progesterone is properly absorbed into your blood. We also measure cholesterol to check whether there are side effects of the treatment.

Additional actions:

- At each visit, we ask you to complete a questionnaire about satisfaction with your breasts, your mood and whether you sleep well.
- At every visit 3D measurements are taken of your breasts.

Different from usual care

Normally, you may see your doctor for a checkup once a year or two. The visits associated with this investigation replace these normal visits.
In addition, two extra actions take place in the form of a questionnaire and 3D measurements.

5. What is expected of you

In order for the examination to run smoothly, it is important that you adhere to the following agreements.

The agreements are that you:

- takes the study treatment according to the explanation.
- does not also participate in another medical scientific study.
- keep appointments for visits.

It is important that you contact the researcher:

- before taking any other medicines. Even if that homeopathic medicines, natural medicines, vitamins and/or medicines from the drugstore.
- if you are hospitalized or treated.
- if you suddenly develop health problems.
- if you no longer wish to participate in the study.
- if your contact details change.

6. Possible Side Effects

Treatment with progesterone and also changing the dose of estradiol can cause common side effects such as headaches and breast tenderness. The chance that serious side effects will occur is very small and probably no higher than with hormone use in general.
Other possible rare side effects of the combined treatments include: nausea, drowsiness, mood changes, vomiting, constipation, fluid retention, jaundice, itching and acne. Please let us know if you experience these side effects.

A rare but important side effect of estradiol and/or progesterone is thrombosis (a blood clot in a vein) or pulmonary embolism (a blood clot in the lung):

You should contact the examiner immediately if you experience: a thick leg, or legs, or sudden shortness of breath

The treatment under investigation may also have side effects that are as yet unknown.
Are you participating in the study? Then you will receive the package leaflet with the medicine.

Measurements

Blood draws may hurt or cause bruising. All in all, we will draw 8ml of blood from you three times. This amount corresponds to the amount of blood collected during a normal check-up visit. For comparison: 500 ml of blood is taken at a time at the blood bank.

7. Potential Pros and Cons

It is important that you carefully consider the possible advantages and disadvantages before you decide to participate to do.

The study treatment may lead to an increase in breast size, but it is certain not.

Disadvantages of participating in the study may be

- possible side effects of the hormone treatment change
- possible inconveniences of the measurements in the study.

Participation in the study also means:

- that you have lost extra time;
- (additional) testing;
- that you have agreements that you must keep;

All these matters have been described above under points 4, 5 and 6.

8. If you don't want to participate or want to stop the study

You decide whether you want to participate in the study. Participation is voluntary.
If you do not want to participate, you will receive the usual follow-up appointments at the outpatient clinic.

If you do participate, you can always change your mind and stop anyway, even during the study.
You don't have to say why you're stopping. You must report this immediately to the researcher.
The data collected up to that point will be used for the research.

If there is new information about the study that is important to you, let the researcher this to you. You will then be asked if you want to continue participating.

9. End of the investigation

Your participation in the study will end if

- all visits as described under point 4 are over
- you choose to stop
- the researcher thinks it's better for you to stop
- the government or the reviewing medical-ethical review committee decides to to stop research.

The entire study ends when all participants are ready. In principle, the progesterone that you may have used during the study will not be available after the study. The attending physician will discuss the options for further medical care with you.

After processing all the data, the researcher will inform you about the most important results of the study. This will happen approximately 6-12 months after your participation.

10. Use and storage of your data and body material

Your personal data will be collected, used and stored for this research. This concerns data such as your name, address, date of birth and data about your health.
Blood is needed for this test. In addition, 3D photos of your breasts are required for this examination. The collection, use and storage of your data, your body material and the 3D photos is necessary to answer the questions asked in this research and to be able to publish the results. We ask your permission for the use of your data, blood and 3D photos.

Confidentiality of your data and body material
To protect your privacy, your data is given a code. Your name and other information that can directly identify you are omitted. Data can only be traced back to you with the key of the code. The key of the code remains safely stored at the VUmc. The data is also not available to you in reports and publications about the research traceable.

Access to your data for control Some people can access all your data in the VUmc. Also to the data without code. This is necessary to be able to check whether the research has been carried out properly and reliably. Persons who have access to your data for control purposes are: the committee that monitors the safety of the research, a monitor who works for the researcher, national and international supervisory authorities, for example, the Health and Youth Care Inspectorate. They keep your data secret. We ask you to give permission for this inspection.

Data retention period Your data must be stored at the VUmc for 25 years. Your body material (blood) will be destroyed immediately after use.

Retention and use of data for other research

After this study, your data may also be important for other scientific research in the field of hormone treatment for transgender people. We ask for your permission to be able to approach you again after the study, for example for a follow-up study. For this, your data will be stored for 25 years. You can indicate on the consent form whether or not you agree to this.

If you do not agree with this, you can simply participate in the current study.

Information about unexpected findings

During this research, something may accidentally be found that is not important for the research, but is important for you. If this is important for your health, you will be informed by your treating physician. You can then discuss what needs to be done with your GP or specialist. You also give permission for this if you participate

to this study.

Withdraw permission

You can always withdraw your consent for the use of your personal data. This applies to this study as well as to storage and use for future research. The research data collected up to the moment you withdraw your consent will still be used in the research.

More information about your rights when processing data

For general information about your rights when processing your personal data, you can consult the website of the Dutch Data Protection Authority.

If you have any questions about your rights, please contact the person responsible for processing your personal data. For this study, that is:

Amsterdam UMC, location VUmc. See Appendix A for contact details.

If you have any questions or complaints about the processing of your personal data, we recommend that you first contact the researchers. You can also contact the Data Protection Officer of the institution or the Dutch Data Protection Authority.

11.Insurance for test subjects

An insurance policy has been taken out for everyone who participates in this study. The insurance covers damage caused by the investigation. Not all damage is covered. In Appendix B you will find more information about the insurance and the exceptions. It also says who you can damage
report.

12.Inform the GP

We always send your GP a letter to let you know that you are participating in the study.
This is for your own safety. If you don't like this, you can't join this
research.

13. Compensation for participating

The study treatment for the study will not cost you anything. For participating in this study you will receive an expense allowance (excluding parking and travel costs) of €50 per visit.

14.Do you have any questions?

If you have any questions, please contact the research team. For independent advice about participating in this study, you can contact the independent doctor. She knows a lot about it
research, but has nothing to do with this research.
If you have any complaints about the study, you can discuss this with the researcher or your attending physician. If you prefer not to do this, you can contact the complaints officer of Amsterdam UMC, location VUmc. All details can be found in **Appendix** A: Contact details.

15.Signing consent form

You will have a cooling-off period of 10 working days. When you have had sufficient reflection time, you will be asked to decide whether to participate in this study. If you give permission, we will ask you to confirm this in writing on the accompanying statement of consent. By your written consent you indicate that you have understood the information

and consent to participate in the study.
Both you and the researcher will receive a signed version of this consent form.

Thank you for your attention.

16.Appendices to this information

A. Contact details B.
Information about the insurance
C. Consent form(s)

Appendix A: contact details for Amsterdam UMC, location VUmc

Executive researchers

Lead researcher

Prof. dr. dr. M. den Heijer:

Knowledge and Care Center for Gender Dysphoria/ Department of Internal Medicine
De Boelelaan 1117

1081 HV Amsterdam

Coordinating researcher:

dr. KMA Dreijerink

Knowledge and Care Center Gender Dysphoria/ Department of Internal Medicine
De Boelelaan 1117

1081 HV Amsterdam

020-4440542 during office hours, outside office hours for urgent medical questions 020-4444444, questions to the internist on duty E-mail address: progesteronstudie@amsterdamumc.nl Study phone: +31 6 83950898

Independent physician:
Dr. EB Conemans

Knowledge and Care Center Gender Dysphoria/ Department of Internal Medicine
De Boelelaan 1117

1081 HV Amsterdam

020-4440542

Complaints and questions about data protection:

Zorgsupport
De Boelelaan 1117

1081 HV Amsterdam

020-4443590

E-mail address: secretariaat.Zorgsup@vumc.nl

You can also contact: The Data Protection Officer via

privacy@vumc.nl The Dutch Data Protection Authority via https://

autoriteitpersoonsgegevens.nl/

Appendix B: information about the insurance

The sponsor has taken out insurance for everyone who participates in this research.
The insurance covers damage caused by participating in the study. This applies to damage during the study or within four years after the end of your participation in the study. You must have reported damage to the insurer within those four years.

The insurance does not cover all damage. At the bottom of this text is a brief description of which damage is not covered.
These provisions are contained in the Compulsory Insurance Decree for medical research involving humans. This decision can be found on www.ccmo.nl, the website of the Central Committee on Research into Human Subjects (see 'Library' and then 'Laws and regulations').

In the event of damage, you can contact the insurer directly.

The insurer of the investigation is:	
Name:	Centramed
Address:	Maria Montessorilaan 9, 2919 DB Zoetermeer
Phone number: 070-3017070	
E-mail:	info@centramed.nl

The insurance offers cover of €650,000 per test subject and €5,000,000 for the entire study and €7,500,000 per year for all studies by the same client.

The insurance does **not cover the following damage:**

ÿ damage from a risk of which you have been informed in the written information. This does not apply if the risk is more serious than anticipated or if the risk is very serious was unlikely;

ÿ damage to your health that would also have occurred if you had not benefited from the study participated;

ÿ damage caused by not (fully) following directions or instructions;

ÿ damage to your offspring, as a result of a negative effect of the research on you or your descendants;

ÿ damage caused by an existing treatment method in research into existing treatment methods.

Appendix C: Subject Consent Form

Progesterone in trans women

- I have read the information letter. I could also ask questions. My questions have been sufficiently answered. I had plenty of time to decide whether to participate.
- I know that taking part is voluntary. I also know that I can decide at any time not to participate or to stop the study. I don't need a reason for that to give.
- I give permission to inform my GP that I am participating in this research
- I give permission for the making, use and storage of 3D photos of my breasts
- I give permission for the collection and use of my data/blood samples to answer the research question in this study. The data is stored for 25 years.
- I know that for the purpose of auditing the investigation, some people may have access to all my data. These people are listed in this information letter. I give permission for that access by these persons.
- I give permission for my general practitioner and/or treating specialist to be informed of unexpected findings that are (or may be) important for my health.
- I give ÿ **well**

  ÿ **none**

  consent to keep my personal data longer and use it for future research into hormone treatment in transgender people
- I give ÿ **well**

  o ÿ **none**

  permission to use the 3D photos of my breasts for other research. The data is stored for 25 years.
- I give ÿ **well**

  ÿ **none**

  permission to contact me again after this study for a follow-up study.
- I want to participate in this research.

Subject Name:

Signature: Datum : __ / __ / __

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I declare that I have fully informed this subject about the above research.

If information becomes known during the study that could influence the subject's consent, I will inform him/her in good time.

Name of researcher (or his representative):

Signature: Datum: _ / _ / _

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<if applicable>

Additional information is provided by:

Name:

Function:

Signature: Datum: _ / _ / _

.....

The subject receives a complete information letter, together with a signed version of the consent form.