I. Patient information

Trial subject information for participation in medical-scientific research

MUSA-MYOVASC study

Ultrasound characteristics of fibroids concerning non-operative treatment

Introduction

Dear Madam,

You are asked to take part in a medical-scientific research. Participation is voluntary and requires your written consent. You received this letter because you were diagnosed with fibroids.
This letter explains what the study implies. Please read this information carefully and contact the investigator if you have any questions. You can also ask the independent expert, who is mentioned at the end of this document, for additional information. You may also discuss it with your partner, friends or family.
Additional information about participating in a study can be found on the website of the national government: https://www.rijksoverheid.nl/onderwerpen/medisch-wetenschappelijk-onderzoek.

1. General information

This research is being carried out by the VU University Medical Center (VUmc). Samsung® and VUmc reimburse the costs of this study.

The Medical Research Ethics Committee of the VUmc has approved this research. General information about the assessment of research can be found in the general brochure on medical research (attachment D).

2. Purpose of the study

The purpose of this study is to determine whether the blood flow of the fibroid is related to the growth of the fibroid, the menstrual blood loss and other complaints. The blood flow of the fibroid is measured by three dimensional (3D) ultrasound. We investigate this blood flow and growth relation for different fibroid treatments.

3. Background of the study

Fibroids are benign tumors growing from the uterine muscle. Fibroids are a common problem; 20-30% of women in the reproductive age have fibroids. Fibroids cause pain during menstruation and in the lower abdomen, which can interfere with your daily activities. The growth rate of fibroids, as well as the difference in fibroid growth rate between women, is currently unknown. There are four treatment options; medication with or without hormones, (minimally) invasive techniques performed by the

radiologist, or an operation. Little is known about the influence of these treatments on the fibroids size, as not much research has yet focused on this topic. Blood flow seems to play an important role and can be measured using three dimensional (3D) ultrasound. The amount of measured vessels is expressed as a number, the "vascular index". We have already investigated the "vascular index" in a smaller study in the VUmc, which showed a higher "vascular index" (so more blood flow) predicted a higher fibroid growth rate then a lower "vascular index". The study population consisted of women without treatment. It is important to re-assess these results in relation to the different therapies. We need to include 760 women in total, more or less 200 women per treatment option. As a result of this study, we hope to be able to inform women better about the expected fibroid growth rate and the advised treatment.

4. What participation involves

The tests in the context of the 'MYOVASC' study (research) are standard care, only some questionnaires are extra (research). Your participation will last about 2 years.

Regular outpatient visits and tests (standard care)

- *Transvaginal ultrasound:* first visit, after 3 months and after 1 year.
- *Taking a blood sample to measure your hemoglobin:* first visit, after 3 months and after 1 year. Measurement of hemoglobin can trace anemia.
- *Menstrual blood loss assessment chart and fibroid-specific quality of life questionnaire:* first visit and after 3 months.
- *In case of an ablation (such as MR-HIFU or Sonata) or embolization therapy: also after 6 months a transvaginal ultrasound and a blood sample to measure your hemoglobin.*

Extra tests in the context of the 'MYOVASC' study (research)

- *Questionnaires:* first visit, and after 3 months, 1 and 2 years. A questionnaire takes about 5 to 15 minutes.
- *In case of an ablation (such as MR-HIFU or Sonata) or embolization therapy: also after 6 months an extra questionnaire.*

5. What is expected of you

In order to carry out the study properly, it is important that you follow the study instructions.

The study instructions:
• If you and your doctor decide to start medication as a treatment for the fibroids, this therapy is the most effective if you follow the instructions of your doctor. In this way all women will use the treatment in the same way, this makes our study reliable.

• It is important for the accuracy of our results that you will be present at all visits, please let us know in case you are unexpectedly not able to attend, so we can reschedule your appointment. Research does take a lot of time, we appreciate your time and cooperation.

It is important that you contact the investigator:
• If there is a change in the treatment of your fibroid during the course of the investigation. For example, stopping medication or starting with it.
• Before using ‘blood thinners’, ‘tamoxifen’ or ‘aromatase inhibitors’. Tamoxifen and 'aromatase inhibitors' are often given in case or a history of breast cancer.
• If you are admitted to hospital and/or treated for a serious illness.
• If you are pregnant.
• If you no longer wish to participate in the research.
• If your contact details change.

Pregnancy
Women who are pregnant or give breastfeeding cannot participate in this research. The hormones during pregnancy or breastfeeding have influence on the fibroids, and therefore on the measurements. Perhaps we can investigate this in the future.

6. Possible inconveniences

The study cannot give rise to any negative side effects. Possible inconveniences you may experience is the time the study takes because of the questionnaires you fill in extra. The transvaginal ultrasound and blood sample are standard care. Moreover, the choice of fibroid treatment is not influenced by the study, this choice you make with your doctor.

7. Possible (dis)advantages

It is important that you carefully consider the possible pros and cons before you decide to participate. Please take your time to come to your decision. We often send you this information before you have your appointment. In case you need more time to decide or have any questions, just tell the researcher or your doctor. We will only include your data after you have provided written permission.

You will not personally benefit from participation in this study. If you participate in this study, it does not mean that the fibroids disappear or give less complaints. Some women prefer a more frequently checkup of their complaints. Then, a possible benefit is the extra questionnaire. Your participation may contribute to increased general knowledge about fibroids and the best treatment.

A disadvantages of participating in this study may be the inconvenience of the time investment because of the questionnaires (see heading: "6. Possible inconveniences").

8. If you do not want to participate or you want to stop participating in the study

It is up to you to decide whether or not to participate in the study. Participation is voluntary. If you do not want to participate, you will be treated according to standard care for your fibroid(s).

If you do participate in the study, you can always change your mind and decide to stop, at any time during the study. You will then be treated according to standard care for your fibroid(s). You do not have to say why you are stopping, but you do need to inform the investigator. It may be interesting to know why you no longer want to participate, because of the possible consequences for the interpretation of the study results.The data collected until that time will still be used for the study.

If there is any new information about the study that is important for you, the investigator will let you know. You will then be asked whether you still want to continue your participation.

9. End of research

Your participation in the study stops when
• All visits are completed
• You choose to stop yourself
• You become pregnant
• You get a surgical treatment
• Your hospital, the government or the Medical Research Ethics Committee, decides to stop the study.

The study is concluded once all the participants have completed the questionnaire 2 years after the intake. After processing the data, the investigator will inform you about the most important results of the study.This will be about 5 years after your participation.

Moreover, you can decide whether we may contact you for longer follow-up after this study. At this moment we do not know the exact content of this possible follow-up yet. An example may be that we will ask you again about your complaints by a questionnaire after several years.

10. Use and storage of your data and bodily material

For this study we require analyses and collection of medical records. Every participant receives a code which is written on your records. Your name and other personal records will be deleted. The code itself is not traceable to the result of the blood sample.

Your data
All your personal and medical records remain confidential. Only the treatment and research team

know which code you have. The key to your personal code remain confidentially within those teams. Research reports also use this personal code and not your name.

Some people are authorized to evaluate your medical and personal information. The purpose is to verify whether the research has been carried out properly and reliably. General information can be found on the website of the general government.

People who can access your records are: the treatment and research team, a controller who monitors the study and the Health Care Inspectorate. They keep your data confidential. By signing the consent statement, you consent to collecting, storing and reviewing of your medical and personal information.

The researcher keeps your records for 15 years.

Your body material
Your blood sample is stored in our hospital according to the standard protocol, this is independent of the MYOVASC study.

11. No participants' insurance

If you participate in this study, we do not expect you to suffer from additional risks. The VUmc has permission of the Medical Research Ethics Committee not to conclude an insurance.

12. Compensation to participate

The additional tests or visits which are not standard care are free of charge, there are no consequences for your own risk. You will not be paid for your participation in this research. You will be reimbursed for your extra travel costs.

13. Any questions?

If you have any questions, please contact the investigator. If you would like any independent advice about participation in this study, you may contact an independent doctor. He knows about the study but is not involved in it.

If you have any complaints about the study, you may contact the committee handling complaints of this hospital. All relevant details can be found in **Attachment A**: Contact Details.

14. Sign permission form

When you have had sufficient time for reflection, you will be asked to decide on participation in this study. Please take your time to decide, in case you need more time to decide or have any questions, just tell the researcher or your doctor. If you give permission, we will ask you to confirm this in writing on the appended consent form. By your written permission you indicate that you have understood the information and consent to participation in the study. Both yourself and the investigator will receive a signed copy of the consent form.

Thank you for your attention.

15. Attachments to this information

A. Contact details
B. Schedule follow-up
C. Permission form(s)

Attachment A: Contact details Amsterdam UMC, location VUMC and location AMC

Principal Investigator:
Prof. Dr. Judith Huirne, Gynecologist.

Researcher:
Drs. Marissa Frijlingh, PhD.
Email: *info@myovasc.nl*

Independent specialist:
Dr. Velja Mijatovic, Gynecologist.

Contact Amsterdam UMC location VUmc:
Women's Clinic secretary office
Telephone number: 020-5663754
Address: Amsterdam UMC, location VUmc | ZH 8F 028 | De Boelelaan 1117 | 1007 MB Amsterdam

Contact Amsterdam UMC location AMC:
Women's Clinic secretary office
Telephone number: 020-5663754
Email: *gyn_benigne@amc.nl*
Address: Amsterdam UMC, location AMC | H4-230 | Meibergdreef 9 | 1105 AZ Amsterdam

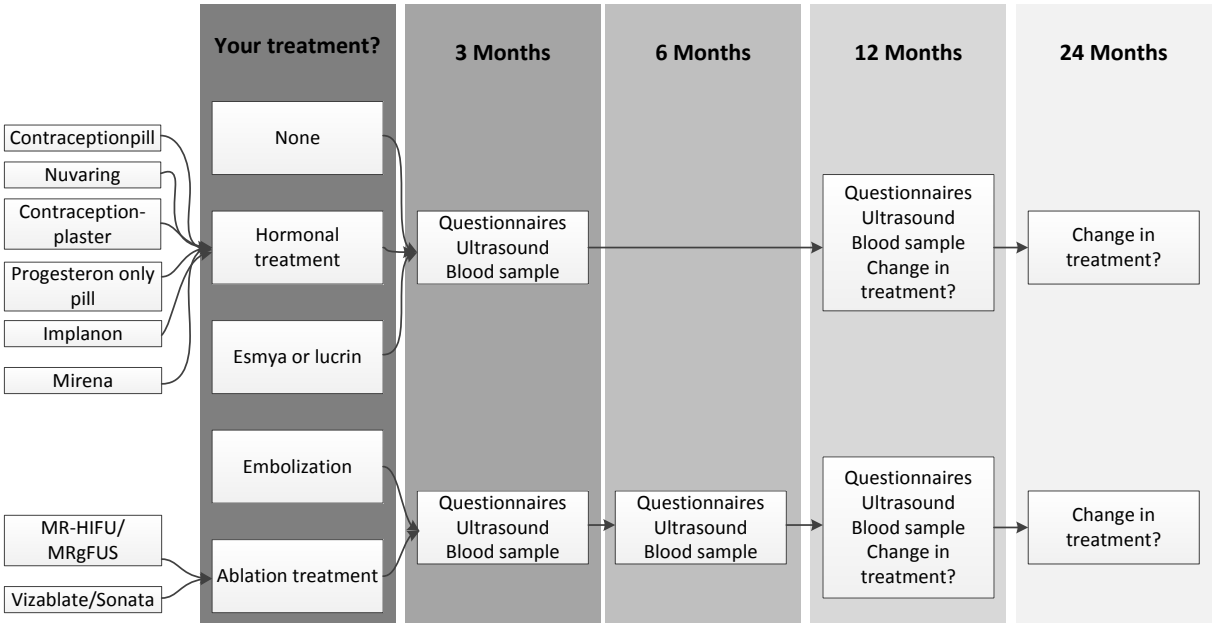
Complaints:
If you have any complaints about the study, please contact your treating physician or the researcher. In case you wish not to, you mail to *klachten@amsterdamumc.nl* or you can contact: 'Patiëntenvoorlichting en Klachtenopvang' (Patient Advice and Liaison Service; 9.00-15.30 hour) | 020-5663355 (location AMC) | Outpatient clinic building A0-144 | P.O. box 22660 | 1100 DD Amsterdam
Or 'Servicecentrum patiënt & zorgverlener VUmc' (Service centrum patient & health care worker VUmc; 9.00-16.30 hour) | 020-4440700 (location VUmc) | PK 0 Hal 08 | Postbus 7057 | 1007 MB Amsterdam

For additional information on your rights with respect to the use of your personal data, general information can be found the website of the Amsterdam UMC: *https://www.amc.nl/web/ik-heb-een-afspraak-1/rechten-en- plichten/patientenvoorlichting/privacystatement-voor-patienten-bezoekers-en-deelnemers- aan-onderzoeken.htm*

For general information on your rights with respect to the processing of your data you can consult the website of the Dutch Data Protection Law at: *https://autoriteitpersoonsgegevens.nl*

For questions or complaints about the use of your personal data, please contact the researcher or the privacy officer by email: *fg@amc.nl* or *privacy@vumc.nl.*

Attachment B: schedule of follow-up



Attachment C: Trial permission form

MUSA-MYOVASC study

Ultrasound characteristics of fibroids concerning non-operative treatment

- I have read the subject information letter. I was able also to ask questions. My questions have been answered answered to my satisfaction. I had enough time to decide whether to participate.
- I know that participation is voluntary. I know that I may decide at any time not to participate after all or to withdraw from the study. I do not need to give a reason for this.
- I know that some people may have access to all my data to verify the study. These people are listed in this information sheet. I consent to the inspection by them.
- I give permission for the collection and use of my data and blood to answer the research question in this study.
- I give permission to keep my records on the location where the study is performed for 15 years after this research.

- I do □ give permission
  □ **Not** consent to being contacted again after this study for a follow-up study.

Name of study subject:
Signature: Date: __ / __ / __

I hereby declare that I have fully informed this study subject about this study.

If information comes to light during the course of the study that could affect the study subject's consent, I will inform him/her of this in a timely fashion.

Name of investigator (or his/her representative):
Signature: Date: __ / __ / __

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* Delete as appropriate.

The study subject will receive the full information sheet, together with a signed copy of the consent form.