Information for participants about taking part in medical-scientific research

What is the role of immune cells in the kidney in lupus nephritis (LN)?

The role of macrophages and monocytes in (proliferative) lupus nephritis; the MAPLE study

Introduction

Dear Sir/Madam,

With this information letter, we would like to ask if you want to take part in medical-scientific research. Taking part is voluntary. You are receiving this letter because you have systemic lupus erythematosus (SLE).

This letter explains what the study is about, what it means for you, and what the advantages and disadvantages are. It is a lot of information. Please read it carefully and decide whether you want to take part. If you want to take part, you can fill in the form in appendix C.

Please ask your questions

You can make your decision based on the information in this letter. We also advise you to do the following:

- Ask the researcher who gives you this information any questions you have.
- Talk with your partner, family, or friends about this study.
- Read the information at www.rijksoverheid.nl/mensenonderzoek.

1. General information

Amsterdam UMC set up this study. Below, we always call Amsterdam UMC the ‘sponsor’. Researchers – these can be doctors, researchers, and research nurses – carry out the study. The study takes place at the AMC location of Amsterdam UMC.
People who take part in medical-scientific research are often called ‘subjects’. Both patients and healthy people can be subjects. This study needs a total of 30 LN subjects, 15 SLE subjects, and 10 healthy subjects. The Medical Ethics Review Committee of Amsterdam UMC has approved this study.

2. What is the purpose of the study?

The purpose of the study is to find out what role specific immune cells play in the start and continuation of LN. We want to look at how many of these cells are present in the kidney before and after treatment. We also want to look at whether changes in the immune cells affect the patient’s health. In addition, we want to check whether certain immune cells can be found in the blood or urine. This may help us detect or monitor LN better in the future.

3. What is the background of the study?

Systemic lupus erythematosus (SLE) is an autoimmune disease that can affect all organs in the body. An autoimmune disease is a disease in which the immune cells attack the body itself, causing inflammation and damage. Normally, immune cells protect the body against germs from outside.

When SLE causes inflammation in the kidneys, we call this LN. Possible effects of LN are loss of protein and blood cells in the urine, high blood pressure, loss of kidney function, and eventually even kidney failure. It is still not fully known what exactly goes wrong in the kidney in LN.

Recent research shows that macrophages, a type of immune cell, play a role in the development of LN. What we do not yet know is exactly which macrophages are present in the kidney and how this changes during treatment. We also do not know exactly how they affect the outcome of treatment.

LN is diagnosed by taking a small piece of the kidney (a kidney biopsy). This must be done before treatment starts. To treat LN better, it is important to understand more about what happens to the immune cells in the kidney. Kidney biopsies and blood and urine values that have already been taken could help with this. For this reason, a second kidney biopsy will be taken 3 months after the start of treatment for this study.

At the moment, there are several treatments for LN. For a long time, treatment with 2 medicines (prednisolone and mycophenolate mofetil, from here on shortened to MMF) was standard. Recently, a third medicine, voclosporin, is sometimes added. We suspect that voclosporin specifically blocks the macrophages in the kidney and may give a better result for some patients. However, using more medicines also increases the risk of side effects.
In daily practice, your doctor decides which treatment is best for you. At the moment, there is no clear preference for one treatment plan over the other. For this study, the choice between treatment with prednisolone and MMF, or treatment with prednisolone, MMF, and voclosporin, will be decided by a random draw (like drawing lots). This is needed so we can look as clearly as possible at the effects of treatment on the immune cells.

4. How does the study work?

How long does the study last?
If you take part in the study, extra blood will be taken on 2 occasions, and you will hand in urine on 2 occasions. These moments are about 3-6 months apart, and are combined with your regular check-ups at the outpatient clinic.

Step 1: are you eligible to take part?

After your treating doctor has given you information about the study and you are interested in taking part, one of our researchers will give you detailed information by phone. During your visit to Amsterdam UMC, you will sign to take part.

First, we check whether you can take part in the study. For this, your doctor will ask you a number of questions and take blood, as usual before your appointment at the outpatient clinic. Based on these results, the researcher decides whether you can take part. If you have an infection, unfortunately you cannot take part.
If you take part, you will get containers for urine. Extra blood will also be taken during the usual blood checks.

Step 2: blood and urine tests
For the study, you do not need to come to the hospital at extra times. During your normal outpatient appointments with your doctor, the following tests will be done (for the study):

- Blood sample. For the study, 9 extra tubes of blood will be taken at the first appointment, and 7 tubes at the blood draw 3 months later. In total, this is 67 ml the first time and 59 ml the second time. This amount does not cause problems in adults. For comparison: someone who donates blood at the blood bank gives 500 ml each time.
    - With the blood test, we check for the presence of specific immune cells.
- Urine sample. You bring the urine to your outpatient appointment on 2 occasions, in the containers given to you earlier.

What is different from regular care?
In principle, nothing changes for you compared to regular care. At two outpatient appointments, extra tubes of blood (see above) will be taken. You will not need an extra needle prick for this: the extra tubes are taken together with the tubes for your check-up appointment. You will also be asked to hand in urine twice.

5. What arrangements do we make with you?

We want the study to go well. That is why we make the following arrangements with you:

- You come to your outpatient appointments.
- You hand in the urine in the containers you were given.
- You may keep taking your prescribed medication as usual. If in doubt, discuss this with your treating doctor or the researcher.

You contact the researcher in these situations:

- You no longer want to take part in the study.
- Your phone number, address, or e-mail address changes.

6. What side effects, harmful effects, or discomfort can you experience?

What discomfort can measurements during the study cause?
Blood draws can be painful or cause bruising. At every visit, as part of regular care, blood is already taken from you. For the study, this will be 59-67 ml extra on 2 occasions. This amount does not cause problems in adults. For comparison: at the blood bank, 500 ml of blood is taken each time. You do not need to fast before a blood draw.

7. What are the advantages and disadvantages of taking part in the study?

Taking part in the study can have advantages and disadvantages. We list them below. Think about this carefully, and talk about it with others.

Taking part in this study does not mean your disease will go away. But by taking part, you help the researchers gain more insight into how SLE and lupus nephritis develop and are treated.

Taking part in the study can have these consequences:

- Taking part in the study costs you extra time.
- You must keep to the arrangements that belong to the study.

Do you not want to take part?
You decide for yourself whether you take part in the study. If you do not want to take part, you will not need to hand in extra urine or have extra tubes of blood taken.

8. When does the study stop?

The researcher will let you know if new information about the study becomes known that is important for you. The researcher will then ask if you want to continue taking part.

In these situations, the study stops for you:

- All samples according to the schedule have been taken.
- You want to stop the study yourself. You may do this at any time. Tell the researcher right away. You do not need to say why you are stopping.
- The researcher thinks it is better for you to stop.
- One of the following bodies decides that the study must stop:
    - the sponsor (Amsterdam UMC)
    - the government, or
    - the medical ethics committee reviewing the study.

What happens if you stop the study?

The researchers use the data and body material (blood and urine) collected up to the moment you stop. If you want, collected body material can be destroyed. Let the researcher know if you want this.

The whole study is finished once all participants are done.

9. What happens after the study?

Will you get the results of the study?
About 2 years after the study ends, the researcher will let you know the main results of the study. If you do not want to know this, tell the researcher. He/she will then not tell you.

10. What do we do with your data and tissue?

If you take part in the study, you also give permission to collect, use, and store your data and body material.

Which data do we store?
We store this data:

- your name
- your sex
- your address
- your date of birth
- data about your health
- (medical) data we collect during the study

Which body material do we store?
We collect, use, and store tubes of blood and urine.
Why do we collect, use, and store your data and body material?
We collect, use, and store your data and body material to answer the questions of this study, and to publish the results. Data and/or body material can be used by the sponsor and by companies that help the sponsor carry out the study.

How do we protect your privacy?
To protect your privacy, we give your data and body material a code. Only this code is put on all your data and body material. The key to the code is kept in a secure place in the hospital. When we process your data and body material, we always use only this code. In reports and publications about the study, no one will be able to trace this back to you.

Who can see your data?
Some people can see your name and other personal data without the code. This may be data collected specially for this study, but also data from your medical file.

These are people who check whether the researchers carry out the study properly and reliably. These people may have access to your data:

- An auditor who works for the sponsor.
- National and international regulatory authorities.

These people keep your data confidential. We ask your permission for these people to view your data. The Health and Youth Care Inspectorate (Inspectie Gezondheidszorg en Jeugd) can view your data without your permission.

How long do we store your data and body material?
We store your data for up to 25 years after the study ends, at the hospital. We also store your body material at the hospital. It is stored for up to 5 years after the study ends, so that new tests related to this study can still be done during that time. As soon as this is no longer needed, we destroy your body material.

What happens with unexpected findings?
During the study, we may accidentally find something that is not directly relevant to the study, but is relevant to your health. The researcher will then contact your specialist. You will then discuss with your specialist what needs to happen. The costs of this are covered by your own health insurance. With the form, you give permission to inform your specialist.

Can you withdraw your permission to use your data?
You can withdraw your permission to use your data at any time. Tell the researcher if you want this. This applies to use in this study and to use in other research. Please note: if you withdraw your permission, and the researchers have already collected data for a study, they may still use this data. For your body material, the researchers will destroy it after you withdraw your permission. But if measurements have already been done with your body material, the researcher may still use those results.

Do you want to know more about your privacy?

- Do you want to know more about your rights regarding the processing of personal data? Go to www.autoriteitpersoonsgegevens.nl.
- Do you have questions about your rights, or a complaint about the processing of your personal data? Contact the person responsible for processing your personal data. For your study, this is:
    - Amsterdam UMC. See appendix A for contact details and website.
- If you have complaints about the processing of your personal data, we advise you to discuss this first with the research team. You can also go to the Data Protection Officer of Amsterdam UMC, or file a complaint with the Dutch Data Protection Authority (Autoriteit Persoonsgegevens).

Where can you find more information about the study?

You can find more information about the study on the following website(s): www.onderzoekmetmensen.nl and/or https://euclinicaltrials.eu. After the study, the website may show a summary of the results. You can find the study by searching for ‘MAPLE study’.

11. Will you get paid for participating in the study?

The study medicines and extra tests for the study cost you nothing. For taking part in this study, you will not get a payment.

12. Are you insured while taking part in the study?

An insurance policy has been taken out for everyone taking part in this study. The insurance pays for damage caused by the study, but not for all damage. Appendix B has more information about the insurance and its exceptions. It also states who to contact if you have any damage to report.

13. We will inform you GP, treating specialist and pharmacist

The researcher will send your GP, treating specialist, and pharmacist a letter or e-mail to let them know you are taking part in the study. This is for your own safety. In case of unclear situations or questions, we may contact your doctor – for example, about your medical history or the medicines you use.

14. Do you have questions?

You can ask questions about the study to drs. S.D. Crum or dr. M. Hilhorst.
Do you have a complaint? Discuss this with the researcher or the doctor treating you. Would you rather not do this? Then go to the hospital’s complaints officer. Appendix A tells you where to find them.

15. How do you give consent for the study?

You can first take time to think calmly about this study. Please take at least 2 days for this. Afterwards, tell the researcher whether you understand the information, and whether or not you want to take part. If you want to take part, fill in the consent form that comes with this information letter. You and the researcher will both get a signed copy of this consent statement.

Thank you for your time.

16. Appendices

A. Contact details for Amsterdam UMC

B. Information about the insurance

C. Consent form(s)

Appendix A: contact details for Amsterdam UMC

Drs. S.D. Crum, physician-researcher, Department of Internal Medicine – Nephrology. Meibergdreef 9 | 1105 AZ Amsterdam | The Netherlands. Tel: 020-5663195 | E-mail: s.d.crum@amsterdamumc.nl

Principal investigator (2nd point of contact):
Dr. M. Hilhorst. Internist-nephrologist and researcher, Department of Internal Medicine – Nephrology. Meibergdreef 9 | 1105 AZ Amsterdam | The Netherlands. Tel: 020-5661300 | E-mail: m.l.hilhorst@amsterdamumc.nl

Data Protection Officer:
E-mail: privacy@amsterdamumc.nl
Complaints: tel: 020 566 3355, e-mail: patientenvoorlichting@amc.nl
For more information about your rights:
https://www.amc.nl/web/sitewide/algemeneprivacyverklaring.htm

Any complaints can be addressed to:
Patient Service Zorgsupport, AMC location
E-mail: PAZO-AMC@amsterdamumc.nl

Patient Service Zorgsupport, VUmc location
E-mail: PAZO-VUmc@amsterdamumc.nl

Appendix B: information about insurance

Amsterdam UMC has taken out insurance for everyone who takes part in the study. This insurance pays for damage that you suffer because you took part in the study. This means damage that occurs during the study, or within 4 years after the end of your participation. You must report any damage to the insurer within 4 years.

Do you have damage caused by the study? Report this to the insurer:

The insurer of the study is:

Insurer name: Centramed B.A.

Address: Postbus 7374, 2701 AJ Zoetermeer

Telephone: 070 301 70 70

E-mail: info@centramed.nl

Policy number: 624.100.044

The insurance provides coverage of €650,000 per subject, with a maximum of €5,000,000 for the whole study, and €7,500,000 for damage resulting from medical-scientific research reported per insurance year.

Please note: the insurance does not cover the following damage:

- Damage caused by a risk we informed you about in this letter. This does not apply if the risk turned out to be bigger than we expected, or if the risk was very unlikely.
- Damage to your health that would also have occurred if you had not taken part in the study.
- Damage caused because you did not follow instructions or guidance, or did not follow them correctly.
- Damage to the health of your children or grandchildren (unless the study specifically concerns an existing pregnancy, birth, or embryos with the aim of achieving a pregnancy – in that case, damage to the child/children concerned is covered).
- Damage caused by a treatment method that already exists, or by research into a treatment method that already exists.

These rules are set out in the ‘Besluit verplichte verzekering bij medisch-wetenschappelijk onderzoek met mensen 2015’ (Compulsory Insurance for Medical-Scientific Research with Humans Decree 2015). This decree can be found in the Dutch government’s legal database (https://wetten.overheid.nl).

Appendix C – Subject Consent Form

For the study:

What is the role of immune cells in the kidney in lupus nephritis (LN)?

- I have read the information letter. I was also able to ask questions. My questions were answered well enough. I had enough time to decide whether to take part.
- I know that taking part is voluntary. I also know that I can decide at any time not to take part after all, or to stop. I do not have to say why I want to stop.
- I give the researcher permission to let my doctors (specialist, GP, and pharmacist) know that I am taking part in this study.
- I give the researcher permission to request information from my GP, specialist, or pharmacist about my medical history or medication.
- I give the researcher permission to inform my GP or specialist about unexpected findings from the study that are relevant to my health.
- I give the researchers permission to collect and use my data and body material. The researchers will only do this to answer the research question of this study.
- I know that some people may already view my data to check the study. These people are named in this information letter. I give these people permission to view my data for this check.

Please tick yes or no in the table below.

I give permission to possibly be asked, after this study, whether I want to take part in a follow-up study.	Yes ☐	No☐

I want to participate in this study.

My name is (subject): ……..

Signature: …… **Date** : ____ / ____ / _____

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

If, during the study, information becomes known that could affect the subject's consent, I will inform the subject in time.

Naam of researcher (or representative):…….
Signature:…… Date: __ / __ / __

Additional information was given by:

Name:……..
Function:……
Signature:…… Date: __ / __ / __

The subject receives a full information letter, together with a signed copy of the consent form.