INFORMATION TO STUDY PARTICIPANTS IN REBIOLUP

You have been diagnosed with a complication of systemic lupus erythematosus that involves the kidneys and can lead to deterioration of the renal function if not treated promptly with adequate treatment. This complication is called lupus nephritis. Based on the results from the kidney biopsy, you have been selected to be initiated at a specific immunosuppressive therapy, which makes you eligible for participation in our study, entitled "Per-protocol **re**peat kidney **bio**psy in incident cases of **lup**us nephritis" (short name: REBIOLUP). This study aims at investigating the value of a repeat kidney biopsy at month 12 after the first biopsy, in terms of optimisation of treatment and thus prevention of subsequent renal flares and deterioration of the renal function. Previous investigations show a discrepancy between blood or urine test results and findings in the kidney biopsy with regard to disease activity, pointing to the fact that the repeat kidney biopsy is imperative for a safe treatment evaluation and the subsequent decision on therapeutic management. However, no structured investigation has been conducted to date to test this hypothesis.

For this reason, we would like to ask you whether you are willing to participate in the aforementioned study, where we want to investigate not only short-term but also long-term effects of your therapy, both regarding routine clinical parameters and parameters at the level of tissue, and the value of the repeat kidney biopsy in improving short-term and long-term prognosis of the disease.

WHAT IS THE PROCEDURE?

You will receive your therapy as planned by shared decision between your treating physician and you. Prior to the first treatment and during follow-up (5 years in total), you are going to undergo clinical assessments and will be able to answer questions about your health and your disease. This procedure will not interfere with the routine care that you would be given if you did not participate in this study. However, 50% of the patients who agree to participate will be randomised to undergo a repeat kidney biopsy approximately 12 months after the initial kidney biopsy. At this point, we do not know whether you will be one of those patients, but by agreeing to participate in the study you consent to undergo a repeat kidney biopsy if you are selected to that study arm during the randomisation process.

The repeat kidney biopsy is conducted following exactly the same process as the initial kidney biopsy, and has the same potential untoward complications. These include the possibility of pain or bleeding by the site of the puncture, and post-procedure infections. However, the risk for these complications is low, unless you belong to a high-risk group, which will lead to withdrawal of your participation in the study. In the event of a complication, these resolve most often spontaneously without the need for further action. In some cases of pain, analgesia (pain killers) may be needed, and in some cases of extensive bleeding, blood transfusion may be needed.

On specific occasions, you will meet a physician who will perform a clinical assessment and ask questions about *e.g.* your health during the last month in order to complete questionnaires of your disease activity, as well as assess current symptoms. These occasions will be at treatment initiation (baseline), and at month 3, 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60 from baseline, at other time points within this period of time if indicated (e.g. if you undergo a worsening), and at exit from the study if this is earlier from month 60. Separate visits to your treating physician may also be planned according to a different schedule.

For the purpose of this study, blood samples from your arm as well as urine samples (according to specific instructions) will be collected prior to your first treatment (baseline), at month 12 and at month 24 from baseline. In total, the volume of blood that will be obtained exceeding the amount obtained for regular assessment will be approximately 50 mL. These samples will be prepared and stored in freezers for future research purposes. Other samples will be collected regularly on the occasions of the predefined visits as described above and will used for routine care, as by good clinical practice and according to European recommendations for the management of lupus nephritis. Very small fragments of kidney tissue from the kidney biopsies will be used for research purposes within the frame of this project. This will not affect the assessments needed for evaluation of the disease activity as by good clinical practice, as these fragments will only be provided to the investigators of the study if the rest of the tissue is sufficient for the routine clinical assessment. Finally, glasses prepared from residual kidney tissue for microscopic assessment will be sent for central digitalisation or research purposes to another participating centre within your country of residence or abroad. This will not affect the assessments needed for evaluation of the kidney biopsies and decision of treatment.

WILLINGNESS AND CONFIDENTIALITY (SECRECY)

The participation in this study is unconstrained (based on free-will). If you accept to participate, this will not entail any consequences regarding your treatment. You will be able to discontinue your participation in the study at any time, without providing any specific reason for your decision.

The data and test results that we collect are going to be processed after pseudonymisation, and only investigators who are directly involved in the research project will have access to the data. You can make use of your right to get informed about the personal data that are registered about you in the databases, from where these data have been retrieved, and to whom these data have been dispensed. You have the right to retrieve a written extract containing this information once a year, free of charge. In case any inaccuracies are identified, these will be corrected. This is a multicentre study, but the local university where you have been enrolled has the full responsibility of your personal data. Only pseudonymised data, where identification of your personal identity is not possible, may be processed centrally for the purposes of this study. Blood, urine and tissue samples may also be shipped to national or international research collaborators, but will be pseudonymised for the recipient so that your identity will not be traceable. These procedures will follow the General Data Protection Regulation (GDPR) 2016/679.

Your personal data will be handled with confidentiality/secrecy according to local legislation in your country and the law of secrecy, which guarantees a high level of confidentiality and secrecy. The blood, urine and tissue samples will be stored in the biobanks of your local university, until a central biorepository for the purpose of this study is available. Only investigators responsible for the research project will have access to the samples and the data that will be collected within the frame of the study.

The following investigators are members of the steering committee of the study:

Ioannis Parodis | Consultant rheumatologist (Stockholm, Sweden)

Farah Tamirou | Consultant rheumatologist (Brussels, Belgium)

Julia Menke | Consultant nephrologist (Mainz, Germany)

Hans-Joachim Anders | Consultant nephrologist (Munich, Germany)

Brad H. Rovin | Consultant nephrologist (Columbus, United States)

Frédéric Houssiau | Consultant rheumatologist (Brussels, Belgium)

We, the undersigned, are responsible local investigators for the study project. You may get in contact with us and ask questions whenever you so wish.

Name Surname | Title | E-mail:

Name Surname | Title | E-mail:

Name Surname | Title | E-mail:

INFORMED CONSENT FORM

I, the undersigned, have received and read the written information.

I ACCEPT:

- to participate in the research study entitled "Per-protocol **re**peat kidney **bio**psy in incident cases of **lup**us nephritis" (short name: REBIOLUP) and have understood that my participation is unconstrained (based on free-will) and can be discontinued whenever I so wish without the need to provide any specific reason.

I APPROVE:

- that, if assigned to that arm, I will undergo a repeat kidney biopsy one year after initiation of treatment;
- that small fragments of the initial and the repeat biopsy will be stored in a biobank at my local university (study centre), and may be transferred to a central biorepository at another participating centre within my country or abroad;
- that the glasses prepared for the microscopic assessment of my kidney biopsies may be sent for central digitalisation to another participating centre within my country or abroad;
- that the blood and urine samples that I have provided will be stored in a biobank at my local university (study centre), and may be transferred to a central biorepository at another participating centre within my country or abroad in the future, prior to analysis;
- that the samples will be utilised as described in the information for study participants, but I have the right to withdraw my consent to the use of my samples at any time, as well as the right to demand that my samples are promptly destroyed or de-identified;
- that pseudonymised samples may be shipped to research collaborators abroad;
- that the samples may be used in future biomedical research that is not described here, the protocols of which will be reviewed and approved by the regional ethics review board; and
- that in case of such research, copies of or information from my medical charts may be dispensed (only to investigators directly involved in this research).

DATE, PLACE:

ID OR CIVIC REGISTRATION NUMBER:

SIGNATURE (STUDY PARTICIPANT):

NAME (STUDY PARTICIPANT):

SIGNATURE (INVESTIGATOR):

NAME (INVESTIGATOR):