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Collaborative Transplant Study | INF 305 | 69120 Heidelberg, Germany

Patient Label

**Collaborative Transplant Study Covid-19 Serum Study**

**"Antibody formation against the graft after SARS-CoV-2 infection"**

***Information Handout***

***for transplanted patients with SARS-CoV-2 infection after transplantation***

***after regaining the capacity to consent***

Dear Patient

You have been hospitalized due to your SARS-CoV-2 infection. As part of your hospitalization, we have included you, with the consent of your legal representative, in our Collaborative Transplant Study Covid-19 Serum Study mentioned above. The purpose of this information document is to explain to you the reasons for study inclusion and the study-related actions that have already been taken. Please read the following information carefully. Once you have received all the information, you can decide for yourself whether you wish to continue to participate in our study or personally revoke the consent you gave through your legal representative. Allow yourself sufficient time and ask the study staff any questions that are important to you. The study is funded by the Institute of Immunology in Heidelberg. In addition, project funding from third parties is sought. There are no conflicts of interest (both financial and personal) for any department or individual involved in the study.

**What is the objective of the study?**

In this study, we would like to investigate whether

(a) patients who had a Corona virus (SARS-CoV-2) infection before or after organ transplantation are more likely to develop antibodies against their transplant than control patients without infection depending on the severity of the disease

b) the formation of such graft-damaging antibodies affects the function of your transplant.

Furthermore, we would like to analyze how the subgroups of antibodies formed by patients with SARS-CoV-2 infection against the Corona virus change during the course of the disease and whether these changes have an impact on the course of the disease.

After transplantation, new formation of graft-damaging antibodies may occur, which has been shown to increase the risk of rejection. We would like to investigate whether transplanted patients with SARS-CoV-2 infection form such graft-damaging antibodies more frequently.

Other aspects we would like to analyze include the influence of blood group and tissue characteristics on the incidence and severity of Covid-19 as well as the impact of the decrease in SARS-CoV-2 antibody strength on the severity of Covid-19 in transplanted patients. The question is whether there are genetically determined factors (such as blood type or various tissue characteristics) that influence the occurrence and severity of Covid-19. Therefore, in order to answer this question, specific testing of genetic material (blood) will be needed. At this time, it is not possible to predict which genetic variants might influence the occurrence and progression of Covid-19; thus, it is difficult to narrow down the scope of the genetic testing. We would also like to investigate whether certain subsets of SARS-CoV-2 antibodies correlate with better control (neutralization) of the virus.

Until now, studies on these questions in transplanted patients have either not been performed at all or did not meet the necessary numerical requirements. The international Collaborative Transplant Study coordinated by us, in which more than 150 liver and kidney transplant centers from all over the world are actively participating, offers the unique opportunity to gather reliable information on the effects of Corona infection on organ transplantation outcomes in a relatively short time. We would like to subsequently make these results available to transplant centers for the benefit of transplanted patients.

**How does the study work?**

As a transplanted patient with SARS-CoV-2 infection, two additional tubes of blood (approximately 15 – 20 ml) will be or have already been drawn from you on the day of hospitalization due to your SARS-CoV-2 infection for testing of immune activation marker sCD30, graft-damaging and SARS-CoV-2 antibodies as well as accurate typing of tissue characteristics (HLA antigens).

60 – 90 days after hospitalization, an additional blood sample (serum blood, approx. 10 ml) will be or has already been taken from you as part of your routine follow-up at the transplant center for study purposes in order to examine the development of the immune parameters mentioned above (sCD30, transplant-damaging antibodies and SARS-CoV-2 antibodies). At this time, the physician in charge of your treatment will also answer questions about the course of your SARS-CoV-2 infection in a questionnaire.

One year after hospitalization due to your SARS-CoV-2 infection, an additional blood sample will be taken (approximately 10 ml) to re-evaluate the development of the immune parameters mentioned above.

From experience we know that the collection of the additional blood tubes requires <1 minute more. Experience has shown that the time required for explaining the study and discussing participation and consent can be expected to be 15 minutes depending on the amount of information required. The study-related additional collection of 10 to a maximum of 20 ml of blood will usually have only a minor impact on the total blood volume and your general condition.

**Do I have a personal benefit?**

Since the findings are only elaborated within the framework of the study and the examination will be pseudonymized[[1]](#footnote-1), there is no direct individual benefit for you. It is planned to publish the results in medical or biological journals and to present the study at national and international congresses for further discussion of the results.

**How and why was I already included in this study?**

Patients like you who become hospitalized due to your SARS-CoV-2 infection may experience rapid progression of the disease with possible intensive care hospitalization and concomitant loss of capacity to consent.

We have decided to include non-consenting patients in the study because we expect increased formation of transplant-damaging antibodies and/or the impairment of graft function, especially in these severe courses. We think, following points 28 and 30 of the Declaration of Helsinki, that, especially from your group of diseased patients, we can gain additional information about the course of the disease in the whole group (transplanted patients with SARS-CoV-2 infection) as well as information to promote the health of the whole group (e.g. prevention of rejection by timely detection of newly formed transplant-damaging antibodies). We estimate that the benefit we can expect from a greater number of participants and especially from the information gain of follow-up of severe SARS-CoV-2 infections is reasonable compared with the burden of collecting approximately 10 – 20 ml of blood in addition to routine blood collection.

Before your inclusion in this study, an information leaflet about this study was sent to your legal representative and his or her proxy consent was obtained after detailed information on the declaration of consent. You now have the opportunity to decide again, after regaining your capacity to consent, whether or not you wish to continue to participate in this study.

**What are the risks associated with participation?**

A small amount of blood will be taken from you three times at the most. Adverse effects or risks are not expected from the blood collection and the amount of blood collected. All blood collections will be obtained as part of routine care. No additional study-related punctures will occur. Blood sampling may cause local irritation, infection, bleeding as well as bruising in addition to mild pain from the puncture in rare cases. There is also a risk of nerve injury with superficial numbness. All these risks have nothing to do with this study, but represent general risks of blood collection.

According to the current state of science, the occurrence of incidental findings is unlikely. Nevertheless, incidental findings may occur in the course of the examinations of the material obtained. In principle, this may result in indications of already existing or future diseases that are not related to the objectives of the study (incidental findings). We will inform you about such findings upon request. However, the notification of incidental findings may have far reaching, even negative consequences for you and your blood relatives' further life. For example, you may be required to provide this information when taking out insurance policies or during a health examination with the aim of obtaining a civil service position. Not least because of these potentially negative consequences, but also because of the constitutionally guaranteed right not to know, the decision on how to deal with such findings is left to you. Therefore, if you do not wish to be informed about incidental findings or only those that are likely to have the potential to prevent or treat disease at an early stage, please tick the appropriate option as part of the consent form. All data will be treated strictly confidentially and will only be evaluated in pseudonymized form.

**Privacy information**

General:

Medical confidentiality and data protection regulations will be observed. During the study, medical findings and personal information will be collected from you and written down in your personal file or stored electronically at the trial site. The data important for the study will additionally be stored in pseudonymized (encrypted) form, evaluated and, if necessary, passed on to university clinics and cooperation partners, possibly also in countries where data protection requirements are lower than in the European Union.

The study management will take all reasonable steps to ensure the protection of your data in accordance with European Union data protection standards. The data is secured against unauthorized access. Decryption will only occur in the event of withdrawal from the study for the purpose of data destruction. As soon as possible according to the research or statistical purpose, personal data will be anonymized [[2]](#footnote-2). Data collected during the study will be kept indefinitely in the Collaborative Transplant Study database in Heidelberg for use in future scientific studies. Any biological material from you that is not needed will also be asserved indefinitely under a pseudonym at the study center after the study is completed in order to evaluate further biomarkers in Covid-19 research in the future. These include, for example, studies of tissue characteristics, blood group and genetic information important for organ transplantation. As soon as possible according to the research purpose, the samples will be pseudonymized. If you do not agree to the use of data for future research purposes, you may restrict your declaration of consent. The retention period of the biomaterials and data cannot be stated precisely, as it is currently not foreseeable which studies on the study blood regarding organ transplanted patients with SARS-CoV-2 infection might be relevant in the future. As a consequence, the biomaterials will be kept until further notice and made available for further medical research regarding transplanted patients with SARS-CoV-2 infection. We will review every five years whether further retention of the biomaterials and data is still necessary. The personal data will be anonymized as soon as possible according to the research purpose.

Your data and samples may also be passed on to recipients in countries outside the EU (clinics, cooperation partners) if one of the following conditions is met:

a. The European Commission has determined that the country has an adequate level of data protection under the law.

b. On the part of the study director, contractual data protection clauses have been agreed with the research partners which have been adopted or approved by the European Commission or the competent supervisory authority. You may obtain a copy of these data protection clauses from the below-listed officials responsible for the study.

In addition, however, data and samples may also be transferred to research partners in third countries for which neither of these two requirements is met. These countries **may** have **a lower level of data protection than the EU**. The study directors mentioned below assure that, also in these cases, the research partners will be contractually obliged, as far as legally possible, to comply with the EU data protection level. Nevertheless, there is a risk that government or private agencies may access your data even though this would not be permitted under European data protection law. In addition, you may be subject to fewer or less enforceable data subject rights in these countries and there may be no independent supervisory authority to assist you in exercising your rights. **In this case, your samples and data can only be passed on if you have given your explicit consent. If you do not agree, you may delete the respective marked paragraph in the declaration of consent.**

We would like to point out that there is currently a high and also legitimate interest in Covid-19 research. Through good cooperation with other transplant centers, we hope to obtain as much data as possible regarding Covid-19 infections in transplanted patients as soon as possible. This requires an exchange of data between different transplant centers. We would like to point out again that the data important for the study will be stored in pseudonymized (encrypted) form, evaluated and, if necessary, passed on to university clinics and cooperation partners, possibly also in countries where data protection requirements are lower than in the European Union.

You have the right to request information from the persons responsible (see below) about the personal data stored about you. Likewise, you may request the correction of inaccurate data and the deletion of data or restrictions on their processing.

The persons responsible for the study-related collection of personal data are:

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If you have any concerns about data processing and compliance with data protection requirements, you may contact the following data protection officer at the facility:

Dr. jur. Regina Mathes

Im Neuenheimer Feld 672

69120 Heidelberg

Tel.: 06221/56-7036

datenschutz@med.uni-heidelberg.de

In the event of unlawful data processing, you have the right to lodge a complaint with the following supervisory authority:

The State Commissioner for Data Protection and Freedom of Information of Baden-Württemberg

P.O. Box 10 29 32, 70025 Stuttgart

Königstraße 10a, 70173 Stuttgart

Tel.: 0711/61 55 41 - 0

Fax: 0711/61 55 41 - 15

E-mail: poststelle@lfdi.bwl.de

Internet: http://www.baden-wuerttemberg.datenschutz.de

For the purposes of the study, it is useful to include data from your medical records with your physicians in charge. We would like to ask you to agree to an excerpt of the transplantation-related data being passed on to the study management and to release your physicians from their medical confidentiality in this respect.

Any collection, storage and transmission of data from your biomaterials in the context of research projects involves confidentiality risks (e.g. the possibility of identifying you), especially with regard to information on your genetic make-up. These risks cannot be completely excluded and increase according to the amount of data that can be linked, especially if you yourself publish genetic data on the Internet (e.g. for genetic research). The study management assures you that it will do everything possible according to the state of the art to protect your privacy and that samples and data will only be passed on to projects that can demonstrate a suitable data protection concept.

**Voluntariness / Resignation**

Participation in the study is voluntary. If you still wish to participate, we ask you to sign the enclosed consent form. You may revoke this consent in writing or verbally at any time in the further course without giving reasons and without incurring any disadvantages.

If you wish to revoke the consent given by your legal representative, please tick the box provided for this purpose on the consent form ("I hereby revoke my consent already given by my legal representative"). If you wish to revoke your current consent at a later stage, please contact the study director or the staff treating you.

If you revoke your consent, you may decide whether the data collected from you for study purposes should be deleted and the samples obtained should be destroyed or whether they may continue to be used for the purposes of the study. Even if you initially agree to further use, you may still change your mind later and request deletion of the data or destruction of the samples; to do this, please also contact the study management or the staff treating you.

Please note that data that have already been included in scientific evaluations or data or samples that have already been anonymized can no longer be deleted or destroyed at your request.

**Do I incur any costs as a result of my participation? / Do I receive payment or reimbursement of expenses?**

Participation in the study is free of charge for you. However, you will not receive any payment either, as the study participation is part of the general transplant follow-up care.

**More information**

For further information as well as for information on general results and the outcome of the study, please contact the following persons:

Responsible Study Physician:

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**We would be grateful for your participation in this research project!**

1. "Pseudonymization" means the processing of personal data in such a way that the personal data can no longer be attributed to a specific data subject without the use of additional information ("key"). This additional information is kept separately and is subject to technical and organizational measures that ensure that the personal data cannot be assigned to an identified or identifiable natural person. [↑](#footnote-ref-1)
2. "Anonymization" is the alteration of personal data in such a way that the data subject can no longer be identified or can only be identified at a disproportionate cost or time. [↑](#footnote-ref-2)