Patient consent form

REMOVE - Investigation of the mechanisms and efficacy of a hemoadsorption procedure for the prevention of vasodilatory shock in cardiac surgical patients with infectious endocarditis - a multi-center, randomized controlled clinical trial with group-sequential design

Dear Patient,

You have been diagnosed with infective endocarditis, which requires surgical treatment of which your doctor has informed you. We want to ask if You would like to participate in a clinical trial, which we would like to present below.

Please read this patient information carefully, which explains the objectives and the course of the clinical trial. A clinical trial doctor will afterward discuss with You the different aspects of this clinical trial. Please do not hesitate at any moment to address any issues that might arise during this conversation. You will be given enough time to decide if You would like to participate in the clinical trial.

Clinical trials are needed to gain or extend insights into the efficacy of new therapies. The study we present here was - as required by law - approved by the responsible ethics committee. It is a study with a medical device (CytoSorb®, a whole blood adsorber).

This study, funded by the Federal Ministry of Education and Research, is carried out in Germany at several hospitals. During the trial, there should be 250 participants in total. The study director is Dr. Mahmoud Diab from the Cardiothoracic Surgery Department of the University Hospital in Jena.

The study is also financially supported by the Firm CytoSorbents (Berlin), which provides the medical device and laboratory testing equipment.

Participation in this clinical trial is voluntary. Only the patients who provide written informed consent are eligible to be included in this study. If You should decide not to participate in this study or if you, due to personal reasons, decide to withdraw Your consent from this study, there will be no disadvantages in Your treatment or breach of Doctor-Patient relationship.

Why is this study being conducted?

A bacterial infection of the inner lining of the heart was diagnosed in You, also known as infective endocarditis. The treatment requires open-heart surgery utilizing the heart-lung machine. It was shown in different studies in Patients suffering from infective endocarditis that there is a surge of the release of pro-inflammatory and vasoactive substances (vasodilatative or vasoconstrictive) during the operation. These can lead to multiorgan and / or cardiovascular failure (vasodilatory shock) during and after surgery. This study aims to investigate whether the CytoSorb® adsorber can remove the pro-inflammatory and vasoactive substances from the blood and thus prevent cardiovascular complications during and after surgery.

Does participating in the study affect my treatment?

As a Patient participating in the study, you will be randomly assigned to one of the two predetermined patient groups using a computer-controlled random procedure (so-called randomization, similar to the throwing of a coin). Your doctor cannot influence the allocation. The

probability to be chosen in one or the other group is the same (50% each), and You will not be informed to which group You belong to.

If you are assigned to the control group, you will be treated according to the current standards of treatment, meaning- the heart surgery procedure will be performed without the utilization of the CytoSorb® adsorber. If you are assigned to the intervention group, the heart surgery will be performed with the utilization of the medical device CytoSorb®.

What exactly is the medical device CytoSorb®, and what does it do?

CytoSorb® is a so-called whole blood adsorber. It is a cylinder that is built into the heart-lung machine. The cylinder contains a unique, novel material that can bind excess amounts of proinflammatory and vasoactive substances from the blood, similar to a filter. CytoSorb® is already approved as a medical device and is already being used in the field of cardiac surgery and kidney replacement therapy (dialysis).

However, the efficacy in patients with infectious endocarditis has not been studied so far. This will be investigated in the present study.

What is the course of this study, and what are the considerations if I take part in it?

After You have signed the consent form, You become a Study-participant. Your doctor will proof if all the necessary criteria have been met. In female patients, those of childbearing age, in order to participate, it is necessary to perform a pregnancy test. Female patients that test negative will be elgabel to take further part in the trial. After a review of the eligibility criteria, the Patient will randomly be assigned to the control or intervention group. The course of the study is the same for participants in both groups. The only difference is in the use of The CytoSorb® in the intervention group.

Beginning from the day before the operation until the ninth day after the surgery, a study worker will collect data from Your medical record, for example, diagnoses, laboratory values, and treatments for the study documentation. These are an integral part of your treatment and are not performed extra for the study. On the 30th day after the surgery, a medical examiner will inquire about Your condition. The interview will take about 10 minutes. If you are no longer in the hospital at this time, a study worker from Your treating clinic will contact You by phone. After that, the study is over for You.

What personal benefit do I have from participating in the study?

If you belong to the intervention group, CytoSorb® will be integrated into the heart-lung machine during the operation. Since there are no controlled studies on the use of CytoSorb® infective endocarditis, it can not be predicted whether or not You will have an immediate benefit. Finding this out is the purpose of this study.

If you belong to the control group, you will be treated according to the current guidelines, as if you have not taken part in the study.

What are the risks associated with participating in the study?

If you have been assigned to the intervention group, CytoSorb® will be installed into the heart-lung machine during your operation. The adsorber has already been used in cardiac surgery and kidney transplant procedures.

In the studies published so far, no undesirable side effects or safety-relevant events have been observed, which can be attributed to the adsorber. The application is considered safe and without complications. Your participation is not associated with any further risk.

If have been assigned to the control group, your participation in the study is not associated with no further risk.

However, irrespective of the group allocation, there are risks of surgery due to your underlying disease, infectious endocarditis.

What are other possible treatment options apart from this study?

If You decide not to participate in this study, you will be treated according to the current standard of care, that is, cardiac surgery without the use of the CytoSorb® Adsorber.

Who can not participate in this study?

You may not participate in this study if you are simultaneously participating in other studies or clinical research projects. There are also several so-called exclusion criteria. If one of them is fulfilled, you can not participate in the study. These criteria are separately requested and checked by the study doctor. Pregnant and lactating women are not allowed to take part in the trial.

Am I insured during the study?

CytoSorb® is an approved medical device and is used according to its intended use. Therefore, the Medical Devices Act does not prescribe insurance. The liability insurance of the hospital remains unaffected. This means that the hospital and its collaborators (study physicians, other personnel) are liable for liability if you suffer damage as a result of their fault. Please note that you are not insured from an accident during travel to and from the study center.

Will new information be shared with me during the study?

You will be immediately informe if there are new findings regarding the treatment of the infective endocarditis or the medical device. At that moment, You can decide whether or not you want to continue to participate in the study. The results of the study – your personal or overall results of all study participants - will not be shared with You.

Who decides if I leave the study? Can I terminate my participation at any time?

Participation in the study is voluntary. You may terminate your participation at any time, without stating your reasons, and without incurring any disadvantages concerning your medical treatment or relationship with your attending physician. The data acquired until that moment will continue to be used.

However, under certain circumstances, it is also possible that the study doctor or the study leader may decide to terminate your participation in the study prematurely, without you influencing that decision. The reasons for this can be z. For example:

• if Your further participation in the study is no longer medically acceptable;

• If the study is terminated for organizational/regulatory reasons at the supervising laboratory;

• If the clinical trial is aborted.

The study doctor will then discuss with you how your further treatment will proceed.

What else can I do for research?

We would kindly ask if you could provide us with a blood sample for research purposes. It is not mandatory for You to provide us with a blood sample in order to participate in the study. You can decide on that separately in the section "Declaration of consent" whether or not you consent to donate the blood sample for the research purpose described below.

The Medical Microbiology in Jena wants to develop new diagnostic methods for the detection of infective endocarditis and requires a single blood sample (Start OP). The blood volume taken is about 2.5 ml (that is about half a teaspoon).

As part of the perioperative preparation, peripheral vein catheters are placed in order to administer medication and iv fluids. The blood sample might be either taken from this venous catheter or during another routine blood control. They are therefore not additionally burdened with punctures.

The sample is then pseudonymized, and given further, which means that apart from your doctor, nobody can match the samples to you.

You will not be involved in any resulting patents or commercial use of the results.

Do I incur costs by participating in the study?

If you participate in this clinical trial, you will not incur any additional costs. However, you will also receive no expense allowance for participating in this study.

What happens to my data? (Privacy information)

During the study, medical findings, types of treatment, prescribed medication and personal information such as your contact information will be collected and recorded at the study center in your personalized medical record on paper or stored electronically. Your private data will be stored separately from your medical data and will be treated confidentially.

The person responsible for data processing in this project is the study leader, Dr. Diab as an authorized representative of the sponsor (the Center for Sepsis Control and Care at the University Hospital Jena).

The study director is commissioned for the data processing center of the Center for Clinical Trials (ZKS) of the University Hospital Jena (Salvador-Allende-Platz 27, 07747 Jena). The necessary study data are stored in the ZKS Jena in a pseudonymous form, evaluated, and if necessary, further passed on to the responsible ethics committee. Pseudonymized means that no name or initials are used,

only a number and / or letter code may be used. Only the study staff at your study center will know the code of your name. These persons are obliged to secrecy. The data is secured against unauthorized access. The study results will be published without any reference to You.

Due to legal regulations, certain persons (authorized third parties) have the right to access your personal data or medical record. These are agents of the contracting authority or the competent authority. These persons are also obliged to secrecy. The inspection and disclosure take place only in the context of the legally regulated tasks of the inspecting persons, namely for the purpose of checking the data and the correctness of the conduct of the study. If you withdraw your consent, no further data will be collected from you, but the data collected to that timepoint will continue to be used.

Regarding your data you have the following rights (Article 13 ff. DSGVO, §§ 32 ff. BDSG-new):

• Right to information

You have the right to information regarding the acquisition of your data, processing it, and if necessary, the transmission of it to third parties during the clinical trial (handing over a copy).

• Right to rectification

You have the right to correct the incorrect acquired personal data concerning you.

• Right to delete

You have the right to delete personal data concerning you, e.g. that data is no longer necessary for the purpose for which it was collected.

We point out, however, that the pseudonymous data collected based on other applicable regulations (ICH GCP Directive) can not be completely removed.

• Right to restriction of processing

Under certain conditions, you have the right to demand the restriction of processing, meaning, the data may only be stored, not processed. This must be requested. Please contact the study doctor or the data protection officer at your study center.

• Right to data portability

You have the right to receive the personal data that you have provided to the person responsible for the clinical trial. This allows you to request that this data be transmitted either to you or, as far as technically possible, to another place designated by you.

• Right of objection

You have the right to object at any time to any specific decision or action taken to process your personal data. In principle, such processing no longer takes place.

• Consent to the processing of personal data and right to revoke this consent

The processing of your personal data is only legal with your consent.

You have the right to revoke your consent to the processing of personal data at any time. However, the data collected up to that point in time may be processed, mentioned also in the Patient Information and Consent Part of our form.

If you would like to use one of these rights, please contact your study doctor or the data protection officer of the study center. You have also the right to issue a complaint to the supervisory authority if you believe that the processing of personal data concerning you is contrary to the GDPR: