Queen Elizabeth Hospital Birmingham, Liver unit, Mindelsohn Way,
Edgbaston, Birmingham,

Patient Information

Study:
Hypothermic oxygenated perfusion (HOPE) of human liver grafts before transplantation - A multicenter, randomized controlled trial

For Patients and Families

1. *Selection of study participants*

You have been asked to participate in this study, because in Switzerland currently not enough organs for liver transplantation are available.
Liver transplantation at our hospital is well organized and follows a standard procedure:
First our patients undergo all necessary medical investigations. According to the results transplant physicians and surgeons include potential liver recipient candidates into the swiss transplant (national) waiting list for liver transplantation. Exclusively medical conditions are important for the selection of the position on the list and the related waiting time for an appropriate organ. In case of liver allocation to a specific recipient on the list, you get a phone call and a medical transport will pick you up for transfer to our hospital. Donor liver procurement is performed and the organ will be transferred under cold conditions to our hospital. Liver vessels of each single donor organ are prepared prior to the transplantation. During the liver transplantation operation firstly, the deceased organ will be resected followed by the implantation of the new liver. During the resection of the deceased organ the new organ remains under cold conditions in ice at 4 degrees in the operation room.

2. Aim of the study

The life of many people strictly depends on a new liver.
Unfortunately, we do not have enough organs for all potential recipients on the waiting list. Today, we therefore have to also use livers of less quality with a much higher risk of functional impairment after transplantation. Our aim is, therefore to improve the quality and function of such livers. The research group of Prof. Dr. P. Dutkowski (Zurich), showed during the last 15 years, that a short, cold and oxygenated liver perfusion prior to implantation improve the function of the liver. These results have been confirmed internationally. With this study, we want to improve liver function after transplantation by such a short and cold machine perfusion.

3. General Information's about this clinical study

The titel HOPE is defined as: Hypothermic Oxygenated Perfusion. This is an organ perfusion with a cold, oxygenated perfusion solution. Following organ procurement, transport and vessel preparation, livers undergo a short, cold perfusion for 1-2 hours prior to implantation in the operation room. Importantly, liver perfusion will be paralleled to the first part of liver transplantation surgery – which is the resection of the deceased liver and will therefore not extend or postpone the implantation of the new liver. Additionally, the liver transplantation technique will not be affected at any time.
In order to achieve representative results, we plan to include 170 patients in this study. The study will take place at University Hospital Zurich and 8-10 other centres in Europe. In 2010, in New York James Guarrera performed a similar study on cold liver machine perfusion before transplantation. Though he could show an advantage of the perfused group, this study was not randomized.

4. Voluntariness of Participation

Your participation in this study is voluntary. You will not have any disadvantages if you do not want to participate. The same is essential, if you decide to withdraw your participation during the ongoing study. You have always the opportunity to discontinue participation. Importantly, it is not necessary to define your reasons for a cancellation. In this case, your data will be included in the study results up to this point. A final clinical examination will be scheduled and performed for your security.

5. Study Procedure

Study participant are admitted to our hospital after liver allocation. The liver transplantation is performed accordingly. The liver is prepared in the operation room and stored in the cold as usual. If

this liver/this case has been allocated to the perfusion group of the study, the liver will be now connected to the perfusion machine. During perfusion, the liver is bathing in cold perfusion fluid. In half of the participants (perfusion group, 85 out of 170) the liver is perfused with the cold and oxygenated perfusion fluid. All other liver grafts will be transplanted without cold perfusion (cold storage group, again 85 out of 170). The allocation of the participants to one of the study groups occurs randomly, performed by a computer. The allocation code may become descrambled at any time. Randomization means, participants are randomly allocated to the study groups in a ratio 1 to 1. You as participant will be allocated to either the perfusion group or the storage group. Importantly, physicians, nurses, coordinators etc. are not able to inform you about the study group you have been allocated to. Surgeons and other doctors, do not have information regarding the group allocation. The study duration involves the time between admission to hospital for transplantation until one year follow up after the transplantation.

Examinations before Transplantation:

Before liver transplantation a number of examinations are performed as soon as you are admitted to hospital. This is standard prior to any liver transplantation with or without participation in our study. Lab test (blood and urine), ECG test for the heart, chest x-ray. Again, this is a standard procedure before any liver transplantation. No additional invasive examinations are necessary if you participate in this study. Pregnancy test are performed before inclusion of a female patient at child-bearing age on the waiting list. This is also performed independently from our study.

Examinations after Transplantation:

Following liver transplantation monitoring of all recipients is firstly performed on the intensive care unit (ICU). Blood tests are performed on a daily basis. This is also standard procedure and not specifically different during the study. Following recovery, all recipients are transferred to the normal transplantation ward, where also daily blood tests are performed. According to the health condition of the recipient after liver transplantation additional tests may be necessary. This is also independent from the study. At the day of discharge from the hospital, a final clinical examination and blood tests will be performed.
All blood tests are standard after liver transplantation independent from participation in this study or not. Blood test include: blood picture, coagulation parameters (INR/Quick), liver enzyme release (AST/GOT, ALT/GPT). During the first year after liver transplantation, other parameters such as Bilirubin, GGT and alkaline phosphatase (AP) are performed on a regular basis during clinical examinations in the outpatient clinic. Such results after transplantation will be included in the study analysis. Importantly, during the first year follow up no additional invasive examinations will be necessary. All tests are performed according to the health condition of the recipient, independently from the study participation. Only the results will be used for study analysis. A standard MRI/MRCP is performed 6 and 12 month after transplantation. This is also done on a regular basis after liver transplantation. All controls after transplantation are performed in our outpatient clinic.

6. Responsibilities of the participant

Study participants are responsible for the following items:

- Follow the instruction of the investigator and follow the study plan including the medical controls
- Inform the investigator regarding your health condition during in-hospital and outpatient appointments.
- Inform the investigator regarding any treatments by other doctors and physicians (not related to our hospital.
- Inform the investigator regarding new drugs, prescribed by another doctor not related to the hospital, where you have been transplanted. This involves also supplements by plants, Asiatic therapeutics and homeopathy.

7. Alternative Treatment Options

If you are not interested in participating in this study, you won`t experience any disadvantages. Importantly, non – participation does not influence the timepoint when you receive a new liver graft. Livers are allocated nationally and according to the medical condition of the potential recipient and independently from this study.

8. Advantages for the participant

Participation may improve the function of your new liver and participation of many liver recipients result in faster data analysis and presentation of results, which are important for all liver recipients in the future. Due to your collaboration, more patients will receive a new liver graft with a better function and better outcome and survival in the future.

9. Potential Risks and Disadvantages

Your decision to participate does not influence the organ allocation. The perfusion solution is produced synthetically, sterile and has not been retrieved from another living organism. Participants are therefore not exposed to a higher risk for transmission of HIV or hepatitis virus infections as compared to other patients or liver recipients in general. During and after the transplant procedure, several blood tests and liver biopsies are regularly necessary. As mentioned above, there will be no deviation from the standard procedure after liver transplantation during your participation in this study. The medical treatment including immunosuppression is not influenced by the study. All liver recipients get standard immunosuppression, with or without participation in our study. The outpatient controls during first year after transplantation will be scheduled on the regular basis every 3 month as usual. Directly after liver transplantation patients will be discharged to recover during rehabilitation for several weeks. The overall risk for participants are very small. Occurrence of unexpected risks is unlikely but cannot be completely excluded.

Women in child-bearing age

Due to the essential immunosuppression, women of child-bearing age are required to use standard reliable contraception methods. Prior to listing, standard pregnancy tests are performed. Medical immunosuppression may lead to fetal injury or even abortion. This procedure is independent from our study and performed regularly in all female liver transplant candidates. Patients who become pregnant during study, should inform the investigator and will be excluded from the ongoing study.

For male participants

Your participation has no expected negative influence on development and function of sperm. Male liver transplant candidates are regularly informed regarding the potential influence of immunosuppressive drugs on fertility. Again, this is independent from the study participation and performed in all liver transplant recipients.

10. New Perceptions

The investigator has the duty to inform the participants regarding new findings on safety and potential risks during the study, which may influence your participation.

11. Data Confidentiality

In this study, personal data of participants are recorded anonymously. These data are recorded exclusively for the analysis of the study by investigators involved in the study. Responsible investigators are allowed to analyse the performance of the study. This is called monitoring and a very important tool in order to control the study procedure. Monitoring experts and responsible ethical commissions are allowed to review original data from participants. Importantly, during the entire study data confidentiality will be preserved. The participants name will not appear anywhere. The principal investigator in Switzerland is responsible for the preservation of the confidentiality of all study related data.

12. Costs

All transplant related examinations are free of charge and covered by the insurance in the country. The study does not require additional examinations, different from the standard transplant procedure. There are no further study related investigations, which require payment by the participant or the participant insurance.

13. Participant Compensation

Liver recipients do not receive any financial compensation for their participation in the study.

14. Involuntary Study Interruption

Your participation may become interrupted by the investigator due to the following reasons: exclusion of the donated liver graft by medical reasons (this is the case, if the liver graft is for example steatotic to a higher degree, and will therefore not be transplanted anywhere) or if the health condition of the participant (liver recipient) does not allow a liver transplantation for medical reasons at the time of allocation. Again, this decision is not dependent on your participation in the study.

15. Covering of potential injuries

In case of occurrence of any untypical, impaired health condition or injuries during or after your participation in the study, despite all precautions, please contact the principal investigator, who will initiate necessary steps for such a case. For these purposes, the University Hospital Zurich has

completed an insurance for the participants. Injuries, that are proven to be associated with the clinical trial and your participation will be covered and replaced.

16. Contact

Many thanks for your interest in our project. For further questions or emergencies please contact the transplant coordination or the local investigator.

Local investigator:
Prof. Paolo Muiesan
Andrea Schlegel

Liver Unit

Queen Elizabeth
Hospital Birmingham
Mindelsohn Way
Edgbaston, Birmingham
B15 2GW

Tel 0121 627 2000