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HOPE for human livers

Submission date	Recruitment status	[ ] Prospectively registered
12/03/2017	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
07/12/2017	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
01/03/2019	Surgery	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
The life of many people strictly depends on a new liver. Unfortunately, there are not enough organs for all potential recipients on the waiting list. Livers of lower quality with a higher risk of functional impairment after transplantation therefore have to be used. The aim is therefore to improve the quality and function of such livers. Hypothermic oxygenated perfusion (HOPE) is organ perfusion with a cold perfusion solution with a lot of oxygen. Following routine liver transport in the cold (standard cold storage), livers undergo a short, cold perfusion for 1-2 hours before implantation. The machine used for this has been introduced into the field of liver transplantation and is used in many centres worldwide. A short, cold and oxygenated liver perfusion before transplantation improves the function of the liver in the recipient. These results have been confirmed internationally. The aim of this study is to improve liver function after transplantation by using a short and cold machine perfusion and analyse outcomes and complications after liver transplantation.

Who can participate?
Patients aged 18 or above who are receiving a liver transplant

What does the study involve?
Livers are randomly allocated into two groups to undergo either conventional cold storage or cold storage plus HOPE before implantation. The liver recipients are followed up to assess complications, liver function, length of hospital and ICU stay, and patient and transplant survival at 1 year.

What are the possible benefits and risks of participating?
Participation may improve the function of the new liver and the results will help liver recipients in the future, as more patients will receive a new liver with a better function, outcome and survival in the future. 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. During and after the transplant procedure, several blood tests and liver biopsies (samples) are regularly necessary. There are no changes from the standard procedure after liver transplantation during 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 the study. The overall risk for participants is very small. Occurrence of unexpected risks is unlikely but cannot

be completely excluded. More than 120 livers have been transplanted after this perfusion technique worldwide (in Switzerland, USA, Italy and Netherlands), where no specific unexpected side effects have been reported yet.

Where is the study run from?
The study takes place at University Hospital Zurich (Switzerland) and 8-10 other centres in Europe, for example in Birmingham (QEHB), London (King's College Hospital) and Edinburgh (UK).

When is the study starting and how long is it expected to run for?
April 2016 to July 2019

Who is funding the study?
Swiss National Science Foundation (Switzerland)

Who is the main contact?
Dr Andrea Schlegel

Study website
http://www.hope-liver.com

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2016-002540-16

IRAS number

ClinicalTrials.gov number
NCT01317342

Secondary identifying numbers
2011-0079/4

Study information

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

Acronym
HOPE study

Study objectives
The purpose of this study is, in a phase II randomized trial, to test a newly developed machine perfusion technique of human liver allografts before transplantation. Significance of planned research: Late biliary injury and graft loss remain a major problem in the era of sick liver transplant recipients and marginal donors. Machine liver perfusion techniques have been recognized as potentially protective, but are still not in use in human liver transplantation, because of low practicability and lack of prospective human studies. The suggested study will demonstrate, for the first time worldwide, the effect of an easy and applicable perfusion technique in human liver grafts. The trialists postulate, therefore, a high acceptance rate among transplant surgeons. In case of convincing success, it can be applied at low cost and low resources in any center worldwide.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Kantonal Ethical Commission Zurich, Switzerland, 06/09/2011, ref: KEKZH2011-0079(KEK-ZH-Nr. 2011-0079/4

Study design
Multicenter randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Liver transplantation

Interventions
Randomization will be performed at the time of liver acceptance. This is usually also the time when the liver recipient is admitted to hospital. The liver will be randomized by the local

investigator or the trial coordinator using an online randomization tool. A computer-generated list of random assignments (block randomization per center (www.randomizer.at) is prepared in advance. Hence, concealed allocation will not be possible. The timepoint for randomization will be at the end of procurement to assure a minimum dropout of cases. The procurement team will call the local or principal investigator, who coordinates the randomization in that center. The randomization list from the randomizer has been incorporated into the newly developed eCRF. All personnel involved in randomization will be trained in the use of the online randomization by the Project Leader or the Principal Investigator of each site.

Liver grafts from brain death donors (DBD) will be randomly divided in two groups, receiving either conventional cold storage (n=85) according to standard criteria of organ preservation or cold storage plus subsequent hypothermic oxygenated perfusion (HOPE), performed ex-situ with the liver assist device, before implantation (n=85).

Follow up of each included patient will be 12 months.

Intervention Type
Device

Phase
Phase II

Primary outcome measure
Major postoperative complications (Clavien Grade > or =III), using the established Clavien classification supported by a recently developed comprehensive complication index (CCI). Complications are summarized in the eCRF from the time of transplantation until 1 year after liver transplantation, which is the end of follow up. In the eCRF complications are monitored during hospital stay, at 3 and 6 and 9 and 12-month outpatient controls after liver transplantation.

Secondary outcome measures
1. Plasma AST and ALT, measured 6 and 12 hours after OLT, and at day 1-7 postoperatively to determine the area under the curve (AUC)
2. Postoperative liver function measured by INR (plasma, at day 1-7)
3. Intra- and extrahepatic biliary complications within the first year after liver transplantation, assessed by serum cholestasis parameters (Bilirubin, Gammaglutamyltransferase, Alkaline Phosphatase) every 3 months and liver MRI including an MCRP 12 months after liver transplantation
4. Length of hospital and ICU stay after transplantation
5. Patient and graft survival at 1 year

Overall study start date
01/04/2016

Completion date
31/07/2019

Eligibility

Key inclusion criteria

1. Candidates for liver transplantation
2. Aged 18 or above
3. Receiving a whole liver graft
4. Full consent for the study

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
170

Key exclusion criteria
1. DCD livers
2. Split grafts
3. Living donor livers
4. Combined grafts
5. Domino liver transplantations
6. Cold storage of more than 12 hrs

Date of first enrolment
01/04/2016

Date of final enrolment
01/05/2018

Locations

Countries of recruitment
Belgium

England

France

Germany

Netherlands

Romania

Scotland

Spain

Switzerland

United Kingdom

Study participating centre
Queen Elizabeth Hospital Birmingham
United Kingdom
B15 2TH

Study participating centre
University Hospital Zurich
Switzerland
8091

Study participating centre
King's College Hospital
London
United Kingdom
SE5 9RS

Study participating centre
Royal Infirmary of Edinburgh
United Kingdom
EH16 4SA

Study participating centre
Hospital Universitario “Reina Sofia”
Cordoba
Spain
14004

Study participating centre
University of Medicine “Carol Davila”
Fundeni Clinical Institute

Bucharest
Romania
030167

Study participating centre
Klinik für Allgemeine und Transplantationschirurgie - University Hospital Essen
Germany
45147

Study participating centre
Universitaire Ziekenhuizen Leuven
Abdominal Transplant Surgery
Belgium
B-3000

Study participating centre
Erasmus Medical Centre
Rotterdam
Netherlands
3015 CE

Study participating centre
University Medical Centre Groningen
Netherlands
9713 GZ

Sponsor information

Organisation
University Hospital Zurich

Sponsor details
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/01462r250

Funder(s)

Funder type
Research organisation

Funder Name
Schweizerischer Nationalfonds zur Förderung der Wissenschaftlichen Forschung

Alternative Name(s)
Schweizerischer Nationalfonds, Swiss National Science Foundation, Fonds National Suisse de la Recherche Scientifique, Fondo Nazionale Svizzero per la Ricerca Scientifica, Fonds National Suisse, Fondo Nazionale Svizzero, Schweizerische Nationalfonds, SNF, SNSF, FNS

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Switzerland

Results and Publications

Publication and dissemination plan
Publication following interim analysis when 40 patients have been randomized into the study, and final publication when the study has been completed. Publication is expected in summer /autumn 2019.

Intention to publish date
01/09/2019

Individual participant data (IPD) sharing plan
Participants data will be collected in an electronic case report form (eCRF) and will be available for a few investigators per centre and the sponsor. Importantly, investigators will exclusively have access to participants data from their own centre. When eCRF training has been completed successfully, the personal password and login details are provided by the clinical trial centre in Zurich, Switzerland (Sponsor, leading trial coordinator) just after the centre received the ethical approval prior to start with the inclusion of patients. Participants give consent to use their data

after transplantation, which will exclusively be used for the trial and are not accessible for any other purpose. Data are completely anonymised and trial numbers are allocated to each participant by the eCRF system automatically.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet		17/08/2017	07/12/2017	No	Yes