A single center Phase-I Clinical Trial to Assess Viability of High Risk Donor Livers using Hypothermic and Normothermic Machine Perfusion with Rewarming Phase Prior to Transplantation

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To study the feasibility, and reliability of ex-situ viability testing of high risk donor livers using DHOPE, rewarming and NMP, by assessing graft survival at 3 months after transplantation.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatic and hepatobiliary disorders
Study type	Interventional

Summary

ID

NL-OMON47272

Source
ToetsingOnline

Brief title
Viability assessment of high risk donor livers using DHOPE, COR and NMP

Condition

- Hepatic and hepatobiliary disorders

Synonym
end-stage liver disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,Tekke Huizinga Fonds,HbO2 Therapeutics LLC ,Jan Kornelis de Cock Stichting

Intervention

Keyword: controlled oxygenated rewarming, ex-situ viability testing, liver transplantation, normothermic machine perfusion

Outcome measures

Primary outcome

The main study parameter is graft survival at 3 months after transplantation.

Secondary outcome

Secondary study parameters:

- Graft and patient survival at 7 days and 1 month.

- Primary non-function (PNF): Occurrence of retransplantation or patient death

within the first 7 days after OLT, without any identifiable cause of graft

dysfunction(12).

- Early allograft dysfunction (EAD), presence of one or more of the following

variables (13):

o Elevation of AST and/or ALT above a defined cut-off value (>2000 IU/mL)

within the first 7 days after OLT;

o Elevated international normalized ratio (INR) of *1.6 on day 7 after OLT;

o Elevated bilirubin levels of *10 mg/dL on day 7 after OLT.

- Development of non-anastomotic biliary strictures (NAS).

- Biochemical analysis of graft function and ischemia-reperfusion injury

determined with serum levels of ALT, AST, AlkP, *GT, INR, lactate, creatinine,

platelets and total bilirubin at postoperative day 0-7 and 1 and 3 months.

Study description

Background summary

Currently, there is a shortage of suitable donor livers. To expand the donor pool, livers from high risk donors, or otherwise termed extended criteria donor (ECD) livers are increasingly accepted. ECD livers carry an increased risk of developing severe complications. Machine perfusion is a promising technique in predicting whether an ECD liver is susceptible to developing one of these complications or not, prior to transplantation. Normothermic machine perfusion (NMP) is conducted at a physiologic temperature of 37 °C, using a perfusion fluid based on an oxygen carrier. This results in a metabolically active liver, offering the ability to assess liver function and viability ex-situ. Aside from NMP, dual hypothermic oxygenated machine perfusion (DHOPE), conducted at 4 - 14°C, is advocated to improve the quality of ECD livers. Hence, this protocol is designed to assess viability of high risk donor livers using NMP, prior to transplantation. DHOPE, being superior in optimizing the quality of ECD livers will be conducted before gradually rewarming the donor liver to a normothermic temperature. During NMP a viability assessment will be carried out. Thus, high risk donor livers that would previously not have been accepted for transplantation, will be transplanted when meeting the viability criteria. Therefore, the donor pool might be expanded.

Study objective

To study the feasibility, and reliability of ex-situ viability testing of high risk donor livers using DHOPE, rewarming and NMP, by assessing graft survival at 3 months after transplantation.

Study design

A single center phase-I clinical trial, in which 10 liver transplants will be included based on empirical experience.

Intervention

Each high risk donor liver accepted for this study will undergo machine perfusion. First, DHOPE will take place, before gradually rewarming the liver till a normothermic temperature. Secondly, after rewarming, NMP will take place.

Study burden and risks

The risks and the burden associated with this study will be limited. If a high risk donor liver is not viable or *poor-functioning* at the moment of viability assessment, the liver will not be transplanted, in order to protect the recipient. Moreover, if there is a device error * disadvantageous for the donor liver * the liver will neither be transplanted. The only drawback concerning this is the fact that the patient will come to the hospital unnecessarily. The advantage is that when a liver is being transplanted the odds are quite high that the liver is of very reasonable quality. Least the liver will be perfused with Hemopure ®, an oxygen carrier. Despite of many studies, Hemopure ® is not yet approved in the Netherlands. However, based on the information on Hemopure ®, as described in this protocol and in the Investigators Brochure, there is no reason to believe that Hemopure ® causes significant damage.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700 RB
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700 RB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:;Recipient
- Adult patients (* 18 years old)
- Given informed consent ;Donor grafts
- Donors with a body weight *40 kg

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:;Recipient
- Simultaneous participation in another clinical trial that might possibly influence this trial
- Mental conditions rendering the subject incapable to understand the nature, scope and consequences of the trial
- Listed for liver transplantation due to fulminant liver failure or retransplantation because of PNF
- Recipient positive test for HIV
- Allergic to one of the components in the perfusion fluid. ;Donor grafts
- Donor positive for HIV, Hepatitis B or C
- Split or partial liver grafts
- Domino donor livers
- Expected cold ischemia time of * 10 hours

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-12-2016

Enrollment:	10
Type:	Actual

Medical products/devices used

Generic name:	Liver Assist
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	24-08-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-11-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-04-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-06-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-11-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-04-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-06-2018

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL58015.042.16
Other	TC=5972