PLEASE NOTE: *This trial has been registered retrospectively.*

Trial Description

Title

Prognostic potential of different tests for liver function in patients with cirrhosis

Trial Acronym

Prognosis

URL of the trial

[---]*

Brief Summary in Lay Language

This study assesses prospectively the liver function of chronic liver failure patients due to cirrhosis treated or evaluated for potential liver transplantation at the University Hospital Charité Berlin, Germany.
Liver function is measured using different liver function test such as 13C-Methacetin-Atemtest (LiMAx-Test) und Indocyaninegrün-Test (ICG-Test).
Additionally a spezial ultrasound examination (FibroScan) is used for fibrosis(/ cirrhosis grading and patients' quality of life is assessed using the chronic liver disease questionnaire (CLDQ)-german version.
Over the course of three years maximum follow up phone calls are performed to assess the actual quality of life after month 6, 12, 24 respectively.

The aim of this study is the determination of the different prognostic values of available diagnostic tests for the mortality/ survival in patients with end stage-liver disease/ cirrhosis. Moreover QoL assessment of patients with different stages of cirrhosis is from outstanding interest for therapy decision making. QoL could influence the decision to perform liver transplantation and lead to changes in the current organ allocation system.
Endpoints are patient death and performed liver transplantation.
Acquired patient data on day one and in course of the evaluation for liver transplantation will be correlated with the waiting time on the transplantation list and with the mortality and morbidity while time on the waiting list. Moreover data will be compared with currently used scores (Child-Pugh-Score; MELD-Score)

There is no planned additional intervention in the course of the study.

The aim of this study is the determination of the different prognostic values of available diagnostic tests for the mortality/ survival in endstage-liver disease/ cirrhosis.

Brief Summary in Scientific Language

The disparity between the number of potential candidates for liver transplantation and the number of available donor organs is constantly growing and waiting list mortality presents a serious problem in medicine. Effective transplant waiting lists allocate the available grafts firstly to those patients, who would have had a poor prognosis without transplantation. Nevertheless, it is a challenging issue to identify these patients, because a certain number of tests and classification systems are available to assess end-stage liver disease.
Liver allocation is currently based on the model of end-stage liver disease score (MELD). The MELD score includes 3 laboratory parameters: International Normalized Ratio (INR), serum creatinine and serum bilirubin. Clinical studies revealed its potential to predict short-term prognosis (6-month mortality). Nevertheless more and more authors criticize the problems and limitations of the MELD-Score.
Therefore additional parameters for the classification of liver function need to be explored for further optimization of the organ allocation system.

In this prospective trial 300 patients evaluated for liver transplantation or with advanced cirrhosis, which are not intended for liver transplantation, will be examined in an observational longitudinal study. All patients need to give their written informed consent. The study protocol includes the initial determination of a broad spectrum of available test for liver function and morphology, and consecutive follow-up interviews at predefined points in time - up to 3 years after enrolment. Liver function capacity will be measured by using the LiMAx test and ICG test, fibrosis/cirrhosis grading is performed using a special sonographic examination technique the FibroScan.
Additionally, we analyse the performance of synthetic capacity of the liver by means of blood parameter values such as IGF-1 (Insulin-like growth factors), pseudocholinesterase, albumine, and coagulatory factors (FII/FVII). All examinations will be carried out during a time frame of 2 days or one hospital stay respectively.

After a minimum of 6 hours fasting each subject undergoes enzymatic liver function capacity measurement using the LiMAx test. Blood samples are drawn from a peripheral vein after placing an intravenous catheter. Prior substrate injection the ratio of 13C02/12C02 concentration was recorded over a period of ten minutes in the native exhaled samples using a non dispersive isotope selective infrared spectroscopy device (FANci, FAN GmbH, Leipzig). After intravenous application of a solution of 2mg/kg/BW 13C-labeled methacetin and subsequent injection of 20 ml 0,9% sodium chloride a maximum of 46 breath samples are collected and analyzed for each patient. Methacetin is selectively metabolized by the Cytochrom P450 1A2 subenzyme exclusively expressed in hepatocytes. The substrate is degraded to acethaminophen and 13- labeled carbon dioxide.
Thus exhalation of the 13CO2 metabolite is detected over a maximum period of 60 minutes.

Within the same session metabolic liver function test is determined using

indocyacin green (ICG), a water soluble non toxic green dye. After injection of 0,5 mg/kg/BW ICG following 10ml Aqua and 20ml 0,9% sodium chloride plasma disappearance rate is measured using a photo spectrometric fingertip. ICG is stable in blood and plasma, bound to plasmaproteins (albumin and α1-lipoprotein). Moreover this agent is taken up by parenchymal hepatic cells, is not metabolized and excreted unchanged in the bile without remaining in the enterohepatic circulation.

Fibrosis cirrhosis grading is performed using a special sonographic examination technique the FibroScan. This special sonographic examination is easy to perform within approximately 10 minutes and does not harm the patient.

Beside routine laboratory parameters, liver function parameters such as PCHE, FII, FVII and IGF-1 as well as hGH, Insulin and c-peptide are analysed.

All examinations are carried out during a time frame of 2 days or one hospital stay respectively.
Moreover patients are followed up to 3 years. Phone calls assessing medical history (cirrhosis related complications; hospital stays), the actual quality of life as well as the actual status (death vs. alive; on waiting list vs. not on waiting list for organ transplantation) are performed after month 6, 12, 24 and 36 respectively.
If patients are lost in course of the follow up information regarding status (death yes-no) and day of death are extracted from the 'Melderegister' according to '25 Abs. 1 Gesetz über das Meldewesen in Berlin (Meldegesetz)'.

The study end-points are liver transplantation or death.

The initial test results will be correlated with the waiting time on the transplantation list and with the mortality and morbidity while time on the waiting list. Moreover the results will be compared with previously and currently used scores (Child-Pugh-score, MELD-score).

The aim of this study is the determination of the different prognostic values of available diagnostic tests for the mortality/ survival in endstage-liver disease/ cirrhosis.

Major hypothesis:
1. Liver function tests allow the determination of prognostic values regarding patient survival
2. Dramatically reduced liver function is associated with inferior 2 year survival

Minor hypothesis:
Liver function tests have superior prognostic predictability compared to currently used models and could influence the actual organ allocation system in the future.

Organizational Data

- DRKS-ID: **DRKS00000614**
- Date of Registration in DRKS: **2012/06/14**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **EA2/066/09 , Ethik-Kommission der Charité - Universitätsmedizin Berlin-**

Secondary IDs

Health condition or Problem studied

- ICD10: **K71.9 - Toxic liver disease, unspecified**
- ICD10: **K72.1 - Chronic hepatic failure**

Interventions/Observational Groups

- Arm 1: **300 patients with liver cirrhosis Child Pugh B or C, which were hospitalized or undergoing evaluation for livertransplantation at the University Hospital Charité, Berlin are enrolled in this non interventional trial. Patients recieve biochemical blood analysis, liver function testing, enzymatic liver function testing using the LiMAx-Test and liverstiffness measurements. Patients quality of life, complication rate and patient death are investigated over a period of up to 3 years.**

Characteristics

- Study Type: **Non-interventional**
- Study Type Non-Interventional: **Other**
- Allocation: **Single arm study**
- Blinding: **Open (masking not used)**
- Who is blinded: **[---]***
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Study Type: **Non-interventional**

Study Type Non-Interventional: **Other**

Allocation: **Single arm study**

Blinding: **Open (masking not used)**

Who is blinded: **[---]***

Control: **Uncontrolled/Single arm**

- Purpose: **Prognosis**
- Assignment: **Single (group)**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

status of the patient: death, liver transplantation, or survival without transplantation at timepoints 6,12, and 24 moths will be prooven via telephone contact with the patient.

Secondary Outcome

Changes of quality of life by means of COLQ- German version and occurence of complications related to cirrhosis will be evaluated on timepoint 0 and after 6, 12 and 24 month respectively using telephon follow up calls. Acquired data will be documented in special designed clinical report forms.

Countries of recruitment

- DE **Germany**

Locations of Recruitment

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2009/07/01**
- Target Sample Size: **300**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **75 Years**

Additional Inclusion Criteria

1. patients with liver cirrhosis fulfilling Child b or c
2. 18-75 years old, both sex
3. patients which signed the informed consent

Exclusion criteria

1. patients listed for other than liver transplantation
2. acute liver failure
3. patients with sver infectious disease
4. uncompliance

Addresses

- **Primary Sponsor**

Klinik für Allgemein-, Viszerall- und Transplantationsmedizin
Mr. Priv.-Doz. Martin Stockmann
Augustenburger Platz 1
13353 Berlin
Germany

Telephone: **+49 30 450 552 001**
Fax: **[---]***
E-mail: **martin.stockmann at charite.de**
URL: **http://www.charite.de/avt/**

- **Contact for Scientific Queries**

Klinik für Allgemein-, Viszerall- und Transplantationschirurgie
Mr. Maciej Malinowski
Augustenburger Platz 1
13353 Berlin
Germany

Telephone: **+49 30 450 552 001**
Fax: **+49 30 450 552 984**
E-mail: **maciej.malinowski at charite.de**
URL: **http://www.charite.de/avt/**

- **Contact for Public Queries**

Contact for Public Queries

Klinik für Allgemein-, Viszerall- und Transplantationschirurgie
Mr. Maciej Malinowski
Augustenburger Platz 1
13353 Berlin
Germany

Telephone: **+49 30 450 552 001**
Fax: **+49 30 450 552 984**
E-mail: **maciej.malinowski at charite.de**
URL: **http://www.charite.de/avt/**

Sources of Monetary or Material Support

- **Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)**

European Commission
B-1049 Brussels
Belgium

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **http://ec.europa.eu/index_en.htm**

Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*