Trial Description

Title

graft function adapted tacrolimus therapy after liver transplantation (GRAFTT)

Trial Acronym

GRAFTT

URL of the trial

http://www.charite.de/avt/forschung/workgroup_for_the_liver/ongoing-projects.html#GRAFTT

Brief Summary in Lay Language

Tacrolimus is an important standard induction and maintenance immunosuppressant drug after liver transplantation (LT). Nevertheless, tacrolimus has a narrow therapeutic window and can cause serious adverse effects. Acute overdosing can provoke renal failure and severe neurological disorders, On the other hand, insufficient levels could lead to graft rejection in the initial post-transplant phase.
The purpose of the study is to improve immunosuppressive therapy until three days after liver transplantation.

Patients receiving primary orthotopic LT will be enrolled in this study.
The aim of this study is to achieve a reduced number of patients suffering from toxic drug reactions or organ rejection.

Our assumption is that medication adaption for real liver function improves graft survival.

Therefore the real liver function is measured after liver transplantation. The dosage of tacrolimus will be adapted on this measured liver function. The measument will be repeated on first day after liver transplantation.

Brief Summary in Scientific Language

Prospective,randomized, controlled open label trial with Prograf® and Advagraf® (GRAFTT)

Do you plan to share individual participant data with other researchers?

[---]*

Description IPD sharing plan

[---]*

Organizational Data

- DRKS-ID: **DRKS00003551**
- Date of Registration in DRKS: **2013/05/31**
- Date of Registration in Partner Registry or other Primary Registry: **2011/12/05**
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **11/0560-ZS EK 11 , Ethik-Kommission des Landes Berlin**

Secondary IDs

- EudraCT-Number (for studies acc. to Drug Law): **2011-004944-23**
- Partner Registry-ID: **EUCTR2011-004944-23-DE (EUCTR)**
- BfArM-No.: **4037842**

Health condition or Problem studied

- Free text: **livertransplantation**
- ICD10: **K72.9 - Hepatic failure, unspecified**

Interventions/Observational Groups

- Arm 1: **Prograf®, with liver function adapted TAC-regime in the first three days after LTx, twice a day, 0,025- 0,1 mg/kg body weight**
- Arm 2: **Advagraf®, with liver fuction adapted TAC-regime, in the first three days after LTx, once a day, 0,05- 0,2 mg/kg body weight**
- Arm 3: **control group with standard tacrolimus regime (Prograf), in the first three days after LTx, twice a day, 0,05 mg/kg body weight**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **Open (masking not used)**
- Who is blinded: **[---]***
- Control: **Active control**
- Purpose: **Treatment**
- Assignment: **Parallel**
- Phase: **IV**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **No**

Primary Outcome

Number of patients suffering from either toxic or insufficient tacrolimus whole blood trough levels during the initial 14 days after liver transplantation (twice levels of <5 ng/mL during post-transplant days 1-14 or one levels >20 ng/mL during post-transplant days 1-14)

Secondary Outcome

1.) Tacrolimus whole blood trough level during post-transplant days 1-14

2.) Total cumulative incidence of inadequate tacrolimus whole blood trough levels during post-transplant days 1-14 (<5 ng/mL or >20 ng/mL)

3.) Creatinine serum levels (day 1-14 after transplantation)

4.) Incidence of Adverse effects:
a.) acute renal failure (days 1-14)
b.) chronic renal insufficiency (until 1 year after transplantation)
c) Neurological effects including
encephalopathy, seizures or coma (days 1- 14)
5.) graft rejection (time frame: 1 year)
6.) Rejection free time interval (time frame: 1 year)
7.) Assessment of graft and patient survival (time frame: 1 year)

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Berlin**

- University Medical Center **Aachen**
- University Medical Center **Heidelberg**
- University Medical Center **Jena**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2012/07/26**
- Target Sample Size: **210**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

Inclusion criteria
-Patients intended for orthotopic deceased-donor LT
- Recipient age ≥18 yrs.
- Capability to understand the purpose and the risk of the study
- Written informed consent prior LT

Exclusion criteria

- Participation in other clinical trials during <28 days before LT
- any organ transplantation before enrollment, High-urgent transplantation, split liver LT, living donor LT, combined multi-organ transplantation, AB0 incompatible grafts, retransplantation
- Recipients with malignant tumors beside HCC respecting the Milan criteria or liver metastasis
-Target trough levels of tacrolimus differing from 10-15 ng/mL in the first 14 days after LTx)
- planned use of other immunosuppressive drugs including ciclosporine A, sirolimus, everolimus, azathioprine in the first 14 days after LTx

- patients with known intolerance of tacrolimus
- patients with a history of substance or drug abuse
- patients with psychiatric disorders or any forms of substance abuse not capable of understanding the purpose and risks of the study
- subjects known to be HIV positive- pregnant woman or breastfeeding mother

Addresses

- **Primary Sponsor**

  Charité Universitätsmedizin Berlin
  Augustenburger Platz 1
  13353 Berlin
  Germany

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- **Contact for Scientific Queries**

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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.)**

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- **Commercial (pharmaceutical industry, medical engineering industry, etc.)**

Astellas Pharma GmbH
Georg-Brauchle- Ring
80992 München
Germany

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Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

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.*