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# Evaluation of iloprost in the postoperative period after liver transplantation

**Submission date**
14/08/2012

**Recruitment status**
No longer recruiting

**Registration date**
02/10/2012

**Overall study status**
Completed

**Last Edited**
14/07/2016

**Condition category**
Injury, Occupational Diseases, Poisoning

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

**Plain English Summary**
Background and study aims
The success of a liver transplantation depends on multiple factors. A poorly functioning liver graft increases the risk of complications, severe infections, and complete organ failure. For this reason, strategies are needed to reduce the number of poorly functioning liver grafts. One such possibility is the use of prostaglandin drugs, one of these being Iloprost. Prostaglandins widen the blood vessels and they prevent the aggregation of platelets, the blood cells responsible for clotting. This should improve the blood supply (perfusion) and functioning of the transplanted liver. The aim of this study is to examine whether the continuous use of Iloprost immediately after transplantation over seven days has a positive effect on the function of the transplanted liver.

Who can participate?
Patients aged over 18 receiving a liver transplant

What does the study involve?
Participants are randomly allocated to one of two groups. In the treatment group, participants receive Iloprost continuously intravenously (into a vein) over seven days; in the control group participants receive a placebo (dummy drug) intravenously with the same dosage.

What are the possible benefits and risks of participating?
Iloprost improves the perfusion of the transplanted liver, which may improve the functioning of the liver graft and may reduce the risk of complications. The most frequent drug-related side effects are flushing, headache, nausea and vomiting. Many of these side effects are dose-dependent and may be reduced or stopped by a dosage adjustment.

Where is the study run from?
Lead centre: Jena University Hospital. Further participating centres: Charite Campus Virchow, University Medicine Berlin; University Hospital of Essen; Goethe University Hospital Frankfurt, University Hospital of Mainz, University Hospital of Heidelberg (Germany)

When is the study starting and how long is it expected to run for?
April 2012 to December 2015

Who is funding the study?
1. Astellas GmbH
2. German Federal Ministry of Education and Research
3. BayerVital GmbH

Who is the main contact?
Dr Erik Bärthel

### Study website
http://www.praise.uniklinikum-jena.de

## Contact information

### Type(s)
Scientific

### Contact name
Prof Utz Settmacher

### Contact details
University Hospital of Jena
Department of General Visceral and Vascular Surgery
Erlanger Allee 101
Jena
Germany
07740

## Additional identifiers

### EudraCT/CTIS number
2010-022660-12

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
PRAISE-ZKS0006, DRKS00003514

## Study information

### Scientific Title
A prospective, multi-center, randomized, double blinded, placebo-controlled study for the evaluation of iloprost in the early postoperative period after liver transplantation

### Acronym
PRAISE

### Study hypothesis

Improved graft viability under treatment with systemically administered prostacyclin analogue iloprost.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
Medical Faculty Ethics Committee, Friedrich Schiller University of Jena, 25/01/2011, ref: 2980-11/10

## Study design
Prospective multi-center randomized double-blinded placebo-controlled trial

## Primary study design
Interventional

## Secondary study design
Randomised controlled trial

## Study setting(s)
Hospital

## Study type(s)
Treatment

## Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet (in German)

## Condition
Liver transplantation

## Interventions
Patients of the treatment group received 1 ng/kg body weight /min iloprost, intravenous administered for 7 days post-liver transplantation, in contrast to the control (placebo) population.

## Intervention Type
Drug

## Phase
Not Applicable

## Drug/device/biological/vaccine name(s)
Iloprost

## Primary outcome measure
Current primary outcome measures as of 07/03/2013:
Primary graft dysfunction (PDF) after liver transplantation characterized as presentation of one or more of the following criteria:

1. Alanine amino transferase / Aspartate amino transferase (ALAT or ASAT) level > 2000 lu/ml within the first 7 postoperative days
2. Bilirubin ≥ 10 mg/dl on postoperative day 7
3. INR ≥ 1.6 on postoperative day 7 or as occurrence of initial non-function (lNF) defined as graft failure originating from the graft itself, excluding hepatic artery thrombosis (HAT), biliary complication, recurrent disease or acute rejection and resulting in retransplantation or patient death within 14 days after initial LT

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2. Bilirubin ≥ 10 mg/dl on postoperative day 7
3. INR ≥ 1.6 on postoperative day 7 or as occurrence of initial non-function (lNF) defined as graft failure originating from the graft itself, excluding hepatic artery thrombosis (HAT)
4. Biliary complication
5. Recurrent disease or acute rejection and resulting in retransplantation or patient death within 14 days after initial LT

## Secondary outcome measures

Current secondary outcome measures as of 07/03/2013:
1. Occurence of any infection up to day 28 after LT
2. Initial non-function (lNF) defined as graft failure originating from the graft itself, excluding hepatic artery thrombosis (HAT), biliary complication, recurrent disease or acute rejection and resulting in retransplantation or patient death within 14 days after initial LT
3. Clotting factor substitution up to day 28 after LT
4. Renal replacement therapy up to day 28 and 180 after LT
5. Liver dialysis up to day 28 and 180 after LT
6. Graft survival at day 28 and 't 80 after LT
7. Patient survival at day 28 and 180 after LT
8. Occurrence of biliary complications at day 28 and 180 after LT
9. Length of ICU stay in days up to day 180 after LT (max)
10. Length of hospital stay in days up to day 180 after LT (maximum)
11. Course of ASAT/ALAT, Quick's value/lNR, Factor V and Indocyanine green plasma disappearance rate (ICG-PDR) until day 7 after LT
12. Change in Sequential Organ Failure Assessment (SOFA)-score from day 1 to day 7 after LT

Previous secondary outcome measures:
1. Initial non-function (lNF) defined as graft failure originating from the graft itself, excluding hepatic artery thrombosis (HAT), biliary complication, recurrent disease or acute rejection and resulting in retransplantation or patient death within 14 days after initial LT 2. Clotting factor substitution up to day 28 after LT
3. Renal replacement therapy up to day 28 and 180 after LT
4. Liver dialysis up to day 28 and 180 after LT
5. Graft survival at day 28 and 't 80 after LT
6. Patient survival at day 28 and 180 after LT
7. Occurrence of biliary complications at day 28 and 180 after LT
8. Length of hospital stay in days up to day 180 after LT (maximum)
9. Course of ASAT/ALAT, Quick's value/lNR, Factor V and Indocyanine green plasma disappearance rate (ICG-PDR) until day 7 after LT
10. Change in Sequential Organ Failure Assessment (SOFA)-score from day 1 to day 7 after LT

### Overall study start date
30/04/2012

### Overall study end date
31/12/2015

# Eligibility

### Participant inclusion criteria
Current inclusion criteria as of 07/03/2013:
1. Full-size liver transplantation
2. Informed consent of the patient or legal representative
3. Aged 18 years or over

Previous inclusion criteria:
1. Full-size liver transplantation
2. Informed consent of the patient or legal representative
3. Age over 18 years

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
18 Years

### Sex
Both

### Target number of participants
356 randomised (900 screened, 430 with written consent)

### Participant exclusion criteria
1. Women of child-bearing potential except women with the following criteria:
1.1. Post menopausal (12 months natural amenorrhea or 6 month amenorrhea with serum FSH > 40 mlU/ml)
1.2. Sterilization 86 weeks after bilateral ovarectomy with or without hysterectomy
1.3. Using an effective method of birth control for the duration of trial:
1.3.1 Implants, injectables, combined oral contraceptives, intra-uterine device (in place for a period of at least 2 months prior to screening) and with negative serum pregnancy test
1.4. Sexual abstinence
2. Pregnancy/lactation
3. Respiratory and/or circulatory instability (noradrenaline > 1 pg/kgBWmin and FiOz > 0.6) after liver transplantation (LT) before randomization
4. Split liver transplantation/living donor related liver transplantation
5. Retransplantation
6. Receiving a multi-organ transplantation

7. Participation on other clinical trials 30 days prior to randomization
8. Known allergic reaction against trial medication
9. Conditions in which bleeding complications may be expected from the effect of lloprost on platelets
10. Severe coronary artery disease or unstable angina pectoris
11. Myocardial infarction within the past 6 months prior to baseline assessment after acceptance of donor organ
12. Acute or chronic heart failure (NYHA ll-lV)
13. Cardiac arrhythmias relevant for the prognosis
14. Suspected pulmonary artery congestion
15. Known allergy or intolerance against tacrolimus, mycophenolate mofetil, basiliximab or corticosteroids

**Recruitment start date**
30/04/2012

**Recruitment end date**
31/12/2015

# Locations

**Countries of recruitment**
Germany

**Study participating centre**
**University Hospital of Jena**
Jena
Germany
07740

# Sponsor information

**Organisation**
Friedrich-Schiller-University Jena (Germany)

**Sponsor details**
Fürstengraben 1
Jena
Germany
07743

**Sponsor type**
University/education

**Website**

http://www.uni-jena.de/

**ROR**
https://ror.org/05qpz1x62

# Funder(s)

**Funder type**
Hospital/treatment centre

**Funder Name**
Universitätsklinikum Jena

**Alternative Name(s)**
Jena University Hospital, UKJ

**Funding Body Type**
Private sector organisation

**Funding Body Subtype**
Universities (academic only)

**Location**
Germany

**Funder Name**
Bayer

**Alternative Name(s)**
Bayer AG, Bayer Corporation, Friedr. Bayer et. comp.

**Funding Body Type**
Government organisation

**Funding Body Subtype**
For-profit companies (industry)

**Location**
Germany

**Funder Name**
Astellas Pharma GmbH (Germany)

# Results and Publications

## Publication and dissemination plan
Not provided at time of registration

## Intention to publish date

## Individual participant data (IPD) sharing plan

## IPD sharing plan summary
Not provided at time of registration

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Protocol article | protocol | 29/01/2013 | | Yes | No |