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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 of protocol

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

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2010-022660-12

Protocol serial number
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 objectives
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

Primary study design
Interventional

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

Study type(s)
Treatment

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

Previous primary outcome measures:
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)

4. Biliary complication
5. Recurrent disease or acute rejection and resulting in retransplantation or patient death within 14 days after initial LT

Key secondary outcome(s)
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

Completion date
31/12/2015

Eligibility

Key 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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key 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

Date of first enrolment
30/04/2012

Date of final enrolment
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)

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

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
Study website	Study website	11/11/2025	11/11/2025	No	Yes