A 24 month, multi-center, open-label, randomized, controlled study to evaluate the efficacy and safety of concentration controlled everolimus to eliminate or to reduce tacrolimus compared to tacrolimus in de novo liver transplant recipients.

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To evaluate the use of concentration-controlled everolimus, with the reduction or the elimination of tacrolimus, to provide superior renal function and to provide non-inferior rates of the composite efficacy endpoint compared to the tacrolimus...

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

Summary

ID

NL-OMON37144

Source
ToetsingOnline

Brief title
Evaluation of efficacy and safety of Certican versus Prograft.

Condition

- Hepatic and hepatobiliary disorders
- Renal disorders (excl nephropathies)

Synonym

Impaired renal function after liver transplantation

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Farmaceutische industrie;Novartis Pharma B.V.

Intervention

Keyword: Certican, Kidney function, Liver transplantation, Prograft

Outcome measures

Primary outcome

• Renal function by the abbreviated MDRD equation

• Treated Biopsy-Proven Acute Rejection

• Death

• Graft Loss

Secondary outcome

• Incidence of new-onset diabetes post-transplantation

• Incidence of CNI-side effects

• Progression of fibrosis in HCV positive patients

• Recurrence rate of hepatocellular carcinoma

• Exploratory objective: change in patterns of specific biomarkers for renal

injury in the urine

Study description

Background summary

This registration trial is designed to address important issues that impact recipients of liver allografts as well as clinicians. The introduction of everolimus may provide superior renal function, by allowing for the reduction or the discontinuation of tacrolimus early post-transplantation, and possibly impacting the development or the rate of progression of fibrosis in HCV positive recipients.

Study objective

To evaluate the use of concentration-controlled everolimus, with the reduction or the elimination of tacrolimus, to provide superior renal function and to provide non-inferior rates of the composite efficacy endpoint compared to the tacrolimus control at 12 months post-transplantation.

Study design

This study is a twenty-four (24) month, multi-center, open-label, randomized, controlled study that will consist of a screening period, a baseline period (3 to 7 days post-transplantation) followed by a run-in period that ends on the day of randomization at 30 days (+/- 5 days) post-transplantation.
A total of 690 patients will be stratified and randomized. Stratification will be based upon HCV status and according to the stratum of renal function (assessed by abbreviated MDRD equation). Randomization will be to one of the three treatment arms in a 1:1:1 ratio as follows: 1) tacrolimus elimination arm; 2) tacrolimus minimization arm; 3) tacrolimus control arm. After discontinuation of group 1, based on a recommendation by the DSMB the remaining newly enrolled patients have been randomised 1:1 to groups 2 and 3.

Intervention

Group 1 (elimination arm): low dose Prograft until month 4 (then elimination) + Certican + steroids
Group 2 (minimalisation arm): low dose Prograft + Certican + steroids
Group 3 (control arm): standard treatment Prograft + steroids

Study burden and risks

The burden (number of visits and evaluations) for the patient associated with participation in this trial does not differ from the burden when following the standard protocol after liver transplantation. The only additional burden is a liver biopsy at baseline (for HCV positive patients only). There is a chance of pain and bleeding after the biopsy. However, these risks do not differ from the risk at the routine biopsies at 1 and 2 year after transplant, and in case of a suspected acute rejection, which are all part of the standard treatment.
Patients randomised to one of the two Certican groups may possibly encounter

the side effects of Certican (as described in the 1B text).

Contacts

Public
Novartis

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Allograft is functioning at an acceptable level by the time of randomization.
2. Confirmed recipient HCV status at Screening.
3. Abbreviated MDRD eGFR >= 30 mL/min/1.73m2.
4. Verification of at least one tacrolimus trough level of >= 8 ng/mL in the week prior to randomization.

Exclusion criteria

1. Recipients of a liver from a living donor, or of a split liver.
2. History of malignancy of any organ system within the past 5 years, other than non-metastatic basal or squamous cell carcinoma of the skin or HCC.
3. Hepatocellular carcinoma that does not fulfill Milan criteria at the time of transplantation as per explant histology of the recipient liver.
4. Women of child-bearing potential, unless they meet certain criteria.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-02-2008
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cellcept
Generic name:	mycophenolatemofetil
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Certican

Generic name:	everolimus
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Prograf
Generic name:	tacrolimus
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	21-12-2007
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-02-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-03-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-11-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-09-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-11-2011

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
EudraCT	EUCTR2007-001821-85-NL
CCMO	NL20355.078.07