A twelve-month, multicenter, randomized, open-label study of safety, tolerability and efficacy of Certican-based regimen versus calcineurin inhibitor-based regimen in de novo liver transplant recipient

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The study is designed to show that Certican® initiation together with reduction and thereafter discontinuation of calcineurin inhibitor (CNI) will improve significantly renal function in de novo liver transplant recipients as compared to...

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

Summary

ID

NL-OMON30363

Source
ToetsingOnline

Brief title
Certican versus calcineurin inhibitor in de novo liver transplant

Condition

- Hepatic and hepatobiliary disorders

Synonym
Therapy after Liver transplant

Research involving

Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Farmaceutische industrie: Novartis

Intervention

Keyword: Calcineurin inhibitor, Certican, Liver transplant

Outcome measures

Primary outcome

*to show superiority of Certican®-based regimen with discontinuation of initial CNI therapy in renal function as compared to continuation of CNI based treatment at 11 months post randomization in liver transplant patients. This will be evaluated by comparing renal function calculated by glomerular filtration rate (cGFR) (Cockcroft-Gault formula) between the two groups of patients

Secondary outcome

To assess the efficacy and safety of the two regimens, evaluated at 11 months post randomization by the comparison between the two groups of:

*Incidence of efficacy failure (defined as the combined endpoint of Biopsy Proven Acute Rejection, graft loss, death, lost to follow up from any reason)
*Incidence of the need for a change in the immunosuppressive regimen other than described in the protocol
*Incidence of renal deterioration defined as a decrease > = 25% in cGFR compared to start of randomized treatment

*Renal function after five months post randomization. Renal function is

measured as cGFR

*Incidence of treated Biopsy Proven Acute Rejection

*Patient and graft survival

*HCV replication in HCV positive patients

*Safety parameters including hypertension, diabetes mellitus (fasting glucose),

hyperlipidemia, anemia, infections and malignancies

Study description

Background summary

The success rate of liver transplantation has drastically increased over the last 20 years. Calcineurin inhibitors (CNI) have contributed largely to the improvement in patient and graft survival after liver transplantation. However long-term use of CNI, cyclosporine or tacrolimus, is associated with side-effects which are source of morbidity.
In addition to CNI therapy pretransplantation renal impairment, post operative acute renal failure, age of recipient, hepatitis C infection, hypertension, diabetes mellitus, hyperlipidemia can contribute to development of chronic renal dysfunction after liver transplantation Ultimately a safe and effective therapeutic intervention which would reduce the incidence of chronic renal dysfunction is not available today.
Recent advances in immunosuppression, especially introduction of nonnephrotoxic agents mycophenolate acid and sirolimus have led to evaluation of new immunosuppressive strategies with CNI minimization or withdrawal in patients with established renal dysfunction.

Study objective

The study is designed to show that Certican® initiation together with reduction and thereafter discontinuation of calcineurin inhibitor (CNI) will improve significantly renal function in de novo liver transplant recipients as compared to continuation of CNI-based treatment.

Study design

A twelve-month, multicenter, open-label, randomized, controlled study with two

parallel groups in de novo liver transplant recipients.
Patients will be randomly assigned to one of the two treatment groups in a ratio of 1:1.

Intervention

*Group I (comparator group):
Simulect® + CNI-based immunosuppressive regimen (cyclosporine A or tacrolimus) according to best local practice + steroids according to best local practice.
*Group II (investigational group):
Simulect® + Certican® based immunosuppressive therapy + steroids according to best local practice.

Study burden and risks

The study design is based on the local practice for liver transplantions. The patiënt will have 4 additional visits on top of the standard visits according to the local practice.
The following assessments will be done during the study:
Physical examination (2x); Vital signs and weigth (17x); blooddraw (min. 13 x); pregnancy test when applicable(1x); liver biopsy in case of signs of acute rejection.

Contacts

Public
Novartis

Raapopseweg 1
6824 DP Arnhem
NL
Scientific
Novartis

Raapopseweg 1
6824 DP Arnhem
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Males or females 18 - 70 years old
2. Liver transplant recipient (living or deceased donor)
3. Patients willing and capable of giving written informed consent for study participation and able to participate in the study for 12 months
4. Patients in whom an allograft biopsy will not be contraindicated
5. Females capable of becoming pregnant must have a negative pregnancy test prior to start of study and are required to practice a medically approved method of birth control for the duration of the study
6. Patients with cGFR > 50 ml/min

Exclusion criteria

1. Recipients of multiple solid organ transplants or patients that have already received a transplant in the past
2. HCV positive patients who need an active anti-viral treatment (HCV-positive patients without active antiviral treatment are allowed)
3. HIV positive patients
4. Patients who are breast feeding
5. Patients with a current severe systemic infection
6. Patients who have received an unlicensed drug or therapy within one month prior to study entry
7. Presence of any hypersensitivity to drugs similar to Certican® (e.g. macrolides)
8. Preexisting (i.e. not related to CNI-damage) renal dysfunction that, according to the judgment of the investigator, will not significantly improve after transplantation.
9. Patients that have received Simulect prior to this study.
10. Patients that have received any immunosuppressive regimen 2 months prior to this study.

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:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-12-2006
Enrollment:	40
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	30-10-2006
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-12-2006
Application type:	First submission

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-02-2009
Application type:	Amendment
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)

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	EUCTR2005-002920-32-NL
CCMO	NL14298.078.06