Extension study to the multicenter, open-label, randomized, controlled study CRAD001H2304 to evaluate the long-term efficacy and safety of concentrationcontrolled everolimus in liver transplant recipients.

Published: 19-03-2010
Last updated: 03-05-2024

To evaluate the long-term safety and efficacy of two concentration-controlled everolimus regimen in de novo liver transplant recipients at Month 36 post-transplantation.

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

Summary

ID

NL-OMON34870

Source
ToetsingOnline

Brief title
Long term 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, Prograf

Outcome measures

Primary outcome

• Renal function;

• The composite efficacy endpoint of graft loss or death;

• The composite efficacy endpoint of treated biopsy proven acute rejection (BPAR), graft loss, or death;

• The rate of progression of HCV related allograft fibrosis.

Secondary outcome

• To evaluate the efficacy endpoint of treated BPAR at Months 36 and 48 posttransplantation

• Evolution of renal function and CNI-related side effects at Months 36 and 48 posttransplantation:

• Study-/ Study-Drug related findings at Months 36 and 48 post-transplantation:

• To evaluate the premature discontinuation of study medication, and discontinuation from the study; • To evaluate the incidence of dose interruption and dose reduction of study medication; • To evaluate the incidence of adverse events (AEs) and serious adverse events (SAEs); • To evaluate the incidence of infections; • To evaluate the incidence of major

adverse cardiac events (MACE).

• Evolution of HCV and HCV related fibrosis at Months 36 and 48

post-transplantation: • To evaluate HCV viral load (HCV-RNA levels); • To

evaluate rates of progression of HCV related allograft fibrosis.

• To evaluate the rate of recurrence of hepatocellular carcinoma (HCC) at

Months 36 and 48 post-transplantation in patients with a diagnosis of HCC prior

to liver transplantation.

Study description

Background summary

The reason for this extension is to evaluate the long-term safety and efficacy of two concentration-controlled everolimus regimen in de novo liver transplant recipients at Month 36 post-transplantation. In addition, patients will be receiving everolimus for up to Month 48 posttransplantation.
The most important long-term safety assessments include evaluation of renal function, progression of HCV related allograft fibrosis, and other treatment related effects at Month 36 posttransplantation compared to extension baseline (Months 24 post-transplantation).

Study objective

To evaluate the long-term safety and efficacy of two concentration-controlled everolimus regimen in de novo liver transplant recipients at Month 36 post-transplantation.

Study design

This study is an up to 24-month extension to the multicenter, open-label, randomized, and controlled study CRAD001H2304.
All patients in the control group will be studied for 12 months (ending with Visit 19). Patients in Groups 1 and 2 will be studied for individually variable duration for up to 24 months. The first patients in these groups will be studied for 24 months, the last patients only for 12 months. The end of study will be reached, when the last patient enrolled in the extension study completes Visit 19.

Intervention

Group 1 (elimination arm): Certican
Group 2 (minimalisation arm): low dose Prograft + Certican
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 are the liver biopsies 3 and 4 years post transplant (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

Completed Month 24 visit of core study and continuously being treated with assigned regimen.

Exclusion criteria

1. Patients with clinically significant systemic infection requiring active use of IV antibiotics at Month 24.
2. Patients who are in a critical care setting at Month 24 requiring life support measures such as mechanical ventilation, dialysis, requirement of vasopressor agents.
3. 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):	20-09-2010
Enrollment:	28

Type:	Actual

Medical products/devices used

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:	19-03-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-06-2010
Application type:	First submission
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	EUCTR2009-017311-15-NL
CCMO	NL31771.078.10