A Multi Center, Prospective, Observational, Open-label, Pharmacokinetic Study of Tacrolimus in Heart and Lung Transplantation Patients during the First Days after Transplantation

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Primary objective: To show that the variability of whole blood total and unbound plasma tacrolimus concentrations during the first 6 days post transplantation is larger than the variation of tacrolimus concentrations in stable clinical situation....

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Observational invasive

Summary

ID

NL-OMON39373

Source
ToetsingOnline

Brief title
Spartacus

Condition

- Heart failures
- Respiratory disorders congenital
- Respiratory disorders NEC

Synonym
Heart and lung transplantation

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: cystic fibrosis, pharmacokinetics, tacrolimus, transplantation

Outcome measures

Primary outcome

The main study parameters are whole blood total tacrolimus concentrations and unbound tacrolimus plasma concentrations together with the pharmacokinetic parameters: AUC, Cmin, Cmax, Tmax, T1/2, Vd, CL, CL/F (=oral clearance).

Secondary outcome

Variables influencing unbound plasma tacrolimus concentrations:

* Renal dysfunction

* Erythrocytes or Hematocrit

* Albumin

* alpha-1-Acid glycoprotein

* High density lipoprotein

* pH

* Daily fluid balance and body weight

* CYP3A4/CYP3A5 gene expression, and P-glycoprotein gene expression

* Hepatic dysfunction: bilirubin and ALAT will be used to quantify hepatic dysfunction

* Diarrhoea or ileus

* Cystic fibrosis

* Plasma concentrations of (val)acyclovir, (val)ganciclovir, tobramycin and

trimethoprim/sulfamethoxazole, if administered, will be measured at steady

state as possible additional factor causing kidney dysfunction

Study description

Background summary

Tacrolimus is an immunosuppressive agent used as prophylaxis for organ rejection in lung, heart, liver and kidney transplantation. In previous studies, high inter- and intra-individual variability in tacrolimus blood concentration has been observed among transplant recipients. The range and the factors explaining variation in tacrolimus blood concentrations during the first days post-transplantation in heart and lung transplant recipients are largely unknown. More insight on factors causing the inter- and intra-individual variability in tacrolimus concentrations is necessary in order to adapt dose regimen to individuals. Individualization of dosing regimen is needed to prevent organ toxicity, if tacrolimus concentration is too high, and organ rejection, if tacrolimus concentration is too low or in other words, to improve safety of tacrolimus and minimize toxicity directly after heart and lung transplantation.

Study objective

Primary objective:
To show that the variability of whole blood total and unbound plasma tacrolimus concentrations during the first 6 days post transplantation is larger than the variation of tacrolimus concentrations in stable clinical situation.

Secondary objectives:
* To show that unbound tacrolimus plasma concentrations can better predict the occurrence of renal dysfunction than whole blood total tacrolimus concentrations.
* Identification of variables influencing the unbound tacrolimus plasma concentrations.
* To evaluate whether variations in tacrolimus concentrations in the first days after lung transplantation in cystic fibrosis patients are higher than without cystic fibrosis.

Long-term objective:
* The data will be used to develop a kinetic model in the future in order to dose tacrolimus more accurately to prevent adverse effects of tacrolimus.

Study design

We will perform a multiple doses, open-label, observational, prospective and single-center study in heart and lung transplant recipients. Pharmacokinetic parameters will be observed in 30 heart and lung transplant recipients up to the first 6 days after transplantation or shorter if patients are discharged from the intensive care earlier. Renal function will be evaluated in the first days and circa 1, 3 and 6 months after transplantation in the out-patient department.

Study burden and risks

Risk: Subjects in this study donate blood in a larger content than in daily practice (circa 50 ml per day with a maximum of 300 ml for 6 days for lung patients as well for heart transplantation patients). At 1, 3 and 6 months an additional 2,5 ml serum per time will be withdrawn. No interventions will be made. No supplementary pain will be caused by extra blood sampling or by urine collection since intensive care patients are already equipped with an arterial line and a urine catheter after lung or heart transplantation and blood sampling in outpatients is standard procedure. Minimal risk is suspected in research subjects.

Benefit: Due to its completeness, this study will be of substantial value for transplantation patients. With the novel knowledge acquired with this study we expect to be able to tailor tacrolimus administration in heart and lung transplantation patients. The result will be less side and toxic effects, and thus an increased patient*s safety.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patients * 18 years;* Patients admitted to the ICC of UMCU after heart or lung transplantation;* Treated with tacrolimus (Prograft®; Astellas Pharma Europe);* Informed consent obtained

Exclusion criteria

* Patients < 18 years;* Patients who die within one day after admission to the ICC of UMCU;* Withdrawal of informed consent;* Allergy towards tacrolimus or macrolides;* Patients on total parenteral nutrition

Study design

Design

Study phase:	4
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-05-2013
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Prograft®
Generic name:	tacrolimus
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	27-04-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-10-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-07-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 20956
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2012-001909-24-NL
CCMO	NL40432.041.12
OMON	NL-OMON20956

Study results

Date completed: 14-09-2015

Actual enrolment: 30

Summary results
Trial is onging in other countries