Pharmacokinetics of tacrolimus in the first days after heart and lung transplantation.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON20956

Source
Nationaal Trial Register

Brief title
SPARTACUS

Health condition

transplantation
tacrolimus
pharmacokinetics

Sponsors and support

Primary sponsor: Prof. J. Meulenbelt, MD, PhD
Head of department of National Poisons Information Center
Intensive Care Center of the division of Anesthesiology, Intensive Care and Emergency Medicine, University Medical Center of Utrecht
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Source(s) of monetary or material Support: Department of National Poisons Information Center
Division Anesthesiology, Intensive Care and Emergency Medicine
University Medical Center of Utrecht

Intervention

Outcome measures

Primary outcome

To show the greater variability of tacrolimus whole blood total and unbound plasma concentrations during the first 6 days post transplantation compared to the variation of tacrolimus concentrations in stable clinical situation.

Secondary outcome

1. To show that unbound tacrolimus plasma concentrations can better predict the occurrence of renal dysfunction than whole blood total tacrolimus concentrations;

2. To study which factors influence unbound tacrolimus plasma concentrations in heart and lung transplant recipients (hematocrit, albumin, α1-acid glycoprotein (AGP), and high density lipoprotein (HDL), pH, extensive volume suppletion or CYP3A4/ CYP3A5 and P-glycoprotein (Pgp) polymorphisms, bowel dysfunction or liver dysfunction);

3. To evaluate whether variations in tacrolimus concentrations in the first days after lung transplantation in cystic fibrosis patients are higher than without cystic fibrosis;

4. The data will be used to develop a kinetic model in the future in order to be able to adjust the tacrolimus dose to the individual patient to prevent or reduce adverse effects of tacrolimus.

Study description

Background summary

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.

Objectives:

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:

1. To show that unbound tacrolimus plasma concentrations can better predict the occurrence of renal dysfunction than whole blood total tacrolimus concentrations;

2. Identification of variables influencing the unbound tacrolimus plasma concentrations;

3. 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:

1. 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.

Design:

We will perform a multiple doses, open-label, observational, prospective and multi-center study in heart and lung transplant recipients.

Population:

Heart and lung transplant recipients admitted to the Intensive Care of a University Medical Center in the first six days post transplantation.

Procedures:

Patients will be included at the outpatient’s department before the transplantation. Tacrolimus will be administered orally twice a day, according to the usual procedure of the Intensive Care Center. Blood and urine will be collected. Presence or absence of cystic fibrosis will be recorded among lung transplant recipients. Concomitant drugs as a cause of kidney dysfunction will be recorded and plasma concentrations will be measured at steady state. Renal function will also be evaluated in a later phase in de outpatient department after

circa 1, 3 and 6 months.

Study objective

More insight on factors causing the inter- and intra-individual variability in tacrolimus concentrations is necessary in order to improve safety of tacrolimus and minimize toxicity directly after heart and lung transplantation.

Study design

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.

Intervention

N/A

Contacts

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Eligibility criteria

Inclusion criteria

1. Patients ≥ 18 years;

2. Patients admitted to the ICC of UMCU after heart or lung transplantation;

3. Treated with tacrolimus (Prograft®; Astellas Pharma Europe);

4. Informed consent obtained.

Exclusion criteria

1. Patients < 18 years;

2. Patients who die within one day after admission to the ICC of UMCU;

3. Withdrawal of informed consent;

4. Allergy towards tacrolimus or macrolides;

5. Patients on total parenteral nutrition.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	01-04-2013
Enrollment:	30
Type:	Actual

IPD sharing statement

Plan to share IPD: Yes

Plan description
The IPD will be shared from march 2020. A clinical study report will be available via EudraCT. Patients' characteristics, pharmacokinetic data and NONMEM analyses will be reported in the clinical stuty report form.

Ethics review

Positive opinion

Date:	20-03-2013
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 39373
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL3741
NTR-old	NTR3912
CCMO	NL40432.041.12
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON39373

Study results

Summary results
doi.org/10.1007/s13318-019-00591-7, doi.org/10.1007/s40262-019-00854-1