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

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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.

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON20956

Bron
NTR

Verkorte titel
SPARTACUS

Aandoening

transplantation
tacrolimus
pharmacokinetics

Ondersteuning

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Overige ondersteuning: Department of National Poisons Information Center

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Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

N/A

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-04-2013

Aantal proefpersonen:	30
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Ja

Toelichting
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.

Ethische beoordeling

Positief advies

Datum:	20-03-2013
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 39373
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten

Samenvatting resultaten
doi.org/10.1007/s13318-019-00591-7, doi.org/10.1007/s40262-019-00854-1