Omzetting naar Envarsus om de ideale tijdpunten voor monitoring te vinden

No registrations found.

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

Summary

ID

NL-OMON25477

Source
NTR

Health condition

Envarsus, pharmocokinetic model, tacrolimus, liver transplantation, levertransplantatie

Sponsors and support

Primary sponsor: LUMC
Source(s) of monetary or material Support: Chiesi

Intervention

Outcome measures

Primary outcome

Population pharmokinetic parameters tacrolimus (Envarsus)

PK dependency on CYP3A5*3, CYP3A4*22 and IL polymorphisms

Secondary outcome

Limited PK sampling

Through concentration - AUC correlation

Changes in quality of life before and after conversion

Study description

Background summary

Prolonged release tacrolimus (Envarsus), is a new formulation of the calcineurin inhibitor tacrolimus. This product was originally developed to improve the bioavailability of tacrolimus and to provide more consistent tacrolimus exposure. Its pharmacologically active compound tacrolimus is characterized by a narrow therapeutic window, and highly variable pharmacokinetics necessitating Therapeutic Drug Monitoring (TDM) to individualize the dose and prevent rejection or toxicity such as leukopenia and renal toxicity (3).

For patient friendly area under the curve (AUC) calculation a population PK model is required. However, at the moment there is no population pharmacokinetic model available for envarsus in contrast to other used formulations (prograft and advagraf). Genetic polymorphisms in CYP3A4 and CYP3A5 are known to cause clinically relevant variability in tacrolimus pharmacokinetics in solid organs transplantation. These genetic variants were never investigated in relationship with patients receiving Melt Dose tacrolimus (Envarsus).

Objective: To develop a population pharmacokinetic model of Envarsus in stable liver transplant recipients suitable and to evaluate the effect of CYP3A5*3, CYP3A4*22 and IL- polymorphisms of both donor and recipient on Envarsus pharmacokinetics for initial dose differentiation and compare it to the current standard Advagraf. The first secondary objective is to develop a limited sampling strategy for accurate AUC estimation of Envarsus. The second secondary objective is the evaluate quality of life of patients on both tacrolimus formulations.

Study design: An open-label, prospective, PK evaluation study

Study population: Adult liver transplant recipients aged 18 years till 70 years on a stable immunosuppressive Advagraf based regimen.

Intervention: Liver transplant recipients on a stable once daily Advagraf dose will be converted to an once daily Envarsus based regime. The dose will be determined based on the conversion ratio of 1:0.7 (SmPC of Envarsus). For the evaluation of the pharmacokinetics of Envarsus there two additional AUCs and one trough concentration of tacrolimus will be measured in addition to routine clinical care. Two weeks after conversion a full AUC measurement (T=0,1,2,3,4,6,8,12,24) will be performed to be able to assess the population

pharmacokinetics of Envarsus.

Study design

Inclusion: AUC advagraf + QoL

1 week after inclusion: conversion

2 weeks after conversion: whole pk curve

12 weeks after conversion: limited sampling + QoL

Intervention

Advagraf is converted to Envarsus. After 3 weeks a whole PK curve is done. After 13 weeks a limited sampling AUC is done

Contacts

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Eligibility criteria

Inclusion criteria

Liver transplant patients at least 6 months after transplantation

Between 18 and 70 years old

Stable on Advagraf based immunosuppressivum for at least 3 months with 2 months unchanged dose

Stable graft function

Able to give informed consent

Exclusion criteria

Infections or complications at inclusion

Bilirubin and albumin level outside clinical reference range

Patients with GFR <30 ml/min at screening

Unstable dosing of concomitant medication with known interaction with tacrolimus

Study design

Design

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

Recruitment

NL

Recruitment status:	Other
Start date (anticipated):	13-09-2017
Enrollment:	55
Type:	Unknown

Ethics review

Positive opinion

Date:	18-01-2018
Application type:	First submission

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
NTR-new	NL6790
NTR-old	NTR6976
Other	LUMC te Leiden : P16.321

Study results