Omzetting naar Envarsus om de ideale tijdpunten voor monitoring te vinden

Gepubliceerd: 18-01-2018 Laatst bijgewerkt: 18-08-2022

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

Samenvatting

ID

NL-OMON25477

Bron
NTR

Aandoening

Envarsus, pharmocokinetic model, tacrolimus, liver transplantation, levertransplantatie

Ondersteuning

Primaire sponsor: LUMC
Overige ondersteuning: Chiesi

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Population pharmokinetic parameters tacrolimus (Envarsus)
PK dependency on CYP3A5*3, CYP3A4*22 and IL polymorphisms

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Onderzoeksopzet

Inclusion: AUC advagraf + QoL

1 week after inclusion: conversion

2 weeks after conversion: whole pk curve

12 weeks after conversion: limited sampling + QoL

Onderzoeksproduct en/of interventie

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

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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

Onderzoeksopzet

Opzet

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

Deelname

Nederland

Status:	Anders
(Verwachte) startdatum:	13-09-2017
Aantal proefpersonen:	55
Type:	Onbekend

Ethische beoordeling

Positief advies

Datum:	18-01-2018
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL6790
NTR-old	NTR6976
Ander register	LUMC te Leiden : P16.321

Resultaten