Modificatie van Tacrolimus gerelateerde toxiciteit na levertransplantatie.

Gepubliceerd: 20-09-2018 Laatst bijgewerkt: 15-05-2024

Ethische beoordeling	Goedgekeurd WMO
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON24720

Bron
NTR

Verkorte titel
MOTTO

Aandoening

Liver transplantation

Betreft onderzoek met
Mensen

Ondersteuning

Primaire sponsor:	Stichting Lever en Maag Darm onderzoek, Erasmus MC
Secundaire sponsoren:	Chiesi Pharmaceuticals B.V.
Overige ondersteuning:	Chiesi BV

Onderzoeksproduct en/of interventie

Toelichting

Uitkomstmaten

Primaire uitkomstmaten

A composite endpoint of any of three events: sustained (>3 months post transplantation) new onset diabetes mellitus, eGFR < 60 ml/minute/1.73 m2 for >3 months or new onset hypertension.

Toelichting onderzoek

Achtergrond van het onderzoek
Chronic use of tacrolimus is associated with significant side effects including new onset diabetes after transplantation (NODAT), renal impairment, hypertension, hyperlipidemia and tremor and other neurotoxic traits. It is known that toxicity of tacrolimus is (partly) related to higher peak serum blood concentrations in the first year after transplantation. Reducing peak levels without reducing effective inhibition of the immune response could therefore theoretically attenuate the toxic effects of tacrolimus. Envarsus®, a prolonged release formulation of tacrolimus which gives less fluctuation of whole-blood tacrolimus concentrations and requires lower dosage for similar systemic tacrolimus exposure has the potential to lower the toxic effects of tacrolimus and decrease the amount of metabolic side effects, as compared to the current standard, Advagraf®.

Inschatting van belasting en risico
As both tacrolimus formulations are approved for this indication and the active drug on both formulations is the same, this study is considered a low risk study. The anticipated benefit of this study is that it may lead to lowering of the metabolic side effects, nefrotoxicity and neurotoxicity of long term tacrolimus treatment.

Contactpersonen

Publiek

Wetenschappelijk

Deelname eisen

Leeftijd
Volwassenen (18-64 jaar)
Volwassenen (18-64 jaar)
65 jaar en ouder

65 jaar en ouder

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- First liver transplantation

- Age between 18 and 75

- Using immediate release tacrolimus

- written informed consent

- Female subject of childbearing potential must agree to practice effective birth control

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- Pregnancy or breast feeding

- eGFR < 30 mL/min/1.73m2

- Systemic infection

- Combined organ transplantation

- Use of a mTOR inhibitor

- Use of other tacrolimus formulations

- Hepatic artery trombosis

- Known allergy to the study drug or any of its components

Onderzoeksopzet

Opzet

Fase onderzoek:	4
Type:	Interventie onderzoek

Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel
Doel:	Behandeling / therapie

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	11-04-2019
Aantal proefpersonen:	106
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Ethische beoordeling

Goedgekeurd WMO

Datum:	01-03-2019
Soort:	Eerste indiening
Toetsingscommissie:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 55491
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL7372
NTR-old	NTR7580
CCMO	NL67040.078.18
EudraCT	2018-002856-34
OMON	NL-OMON55491

Resultaten

Datum resultaten gemeld: 27-10-2023

Totaal aantal deelnemers: 106

Samenvatting resultaten
Significantly less liver transplant recipients reached the composite primary endpoint at 12 months in the LCP-tacrolimus group compared to the extended-release tacrolimus group (50.9%, 95%-CI 37.9% - 63.9% versus 71.2%, 95%-CI 57.7% - 81.7%, p=0.005). This significant difference was observed both in the intention-to-treat and in the per protocol analysis. No differences in rejection rate, graft and patient survival were found. In conclusion, LCP-tacrolimus has a more favorable cardiovascular risk profile and results in less chronic kidney disease as compared to ER-tacrolimus in the first year after liver transplantation with comparable efficacy.

Karakteristieken onderzoekspopulatie
106 included were adult patients, between 18 and 75 years, after a primary LT.

Deelnemers doorstroom
"A total of 106 patients was included, of whom 52 randomized to the ER-tacrolimus and 54 to the LCP-tacrolimus arm. Most of the patients was transplanted because of HCC (31/106, 29.2%), primary sclerosing cholangitis (18/106, 16.9%) or (non)alcoholic stea

Ongewenste voorvallen
"In total, 160 SAEs were reported: 47.5% (76/160) in the ER-tacrolimus group and 52.5% (84/160) in the LCP-tacrolimus group. SAEs most frequently reported were fever (23.1%, 37/160), cholangitis and bile duct obstruction (10%, 16/160) and infections (10%,

Onderzoeksvariabelen / uitkomstmaten
"In this randomized controlled study, it was observed that LT recipients using LCP-tacrolimus have significantly better clinical outcomes, i.e. lower incidence of CKD, PTDM and new-onset hypertension compared to LT recipients using the ER-tacrolimus at no

Datum eerste publicatie onderzoek
30-06-2023