Immunomonitoring of stable renal transplantation patients

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

Samenvatting

ID

NL-OMON29204

Bron
Nationaal Trial Register

Verkorte titel
CHDR1950

Aandoening

Immunosuppression

Ondersteuning

Primaire sponsor: CHDR
Overige ondersteuning: CHDR

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Pharmacokinetic endpoints
– Tacrolimus whole blood concentrations

– MPA plasma concentrations
– Prednisolone plasma concentration

Pharmacodynamic endpoints
– Proliferation of T cells in stimulated whole blood
– Cytokine production in stimulated whole blood
– T cell activation marker expression in stimulated whole blood
– Circulating regulatory T and B cell subsets

Safety and tolerability endpoints
– Treatment-emergent (serious) adverse events ((S)AEs).
– Concomitant medication
– Clinical laboratory tests

Toelichting onderzoek

Achtergrond van het onderzoek

Kidney transplantation is a successful treatment option for patients with end-stage renal disease. To prevent allograft rejection, renal transplant patients need long-term immunosuppressive therapy with tacrolimus, mycophenolate mofetil (MMF) and prednisolone. The disadvantages of this maintenance treatment regimen, however, is the large intra- and interpatient variability in clinical outcome, especially for tacrolimus. Too little exposure leads to a risk of acute rejection and formation of donor-specific antibodies, while too much exposure leads to an increased risk of infection and nephrotoxicity.
To minimize adverse effects and improve effectiveness of the current treatment regimen, therapeutic drug monitoring (TDM) is routinely
performed. For tacrolimus, the most common method of TDM is measuring pre-dose trough concentration (C0) in whole blood. These
trough concentrations, however, are highly variable and the correlation with clinical outcome is still debatable. TDM is not standardly
performed for MMF and prednisolone treatment, and therapy is usually not individualized. To improve dosing strategies and minimize adverse effects, the current TDM should be optimized. For that reason, we have developed several whole blood-based PD readout measures for the quantification of immunosuppression. These readout measures (PHA-induced cytokine production, T cell proliferation and T cell activation marker expression) were previously tested in healthy volunteers and have shown to be suitable for quantification of the immunosuppressive effect of a single dose of tacrolimus, cyclosporine A and mycophenolic acid. Besides the high variability and small therapeutic window of tacrolimus, the patient’s age also affects clinical outcome. Elderly transplantation patients are generally prescribed lower doses of tacrolimus, while the dose-normalized C0 concentrations are higher than in the younger patients. Moreover, aging causes the number of effector lymphocytes to decrease, which result in a reduced immune response to the transplanted organ. These age-related changes are one of the reasons that elderly transplant recipients are more likely to

suffer from side effects of over-immunosuppression, such as diabetes and de novo malignancies. To investigate if the relationship between drug concentration and cellular PD measures is different in older patients, both young (<40 years) and elderly (>60 years) kidney transplantation patients will be included in this study.

Doel van het onderzoek

To improve dosing strategies and minimize adverse effects, the current TDM should be optimized. We advocate that PD-based instead of PK-based therapeutic drug monitoring, by using clinically relevant immune tests to quantify the immunosuppressive state of the individual patient, may improve the clinical outcome. For that reason, we have developed several whole blood-based PD readout measures for the quantification of immunosuppression. These readout measures (PHA-induced cytokine production, T cell proliferation and T cell activation marker expression) were previously tested in healthy volunteers and have shown to be suitable for quantification of the immunosuppressive effect of a single dose of tacrolimus, cyclosporine A and mycophenolic acid. In the current clinical study we aim to evaluate if the selected PD readout measures are also suitable for immunomonitoring of renal transplantation patients receiving long-term triple immunosuppressive therapy.

Onderzoeksopzet

Day 1

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)

- Male or female kidney transplantation patients, 18 to 45 years of age or >60 years of age
- Patients that have undergone a kidney transplantation > 2 years before study start
- Patients on maintenance immunosuppression with low-dose prednisolone, MMF and tacrolimus adjusted to target trough levels.
- Patients that have the ability to communicate well with the Investigator in the Dutch language and willing to comply with the study restrictions

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- The use of any medication other than the patient’s standard treatment within less than 5 half-lives prior to study participation, if the investigator judges that it may interfere with the study objectives;
- The use of immunosuppressive or immunomodulatory medication, other than the patient’s standard treatment, within 3 months before study participation;
- Any known factor, condition, or disease that might interfere with study conduct or interpretation of the results, in the opinion of the investigator.
- Unwillingness or inability to comply with the study protocol for any other reason.

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:	Werving nog niet gestart
(Verwachte) startdatum:	22-06-2020
Aantal proefpersonen:	20
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Ja

Toelichting
All IPD that underlie results in a publication and study report can be shared. This IPD will always be fully anonymized and includes individual concentration-effect relationships and individual correlations between different effect measures.

Ethische beoordeling

Positief advies

Datum:	18-05-2020
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 55264
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL8639
CCMO	NL73304.056.20
OMON	NL-OMON55264

Resultaten

Samenvatting resultaten
N.A.