Randomized, placebo-controlled study to immunomonitor Mycophenolate mofetil (MMF) in healthy volunteers

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Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON28654

Bron
NTR

Verkorte titel
CHDR1902

Aandoening

Renal transplantation

Ondersteuning

Primaire sponsor: CHDR
Overige ondersteuning: CHDR

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Pharmacokinetic endpoints:
- Whole blood cyclosporine A levels
- Cellular cyclosporine A levels

Pharmacodynamic endpoints:
- T cell proliferation
- Cytokine production
- IMPDH activity

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 immunosuppression that is mostly calcineurin inhibitor-based. These calcineurin inhibitors are combined with Mycophenolate mofetil (MMF).
Although most other medications used as maintenance immunotherapy after solid organ transplantation are dosed to achieve target concentration ranges in plasma or blood, MMF is usually administered at a fixed dose, and thus not individualized. However, a too low dose 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. Because of the large pharmacodynamic intra- and interpatient variability, therapeutic drug monitoring should be routinely performed to maintain optimal drug concentration and minimize the risk of overexposure.
For this reason, quantitative measures for optimizing MMF dose and regimen are required to minimize the risk of toxicity and improve long-term allograft survival. Immune-monitoring of transplantation patients, using functional immune tests, can assist in finding the optimal dosing strategy. In this study we therefore aim to identify clinically relevant immune tests for quantification of immunosuppression, which can help understanding the inter- and intra-patient variability in the response to MMF treatment.

Doel van het onderzoek

This study aims to apply state-of-the-art immune tests quantifying the immunosuppressive state in individuals, and the relationship between these pharmacodynamic tests and the pharmacokinetic profile (in whole blood and intracellular) after a single dose of MMF.

Onderzoeksopzet

-1h, 0.5h, 1h, 2h, 3h, 4h, 24h, 8d

Onderzoeksproduct en/of interventie

Mycofenolaat mofetil

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Willing to give written informed consent and willing and able to comply with the study protocol;
2. Healthy male or female subjects, 18 to 55 years of age (inclusive) at screening. The health status is verified by absence of evidence of any clinical significant active or uncontrolled chronic disease following a detailed medical history and a complete physical examination including vital signs, laboratory measurements and 12-lead ECG;
3. Body mass index (BMI) between 18 and 30 kg/m2, inclusive, and with a minimum bodyweight of 50 kg;
4. All women of child bearing potential and all males must practice effective contraception during the study and be willing and able to continue contraception for at least 90 days after their last dose of study treatment;
5. All women of child bearing potential must be willing to take a pregnancy test at screening, check-in and follow-up. Men cannot donate any sperm during the study and for three months after EOS.
6. Has 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)

1. Any disease associated with immune system impairment, including auto-immune diseases, HIV, any confirmed history of severe allergic reaction and transplantation patients;
2. Evidence of any other active or chronic disease or condition that could interfere with, or for which the treatment of might interfere with, the conduct of the study, or that would pose an unacceptable risk to the subject in the opinion of the investigator (following a detailed medical history, physical examination, vital signs (systolic and diastolic blood pressure, pulse rate, body temperature) and 12-lead electrocardiogram (ECG) at screening or pre-dose. Minor deviations from the normal range may be accepted, if judged by the Investigator to have no clinical relevance;
3. Clinically significant abnormalities, as judged by the investigator, in laboratory test results (including hepatic and renal panels, complete blood count, chemistry panel and urinalysis) at screening or pre-dose. In the case of uncertain or questionable results, tests performed during screening may be repeated before randomization to confirm eligibility or judged to be clinically irrelevant for healthy subjects;
4. Positive Hepatitis B surface antigen (HBsAg), Hepatitis C antibody (HCV Ab), or human immunodeficiency virus antibody (HIV Ab) at screening, or other known infection requiring antibiotic therapy within the last three months prior to the study;
5. Use of any medications (prescription or over-the-counter [OTC]), within 21 days of study drug administration, or less than 5 half-lives (whichever is longer). Exception is paracetamol (up to 4 g/day). Other exceptions will only be made if the rationale is clearly documented by the investigator;
6. Received immunosuppressive or immunomodulatory medication within 30 days prior to enrolment or planned to use during the course of the study;
7. Use of any vitamin, mineral, herbal, and dietary supplements within 7 days of study drug administration, or less than 5 half-lives (whichever is longer). Exceptions will only be made if the rationale is clearly documented by the investigator;
8. Participation in an investigational drug or device study within 3 months prior to first dosing;
9. History of abuse of addictive substances (alcohol, illegal substances) or current use of more than 14 units alcohol per week, drug abuse, or regular user of sedatives, hypnotics, tranquillisers, or any other addictive agent;
10. Positive test for drugs of abuse at screening or pre-dose;
11. Alcohol will not be allowed from at least 24 hours before screening and every return visit, and during unit stay;
12. Smoking cigarettes (or equivalent) and/or using nicotine based products within 3 months prior to study drug administration;
13. Is demonstrating excess in xanthine consumption (more than eight cups of coffee or equivalent per day) from 7 days prior to the first dose of the study drug until EOS;
14. Any confirmed significant allergic reactions (urticaria or anaphylaxis) against any drug, or multiple drug allergies (non-active hay fever is acceptable);
15. Loss or donation of blood over 500 mL within three months prior to screening or intention to donate blood or blood products during the study and up until 6 weeks after the EOS;
16. If a woman, pregnant, or breast-feeding, or planning to become pregnant during the

study;
17. Any known factor, condition, or disease that might interfere with treatment compliance, study conduct or interpretation of the results such as drug or alcohol dependence or psychiatric disease.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Enkelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	24-06-2019
Aantal proefpersonen:	16
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:	17-06-2019
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 48101
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL7804
CCMO	NL69579.056.19
OMON	NL-OMON48101

Resultaten