Immunomonitoring of Cyclosporin A in healthy volunteers

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Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON23897

Bron
Nationaal Trial Register

Verkorte titel
CHDR1860

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 activation
- T cell proliferation
- Cytokine production

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. A calcineurin inhibitor (CNI) that has been widely used in the past, but still used as immunosuppressive therapy today, is Cyclosporin A (CsA). One of the disadvantages of CNI-treatment is the small therapeutic window. 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.
For this reason, quantitative measures for optimizing CNI regimen are required to minimize the risk of toxicity and improve long-term allograft survival. By immune-monitoring transplantation patients, using functional immune tests, the immunosuppressive state can help finding the right 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 intrapatient variability in the response to Cyclosporin 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 Cyclosporin A.

Onderzoeksopzet

-1h, 1h, 2h, 6h, 24h, 8d

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 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. 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. 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
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).
6. Received immunosuppressive or immunomodulatory medication within 30 days prior to enrollment 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).
8. Use of oral hormonal contraception within 30 days prior to enrollment or planned to use during the course of the study;
9. Any nutrients known to modulate CYP enzyme activity, such as grapefruit(juice), bitter lemon or tonic within 3 days of study drug administration;
10. Participation in an investigational drug or device study within 3 months prior to first dosing;
11. 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;
12. Positive test for drugs of abuse at screening or pre-dose;
13. Alcohol will not be allowed from at least 24 hours before screening and every return visit;
14. Smoking cigarettes (or equivalent) and/or using nicotine based products within 3 months prior to study drug administration;
15. 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;
16. Any confirmed significant allergic reactions (urticaria or anaphylaxis) against any drug, or multiple drug allergies (non-active hay fever is acceptable);
17. 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;
18. If a woman, pregnant, or breast-feeding, or planning to become pregnant during the study;
19. 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 gestopt
(Verwachte) startdatum:	04-03-2019
Aantal proefpersonen:	16
Type:	Werkelijke 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:	14-03-2019
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	NL7601
CCMO	NL68839.056.19

Resultaten