Research into the effects of Tacrolimus on the immune system in healthy volunteers

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Tacrolimus (FK506) is the main immunosuppressant that is prescribed after kidney transplantation. One of the disadvantages of Tacrolimus is the small therapeutic window. In transplantation patients therapeutic drug monitoring is routinely performed...

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

Samenvatting

ID

NL-OMON20026

Bron
NTR

Verkorte titel
Immunomonitoring of tacrolimus

Aandoening

Kidney transplantation, niertransplantatie

Ondersteuning

Primaire sponsor: Centre for Human Drug Research (CHDR)
Overige ondersteuning: Centre for Human Drug Research (CHDR)

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Pharmacokinetic endpoints
- Whole blood tacrolimus levels
- Cellular tacrolimus levels in T-cells and/or PBMCs

Pharmacodynamic endpoints
Drug effects will be monitored in vitro and ex vivo by:
- Calcineurin activity
- T cell proliferation
- T cell activation (cell surface markers)
- T cell activation (cytokine release)

Toelichting onderzoek

Achtergrond van het onderzoek

Tacrolimus (FK506) is the main immunosuppressant that is prescribed after kidney transplantation. One of the disadvantages of Tacrolimus is the small therapeutic window, which makes it difficult to maintain optimal drug concentrations in patients. In this study we therefore aim to identify clinically relevant immune tests for quantification of immunosuppression, which can help predict the right dose of tacrolimus. With these immune tests we quantify T cell proliferation, expression of T cell activation markers and cytokine production. Furthermore, the whole blood tacrolimus concentration is compared to intracellular drug concentrations and correlated to the functional immune tests.

Doel van het onderzoek

Tacrolimus (FK506) is the main immunosuppressant that is prescribed after kidney transplantation. One of the disadvantages of Tacrolimus is the small therapeutic window. In transplantation patients therapeutic drug monitoring is routinely performed to maintain optimal drug concentrations. However, toxicity and rejection still occur in patients with an acceptable drug concentration. For this reason, quantitative measures for optimizing Tacrolimus regimen are required to improve long-term allograft survival. By immune-monitoring transplantation patients, using functional immune tests, the immunosuppressive state can help optimizing dosing strategies. In this study we therefore aim to identify clinically relevant immune tests for quantification of immunosuppression, which can help predict the right dose of tacrolimus.

Onderzoeksopzet

- Screening up to 42 days before study start

- Admission at day -1

- Dosing at day 0

- Return visits at day 2 and day 4

- End of study visit at day 8

Onderzoeksproduct en/of interventie

0.05 mg/kg Prograf (Tacrolimus)

Contactpersonen

Publiek

A.E. in 't Veld
Zernikedreef 8

Leiden 2333 CL
The Netherlands
+31 (0)71 7517164

Wetenschappelijk

A.E. in 't Veld
Zernikedreef 8

Leiden 2333 CL
The Netherlands
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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 at screening;

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 grapefruit(juice), bitter lemon or tonic within 3 days of study drug administration;

9. Participation in an investigational drug or device study within 3 months prior to first dosing;

10. 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;

11. Positive test for drugs of abuse at screening or pre-dose;

12. Alcohol will not be allowed from at least 24 hours before screening and every return visit;

13. Smoking cigarettes (or equivalent) and/or using nicotine based products within 3 months prior to study drug administration;

14. Is demonstrating excess in xanthine consumption (more than eight cups of coffee or equivalent per day);

15. Any confirmed significant allergic reactions (urticaria or anaphylaxis) against any drug, or multiple drug allergies (non-active hay fever is acceptable);

16. 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;

17. If a woman, pregnant, or breast-feeding, or planning to become pregnant during the study;

18. 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:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	04-07-2018
Aantal proefpersonen:	12
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	02-08-2018
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	NL7221
NTR-old	NTR7420
Ander register	: CHDR1644

Resultaten