Model Informed preciSion doSIng tO iNdividualise and optimize pharmacotherapeutic treatment (MISSION) - Appendix 1: Prospective evaluation of Model informed precision dosing (MIPD) for tacrolimus and mycophenolic acid in paediatric patients with a kidney disease

Published: 13-02-2024
Last updated: 02-12-2024

Overall objective:To improve the existing drug prescribing and treatment monitoring process.Objective appendix 1: To prospectively evaluate the predictive performance of the MIPD strategy for tacrolimus and mycophenolic acid in paediatric patients...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal disorders (excl nephropathies)
Study type	Observational invasive

Summary

ID

NL-OMON56572

Source
ToetsingOnline

Brief title
MISSION

Condition

- Renal disorders (excl nephropathies)

Synonym
kidney diseases

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Health-Holland,InsightRX

Intervention

Keyword: Model informed precision dosing, mycofenolic acid, pediatrics, tacrolimus

Outcome measures

Primary outcome

Appendix 1:

• The bias and precision calculated as Mean Prediction Error (MPE) and Root

Mean Squared Percentage Error (RMSE) and written in their relative values for

easy interpretation (%MPE and %RMSE).

• 95 percent confidence intervals (95% CI*s) of the MPE and the RMSE

• Target attainment calculated as the percentage of cases in which the

subsequent AUC lies within the target range.

• Model fit calculated as percentage of poor, intermediate and good fit.

Secondary outcome

Appendix 1:

NA

Study description

Background summary

Despite the fact that patients can differ greatly from each other, most drugs are dosed according to a *one-size-fits-all* approach. This approach could result in risks for undertreatment as well as unnecessary adverse effects because of substantial between-patient variability in drug pharmacokinetics (PK). This highlights the necessity of tailoring the drug dose to individual needs for more precise therapy. In current practice, therapeutic drug monitoring (TDM) is used for drugs with a narrow therapeutic index, where small changes in drug concentrations can significantly affect the drug's efficacy and toxicity. In contrast to regular TDM, model-Informed precision dosing (MIPD) uses pharmacometric models, simulation, and Bayesian forecasting tools designed to predict the optimal dose of a drug for a patient, taking individual demographic and clinical patient characteristics into account. This leads to a more individualised and precise dose advice. Plenty of studies suggest benefits of the use of MIPD, however implementation of MIPD in clinical practice is lagging behind. Therefore, we aim to develop, implement and evaluate MIPD in clinical practice for different indications, populations and drugs.
In the first project (appendix 1), we will focuss on tacrolimus and mycoophenolic acid in peadiatric patients with a kidney disease.

Study objective

Overall objective:To improve the existing drug prescribing and treatment monitoring process.
Objective appendix 1: To prospectively evaluate the predictive performance of the MIPD strategy for tacrolimus and mycophenolic acid in paediatric patients with a kidney disease

Study design

Appendix 1:
This is a prospective observational study of MIPD in clinical practice for kidney disease patients using tacrolimus and mycophenolic acid in Radboudumc. Dose individualization in these patients using the InsightRX platform is performed as standard care, meaning that the selected models and drug levels measured at t=0, t=1 and t=2 hours will be used to calculate the AUC. Based on the estimated AUC, the pharmacist gives a dose recommendation to the physician, who can then modify the dosage of mycophenolic acid or tacrolimus. The selected dose and the measured MPA and tacrolimus concentrations will be used to predict a future AUC.
In this study an extra AUC will be measured; At the regular follow-up visit, usually after 1 to 5 months , another 3 samples (t=0, t=1 and t=2 hours) will be analysed. We will compare the predicted AUC with the newly estimated AUC (based on the 3 obtained samples) by calculation of the root mean squared error (RMSE) and the mean prediction error (MPE). In addition, we will calculate in which percentage of cases the subsequent AUCs lies within the target range. The target AUC*s are in accordance with the local guidelines.

Study burden and risks

Appendix 1:
Concerning the single intervention of the study is blood sampling, the risks are considered as negligible.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert Grooteplein-zuid route 864 10
Nijmegen 6500HB
NL
Scientific
Radboud Universitair Medisch Centrum

Geert Grooteplein-zuid route 864 10
Nijmegen 6500HB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

-Kidney disease patients using tacrolimus and/or mycophenolic acid
-Age between 0 and 18 yearse- judgement of clinician

Exclusion criteria

- Incapacitated patients
- No informed consent

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-05-2024
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	13-02-2024
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	25-09-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL85390.091.23