Avoiding tacrolimus under- and overexposure by using a new dosing algorithm for pediatric renal transplant recipients

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To minimize the occurrence of sub-therapeutic and supra-therapeutic C0 of tacrolimus on day 3, 7 and 10 after transplantation by basing the starting dose of tacrolimus on a dosing algorithm, rather than the standard bodyweight-only-based approach....

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON44606

Source
ToetsingOnline

Brief title
Tacrolimus starting dose in children based on an algorithm

Condition

- Other condition

Synonym
kidney transplantation

Health condition

Voorkomen afstoting na niertransplantatie

Research involving

Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Subsidie van Stichting de Merel

Intervention

Keyword: child, kidney, tacrolimus, transplantation

Outcome measures

Primary outcome

The main study parameter is the percentage of children within the target C0

range of tacrolimus on day 3, 7 and 10 after kidney transplantation.

Secondary outcome

Secondary study endpoints of the study are:

* The proportion of patients with markedly supra- (>20 ng/mL) or

sub-therapeutic (<5 ng/mL) tacrolimus C0 on day 3 after transplantation.

* The time to reach the target C0 (10-15 ng/mL).

* Incidence of BPAR and (serious) adverse events within the first 10 days after

transplantation.

Study description

Background summary

Bodyweight-based dosing of the immuosuppressant tacrolimus in children is considered standard care, even though the available evidence is thin. Other factors including ethnicity, age, genotype (CYP3A5), co-medication and haematocrit influence the clearance of tacrolimus significantly. Even with therapeutic drug monitoring (TDM), it can take up to 14 days to reach the target tacrolimus predose concentration (C0). Underexposure to tacrolimus is associated with rejection and overexposure to the drug with toxicity. We have

developed a dosing algorithm in our population which bases the starting dose of tacrolimus on bodyweight, CYP3A5 genotype and donor type. The hypothesis is that more patients will be within the target C0 range on day 3 after transplantation using the dosing algorithm.

Study objective

To minimize the occurrence of sub-therapeutic and supra-therapeutic C0 of tacrolimus on day 3, 7 and 10 after transplantation by basing the starting dose of tacrolimus on a dosing algorithm, rather than the standard bodyweight-only-based approach. More specifically, we will investigate whether a tacrolimus starting dose based on the algorithm will lead to a sufficient percentage of patients being within the tacrolimus target C0 on days 3, 7 and 10 after transplantation, w.r.t. the percentage found in one historic control group of patients who have received a standard starting dose of tacrolimus; in that case an international randomized trial might be an option.

Study design

Prospective, multi-centre, open-label, therapeutic intervention study

Intervention

All participants will receive the tacrolimus starting dose based on a dosing algorithm which bases the dose on bodyweight, CYP3A5 genotype and donor type, rather than the standard bodyweight-based dose.

Study burden and risks

There is no extra burden for the included children.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Age 2-18 years old
* Patients receiving a kidney from a blood group AB0-compatible donor
* Patients who will receive tacrolimus as part of the initial immunosuppressive therapy
* Signed written informed consent

Exclusion criteria

* Recipients of a non-renal organ transplant at the same occasion
* Recipients receiving immunosuppressive therapy (except steroid treatment) within the preceding 28 days.
* Recipients using medication known to have a relevant pharmacokinetic interaction with tacrolimus

Study design

Design

Study phase:	4
Study type:	Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-11-2017
Enrollment:	28
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Modigraf 0.2 mg, granules for oral suspension
Generic name:	Modigraf 0.2 mg, granules for oral suspension
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Modigraf 1 mg, granules for oral suspension
Generic name:	Modigraf 1 mg, granules for oral suspension
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Prograft capsules, 0.5 mg
Generic name:	tacrolimus capsules 0.5 mg
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Prograft capsules, 1 mg
Generic name:	tacrolimus capsules, 1 mg
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Prograft capsules, 5 mg
Generic name:	tacrolimus capsules, 5 mg
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	10-08-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-09-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-12-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-12-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-12-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 27765

Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2017-001681-24-NL
CCMO	NL61720.078.17
OMON	NL-OMON27765