Determining the stability of TRECs - an important measure for thymic activity.

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Measuring the stability (and thereby half-life) of TRECs.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immunodeficiency syndromes
Study type	Observational invasive

Summary

ID

NL-OMON37746

Source
ToetsingOnline

Brief title
TREC study

Condition

- Immunodeficiency syndromes

Synonym
T cell dynamics during immune suppression, TREC stability

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: NWO

Intervention

Keyword: immune suppression, T cell division, TREC

Outcome measures

Primary outcome

The stability (and thereby half-life) of TRECs.

Secondary outcome

The changes in telomere length of naive T cells in patients treated with the

immune suppressives mycophenolate mofetil and/or azathioprine.

Study description

Background summary

T cell receptor excision circles (TRECs) arise as a by-product during VDJ recombination of T cell receptors in the thymus. TRECs are an important parameter in many immunological studies to measure T cell production by the thymus, as well as peripheral T cell division. It is generally assumed that TRECs are extremely stable and remain present in T cells and their daughter cells for years - or even lifelong. This assumption is crucial for the interpretation of TREC data. However, the half-life of TRECs has never been experimentally determined because this is impossible when T cells undergo cell division. Therefore, we are planning to measure TRECs in patients using immune suppressives which inhibit lymphocyte division.

Study objective

Measuring the stability (and thereby half-life) of TRECs.

Study design

This is a cross-sectional, non-interventional study with invasive procedures. During the study, a blood sample (80 ml in total) will be drawn from each subject. From this sample, naive T cells will be isolated. From the DNA of these cells, both the TREC content and telomere length will be determined using quantitative (q)PCR. Telomere length is a control parameter, since a decrease in TREC content could either derive from residual cell division (thereby also decreasing telomere length), or by intrinsic instability of TRECs.
Cell lysates will be used to measure telomerase activity. Telomerase activity leads to enhanced telomere length, while this would decrease during cell

division.

Study burden and risks

A blood volume of 70 ml, and one red top tube will be drawn (80 ml in total). If it is impossible to combine this visit with a standard visit to the UMC Utrecht, an extra visit will have to planned for this study. This is a light burden. Dialysis patient visit the UMC Utrecht on a regular basis and therefore will not need an additional visit for this study.
The risk of the single blood draw is very low. For dialysis patients this blood draw does not come with an additional burden, since the blood will be drawn via the dialysis needle.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

kidney transplantation(s);
longterm (>10 years) immune suppression by mycophenolate mofetil and/or azathioprine

Exclusion criteria

chronic graft rejection;
thymectomy;
T cell defect(s) prior to transplantation

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-05-2013
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	25-05-2012
Application type:	First submission

Review commission:	METC NedMec
Approved WMO Date:	10-08-2012
Application type:	Amendment
Review commission:	METC NedMec

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	NL38931.041.12