T cell homeostasis after ATG induced lymphocytopenia in renal transplant patients; studied through in vivo 2H2O labeling

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To get more insight into the T cell homeostasis in lymfocytopenic, ATG treated patients and normocytopenic patients treated with standard maintenance immunosuppressive drug therapy.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	White blood cell disorders
Study type	Observational invasive

Summary

ID

NL-OMON35541

Source
ToetsingOnline

Brief title
T cell homeostasis during lymphocytopenia

Condition

- White blood cell disorders
- Immune disorders NEC
- Genitourinary tract disorders NEC

Synonym
low white blood cells, lymphocytopenia

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: 2H2O, ATG, Homeostasis, T cell

Outcome measures

Primary outcome

The amount of 2H2O incorporated into the DNA within the naïve CD4+ and CD8+ T cells will be measured. With special mathematical formulas the production rate and half-life of cells can be calculated. T cell homeostasis in the ATG treated patients, versus the standard immunosuppressive treated patients and versus the healthy volunteers will be analysed through comparing production rates and half-life of the naïve T cells. For that purpose we will use methods that have been described in the literature, and we will collaborate with these same investigators.

Secondary outcome

Production rates and half-life of the CD31+ CD4 naive T cells.

Study description

Background summary

Patients who have received a renal allograft are treated with maintenance immuosuppressive drug therapy, consisting of prednisolone, tacrolimus and mycophenolate mofetil. When their clinical course is complicated by an acute humoral graft rejection, they are treated with a course of Anti-Thymocyte Globulin for 14 days. As a consequence, the T cell pool rapidly becomes depleted. This T cell depletion is known to show a slow recovery. Especially the CD4+ naïve cells fail to recover completely, whereas the CD8+ naïve cells

very slowly recuperate to pre-treatment values. A possible explanation for this difference in recovery might be that the CD4+ naïve T cells rely more on the thymus and CD8+ naïve cells rely more on homeostatic proliferation. In previous studies with 2H2O labelling of lymphocytes in healthy volunteers however, CD4+ naïve T-cells were shown to have a higher production rate than CD8+ naïve T cells.
Through in vivo labelling of lymphocytes with 2H2O , we believe to discover more about the T cell - and especially naïve T cell homeostasis in the lymphopenic situation after ATG treatment. By in vivo labelling the cells of renal transplant patients who receive standard maintenance immunosuppressive therapy and who were not treated with ATG, we can control for any effect of standard maintenance immunosuppressive drug therapy on the T-cell homeostasis.

Study objective

To get more insight into the T cell homeostasis in lymfocytopenic, ATG treated patients and normocytopenic patients treated with standard maintenance immunosuppressive drug therapy.

Study design

Participants will be labelled with 2H2O for a period of 9 weeks, with a downlabelling period of 21 weeks. Using gas chromatography mass spectrometry, 2H2O within different subsets of sorted T cells will be measured.

Study burden and risks

Blood and urine samples will be collected before 2H2O labelling, at week 2 or 3, week 5 or 6, week 9, week 11, week 14, week 18 and week 30 after labelling. This will in total be 8 x 56ml blood.
According to literature and previous studies, in vivo isotope labelling with 2H2O is harmless. Patients are admitted into the hospital for observation during initial oral administration of 2H2O, because rare adverse effects of transient vertigo or dizziness have been reported

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
1105 AZ Amsterdam
NL
Scientific

Academisch Medisch Centrum

Meibergdreef 9
1105 AZ Amsterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Renal transplantation patients treated with standard maintenance immunosuppressive therapy who were treated with ATG because of acute humoral graft rejection and renal transplantation patients treated with standard maintenance immunosuppressive therapy alone. Healthy volunteers, without relevant medical history.

Exclusion criteria

Patients with intercurrent medical problems

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial

Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-10-2011
Enrollment:	9
Type:	Actual

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL28386.018.09