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# Immunmonitoring in kidney transplant recipients

| Submission date | Recruitment status | [_] Prospectively registered |
|---|---|---|
| 23/01/2017 | No longer recruiting | [_] Protocol |
| **Registration date** | **Overall study status** | [_] Statistical analysis plan |
| 26/01/2017 | Completed | [_] Results |
| **Last Edited** | **Condition category** | [_] Individual participant data |
| 26/01/2017 | Urological and Genital Diseases | [_] Record updated in last year |

## Plain English summary of protocol

Background and study aims
People who receive a kidney transplant need to take medication that suppresses the body's immune system (the body's defense mechanism) in order to make sure their body does not reject the new kidney. These medications, known as immunosuppressant drugs, can lead to serious side effects such as infections and increases in cardiovascular risk (risk of heart attack or stroke). In order to help kidney transplant patients, the monitoring of immunosuppressive medication needs to be improved. New tools have been developed in order to monitor how well the medication works as the standard monitoring tools are not able to directly measure the effects of the medication in individual patients. The aim of this study is to compare the normal method of monitoring immunosuppressive medication (cyclosporin A (CsA)) to the new monitoring tool to see if it improves patient's health and lowers their cardiovascular risk.
Who can participate?
Adults who have received a kidney transplant and are receiving immunosuppressive medication

What does the study involve?
Participants are randomly allocated to one of two groups. The first group receives standard monitoring of their immunosuppressive medication CsA. This includes a blood test done prior to taking the medication in order to measure the amount of CsA found in the blood. The second group receives the new monitoring process, which includes a blood test done prior to taking the medication and again two hours later in order to compare specific markers in the blood to see how well CsA is working. At the start of the study and again after six months, participants have their cardiovascular risk measured. At the start of the study and again after one, three and six months, participants have blood tests to check for signs of organ rejection.

What are the possible benefits and risks of participating?
There are no direct benefits of participants however it can help improve immunosuppressive medications for them in the future. There are no notable risks to participants other than discomfort from blood tests.

Where is the study run from?
Renal Center Heidelberg (Germany)

When is the study starting and how long is it expected to run for?
August 2011 to December 2014

Who is funding the study?
Renal Center Heidelberg (Germany)

Who is the main contact?
Dr Claudia Sommerer

# Contact information

### Type(s)
Scientific

### Contact name
Mrs Claudia Sommerer

### Contact details
University Hospital Heidelberg
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# Additional identifiers

### Clinical Trials Information System (CTIS)
2011-003547-21

### Protocol serial number
RCHD–CsA1004

# Study information

### Scientific Title
A randomized open-label trial to evaluate the cardiovascular risk in stable renal allograft recipients on a ciclosporin A (CsA) based regimen monitored either by residual expression of nuclear factor of activated T-cells (NFAT) – regulated genes or CsA trough levels

### Acronym
The CIS Study

### Study objectives
Monitoring of ciclosporin A therapy by residual nuclear factor of activated T-cell (NFAT)-regulated gene expression (RGE) is superior to standard C0 monitoring in terms of pulse wave velocity, an established sensitivity marker for the assessment of cardiovascular risk.

### Ethics approval required

Old ethics approval format

## Ethics approval(s)
Independent Ethics Committee of Institution University Hospital Heidelberg Ethikkommission, 31 /05/2013, ref: AFmo-622/2012

## Study design
Single-centre prospective randomised controlled parallel-group trial

## Primary study design
Interventional

## Study type(s)
Other

## Health condition(s) or problem(s) studied
Renal transplantation

## Interventions
Participants are enrolled consecutively after providing written informed consent. Randomization is performed in a 1:1 ratio by a web-based validated randomization tool and are allocated to one of two groups. All participants receive ciclosporin A (CsA) and mycophenolic acid in the standard dosage.

Standard Monitoring Group:
Participants receive CsA orally, at a dose adjusted to reach the specified exposure target CsA CO levels of 80 to 150 µg/L. This therapy is monitored by the CsA CO monitoring (80-150 ng/ml), which means blood samples are taken from participants in the morning before medication is ingested and the level of CsA concentration is measured. Adjustment to the CsA dosages are made if necessary at each study visit (baseline, month 1, month 3, month 6 and end of study) due to adverse events.

Investigation Group:
Participants receive CsA orally at a dose adjusted to to the results of the new monitoring tool. The CsA therapy is monitored by activated T-cell (NFAT)-regulated gene expression (RGE) of 15 to 30%. The expression of the NFAT-regulated genes (interleukin 2, granulocyte-macrophage colony stimulating-factor, interferon- y) is determined by qRT-PCR at CsA CO and C2. This means that blood is taken in the morning prior to the medication being ingested and then two hours after. Cytokine gene expression is measured in these samples. Adjustment to the CsA dosages are made if necessary at each study visit (baseline, month 1, month 3, month 6 and end of study) due to adverse events.

Following the study, participants receive CsA according to their local center practice. All participants are followed regularly at the end of the study.

## Intervention Type
Other

## Primary outcome(s)
Cardiovascular risk is assessed by measuring pulse wave velocity by measuring pulse wave velocity by SphygmoCor at baseline and at 6 months.

### Key secondary outcome(s))
1. Aortic pulse pressure and central blood pressure is measured using SphygmoCor at baseline and 6 months
2. Blood pressure is measured using a sphygmomanometer at baseline and 6 months
3. Glucose is measured by enzymatic method at baseline and 6 months
4. Cholesterol (LDL and HDL cholesterol) is enzymatic method measured by at baseline and 6 months
5. Triglyceride is measured by enzymatic method at baseline and 6 months
6. S-creatinine is measured by enzymatic method at baseline and 6 months
7. Proteinuria is measured by enzymatic method at baseline and 6 months
8. Myocardial infarction is assessed through reviewing patient's records at baseline, 1 month, 3 months, and 6 months
9. Apoplexy is assessed through reviewing patient's records at baseline, 1 month, 3 months, and 6 months
10. Peripheral arterialocclusive disease rate is assessed by reviewing patients records at baseline, 1 month, 3 months, and 6 months
11. Ciclosporin A induced side effects are assessed through reviewing patient's records at baseline, 1 month, 3 months, and 6 months
12. Incidence and severity of Adverse Events (AEs) and Serious Adverse Events (SEAs) are assessed by reviewing patient notes at baseline, 1 month, 3 months, and 6 months
13. Renal allograft function is assessed by measuring S-creatinine (enzymatic method, standard lab) and 7-MDRD formula at baseline, 1 month, 3 months, and 6 months
14. Biopsy proven acute rejections (classified by BANFF criteria), graft loss, death, and loss-to-follow-up are assessed by reviewing patient notes at baseline, 1 month, 3 months, and 6 months

### Completion date
31/12/2014

## Eligibility

### Key inclusion criteria
1. Over the age of 18 years old
2. Received a renal allograft from a deceased or living donor at least six months prior to study entry
3. Stable renal allograft function, defined as serum S-creatinine ≤ 3.•5 mg/dL and Δ serum S-creatinine ≤ 30% during the previous last three months
4. Receiving CsA microemulsion, mycophenolic acid, and steroids

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Adult

### Lower age limit
18 years

**Sex**
All

**Key exclusion criteria**
1. History of biopsy-proven acute rejection classified as Banff grade ≥ II
2. Chronic active antibody-mediated rejection
3. Chronic T-cell mediated rejection prior to enrollment

**Date of first enrolment**
23/10/2013

**Date of final enrolment**
01/06/2014

# Locations

**Countries of recruitment**
Germany

**Study participating centre**
**University Hospital Heidelberg**
Department of Nephrology
Renal Center Heidelberg
Im Neuenheimer Feld 162
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69120

# Sponsor information

**Organisation**
Renal Center Heidelberg

**ROR**
https://ror.org/013czdx64

# Funder(s)

**Funder type**
Hospital/treatment centre

**Funder Name**

# Results and Publications

### Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will made available at a later date.

### IPD sharing plan summary
Not expected to be made available