

# Do Serum Alemtuzumab Concentrations Predict Donor T Cell Chimerism after Non-Myeloablative Matched Sibling Donor Stem Cell Transplantation in Sickle Cell Disease Patients? (PREDICT study)

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To investigate whether serum alemtuzumab concentrations are predictive of the robustness of engraftment in SCD patients undergoing a matched sibling donor transplantation with alemtuzumab/TBI conditioning resulting in mixed chimerism.

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruiting
<b>Health condition type</b>	Haemoglobinopathies
<b>Study type</b>	Observational invasive

## Summary

### ID

NL-OMON51521

### Source

ToetsingOnline

### Brief title

Do Alemtuzumab Levels Predict T cell chimerism after SCT for SCD?

### Condition

- Haemoglobinopathies

### Synonym

hemoglobinopathy, Sickle cell disease

### Research involving

Human

## Sponsors and support

**Primary sponsor:** Hematologie

**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** Alemtuzumab, Chimerism, Sickle cell disease, Stem cell transplantation

## Outcome measures

### Primary outcome

The correlation between serum alemtuzumab concentration and levels of donor chimerism.

### Secondary outcome

The correlation between serum alemtuzumab levels and patients with and without successful engraftment. Correlation of serum alemtuzumab levels and the dosing of alemtuzumab in mg/kg, number of patient lymphocytes and total number of infused enucleated donor-derived cells.

## Study description

### Background summary

Non-myeloablative allogeneic stem cell transplantation (SCT) has become a feasible curative treatment option for sickle cell disease (SCD) patients with an available matched sibling donor. Chemotherapy free conditioning with alemtuzumab and 3 Gy total body irradiation (TBI) is increasingly being used as preferred conditioning scheme for these patients. This regimen typically results in mixed donor chimerism and has only few toxic effects. However, the risk of graft failure (rejection) is still significant, with an occurrence of 13% in the latest series. Levels of T cell chimerism are crucial for the success of this kind of transplantation. A donor T cell level of at least 50% at 1-year post-transplantation seems to be sufficient to allow the discontinuation of immunosuppressive medication without risk of graft rejection. Low levels of alemtuzumab prior to or shortly after SCT are thought to facilitate rejection of the donor graft. Recently, a positive correlation

between alemtuzumab levels on day+14 was found with levels of T cell chimerism +2 and +4 months post-transplantation in adult SCD patients receiving matched sibling donor SCT. However, in this study alemtuzumab levels prior to the infusion of hematopoietic stem cells and beyond day +28 post-transplantation were not measured. Furthermore, the alemtuzumab levels were measured in 2 patient groups undergoing two different conditioning regimens.

Here, we aim to thoroughly investigate the correlation of alemtuzumab levels and T cell chimerism. To our knowledge, this will be the first study involving SCD patients receiving matched sibling donor SCT with alemtuzumab/TBI conditioning that includes alemtuzumab level measurements before the infusion of hematopoietic stem cells and beyond 1-month post-transplantation. Findings from this study will improve the insights into the etiology of graft failure in these patients and might ultimately lead to a more personalized approach in dosing alemtuzumab in order to achieve a more robust and stable engraftment of donor hematopoietic stem cells.

### **Study objective**

To investigate whether serum alemtuzumab concentrations are predictive of the robustness of engraftment in SCD patients undergoing a matched sibling donor transplantation with alemtuzumab/TBI conditioning resulting in mixed chimerism.

### **Study design**

Prospective observational laboratory study. Serum alemtuzumab concentration will be measured at various time points before and after stem cell infusion (days -3, 0, +7, +14, +28, +60).

### **Study burden and risks**

For subjects included in this study no direct positive effect can be expected. The burden for participants will be limited to 4 ml extra blood being drawn when routine blood tests are planned. Time points T0 and T3 might not coincide with routine blood examinations. However, these samples will be drawn via a central venous catheter, leading to minimal burden and no risk to the patients. Findings from this study could lead to a more personalized approach in future patients in whom alemtuzumab doses could be adjusted to further reduce the risk of graft rejection.

## **Contacts**

### **Public**

Selecteer

Meibergdreef 9 9  
Amsterdam 1105AZ  
NL  
**Scientific**  
Selecteer

Meibergdreef 9 9  
Amsterdam 1105AZ  
NL

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

### Age

Adolescents (16-17 years)

Adults (18-64 years)

### Inclusion criteria

- o Age 16 years and older
- o High performance liquid chromatography (HPLC) confirmed diagnoses of SCD (all genotypes)
- o Planned for a non-myeloablative MSD transplantation with alemtuzumab/TBI at the Amsterdam UMC
- o Willing and able to provide written informed consent

### Exclusion criteria

- No specific exclusion criteria

## 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): 15-07-2022

Enrollment: 25

Type: Actual

## Ethics review

Approved WMO

Date: 04-07-2022

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**

CCMO

**ID**

NL80603.018.22