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.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Haemoglobinopathies
Study type	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

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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	ID
CCMO	NL80603.018.22