Impact of alemtuzumab exposure on immune reconstitution, autoimmunity, risk of infection, chimerism and graft-versus-host disease in children with non-malignant diseases undergoing allogeneic stem cell transplantation - an International Multicenter Observational Study.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON22218

Source
Nationaal Trial Register

Brief title
ARTIC

Health condition

Diagnosis of severe congenital immune deficiency or of congenital hematological disorder with indication for allogeneic stem cell transplantation

Sponsors and support

Primary sponsor: Leiden University Medical Center
Source(s) of monetary or material Support: LUMC, University Children's Hospital Zurich,

EMDO private foundation, Wolfermann-Nägeli private foundation, Daccò private foundation

Intervention

Outcome measures

Primary outcome

Cumulative Alemtuzumab exposure (AUC) till day +7

Secondary outcome

• Immune reconstitution
• Chimerism after alloHSCT
• Incidence of acute and chronic graft-versus-host-disease and grading
• Overall survival
• Event free survival (defined as without death or retransplantation)
• Cumulative incidence of treatment-related mortality
• Cumulative incidence of graft failure (defined as non-engraftment or rejection)
• Incidence of viral primary infections or reactivations within the first 100 days
• Incidence of Donor Lymphocyte Infusion within the first 100 days
• Incidence of bacterial, parasitic and fungal primary infections within the first 100 days
• Incidence of secondary autoimmune reactions
• Incidence of secondary immune-mediated endocrine disorders

Study description

Background summary

In children, Alemtuzumab is increasingly administered off-label prior to allogeneic stem cell transplantation according to European guidelines. However, pediatric data on Alemtuzumab pharmacokinetics (PK) suggest large inter-patient variability, which significantly impacts biological efficacy and clinical outcome. Since optimal dosing of Alemtuzumab in children prior to HSCT is currently unknown, the need for further PK analyses allowing the evaluation of current clinical practice as well as possibly supporting improved patient care in this vulnerable participants group is urgent.
The aim of our observational study is to evaluate current clinical practice and develop a comprehensive population pharmacokinetic model for Alemtuzumab in children with non-malignant diseases treated with reduced intensity conditioning regimens prior to stem cell transplantation. This model will provide essential additional information on Alemtuzumab treatments and support the establishment of a rigorous therapeutic drug monitoring.

Study objective

Primary Hypothesis
High interindividual variability of Alemtuzumab PK in children transplanted for severe non-malignant diseases crucially impacts the cumulative exposure to Alemtuzumab given intravenously as part of a reduced intensity conditioning regimen pre and post allogeneic stem cell transplantation.

Secondary Hypothesis
The exposure to Alemtuzumab correlates significantly with immune reconstitution, risk of acute and chronic GvHD and primary clinical outcome defined as incidence of infectious complications, reactive autoimmunity and secondary immune-endocrine disorders in children with non-malignant diseases undergoing alloHSCT.

Study design

Alemtuzumab levels measured during Alemtuzumab administration as well weekly till 6 weeks after allogeneic stem cell transplantation.

Contacts

Public
Leiden University Medical Center (LUMC)
Federica Achini

+31715297820
Scientific
Leiden University Medical Center (LUMC)
Federica Achini

+31715297820

Eligibility criteria

Inclusion criteria

• diagnosis of severe congenital immune deficiency or of congenital hematological disorder with indication for allogeneic stem cell transplantation (HSCT)
• age at diagnosis and at the time of HSCT ≤ 18 years
• Alemtuzumab treatment intravenously is given as part of a treosulfan- or a busulfan-based reduced intensity conditioning regimen prior to HSCT

• all donor types and hematopoietic stem cell sources will be considered
• HSCT is performed in a study participating center
• written consent of the parents (legal guardian) and of the patient herself or himself if ≥14 years old (≥12 years old in the Netherlands)
• in case of multiple HSCT per patient, further transplantations will only be considered if a minimal serotherapy-free interval of 3 months is preceding the second transplant

Exclusion criteria

• patients who do not fulfill the inclusion criteria
• patients with known hypersensitivity to Alemtuzumab
• patients treated with other serotherapy drugs (e.g. anti-thymocyte globulin – ATG) within the same conditioning regimen prior to HSCT
• patients who received any other serotherapy in the last 3 months before starting this observational study
• known HIV-positivity
• active malignancy
• pregnancy/lactation

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	26-11-2019
Enrollment:	30
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion
Date: 26-11-2019
Application type: First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 55607
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL8185
CCMO	NL68506.058.19
OMON	NL-OMON55607

Study results