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.

Gepubliceerd: 26-11-2019 Laatst bijgewerkt: 15-05-2024

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...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON22218

Bron
Nationaal Trial Register

Verkorte titel
ARTIC

Aandoening

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

Ondersteuning

Primaire sponsor: Leiden University Medical Center
Overige ondersteuning: LUMC, University Children's Hospital Zurich, EMDO private foundation, Wolfermann-Nägeli private foundation, Daccò private foundation

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Cumulative Alemtuzumab exposure (AUC) till day +7

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

• 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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

• 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

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	26-11-2019
Aantal proefpersonen:	30
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	26-11-2019
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 55607
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten