PK/PD of corticosteroids in graft-versus-host disease after hematopoietic cell transplantation in children

Published: 08-07-2020
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To assess the PK/PD relationship of prednisolone as either prophylaxis or therapy of GVHD in children after HCT.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Immunodeficiency syndromes
Study type	Observational non invasive

Summary

ID

NL-OMON54530

Source
ToetsingOnline

Brief title
PIKACHU-study

Condition

- Immunodeficiency syndromes

Synonym
Graft-versus-host disease, reversed rejection

Research involving
Human

Sponsors and support

Primary sponsor: Prinses Máxima Centrum voor Kinderoncologie
Source(s) of monetary or material Support: Ministerie van OC&W,Harmannus Ehrhardt Stichting;gift Maxima Foundation

Intervention

Keyword: Graft-versus-host disease, Pharmacodynamics, Pharmacokinetics, Population PK/PD

Outcome measures

Primary outcome

PK parameters of prednisolone as either prophylaxis or therapy of GVHD in children after HCT will be assessed, even as other determinants for development of a population PK model using non-linear mixed effect modelling NON-MEM.

Secondary outcome

Exposure to prednisolone as measured by area-under-the-curve (AUC), maximum concentration (Cmax) or time-above-threshold will be related to treatment outcome. Treatment outcome is defined as occurrence and grade of GVHD in case of prophylactic therapy and defined as the need for escalation of therapy for treatment of GVHD. Biomarkers will be assessed using cell (mostly flowcytometry) and protein (Luminex and Olink) assays.

Study description

Background summary

One of the biggest obstacles in hematopoietic cell transplantation (HCT) remains the devel-opment of graft-versus-host disease (GVHD), which occurs in approximately 40% of stem cell recipients. First-line treatment to either prevent or treat GVHD is high dose systemic cor-ticosteroids. However, the incidence of the development of GVHD in children receiving corti-costeroids as prophylactic treatment is still high. Besides, only a minority of the patients de-veloping GVHD responds adequately to corticosteroid treatment, often with

lifelong therapy and reduced quality of life. Overall mortality after developing GVHD is around 30%. In current clinical practice, corticosteroid dosing is highly empirical and might result in very variable exposure levels in children. We hypothesize that precision dosing of corticosteroids, to reach an optimal exposure in every individual patient, will increase response rates in pediatric HCT. A pharmacokinetic/pharmacodynamic (PK/PD) relationship of corticosteroids has been suggested in other diseases where exposure to corticosteroids is associated with clinical out-comes. To date, this has not yet been investigated in the setting of GVHD. As a first step to optimize therapy for GVHD, we will study the PK/PD relationship of prednisolone in pediatric patients. If such a relationship exists, optimal dosing strategies can be developed.

Study objective

To assess the PK/PD relationship of prednisolone as either prophylaxis or therapy of GVHD in children after HCT.

Study design

Prospective observational study.

Study burden and risks

Patients will not have direct benefit from participating in this study. The data obtained in this study will be used to assess the population PK and PD of prednisolone in children after HCT. Burden will be minimal since for pharmacokinetics 4 to 5 (additional to SOC) blood samples of 2 ml once or twice will be drawn (limited sampling strategy) and any samples possible of 9 ml to study biomarkers (maximum of 8 samples, PMC only). The volume of blood that is drawn for the study does not exceed the recommended maximum. The applied sampling strategy is minimally invasive, since all the patients that are included already have a central line or a venous access to draw blood for SOC. Sampling will only be requested during hospitalization or during routine outpatient clinic visits after HCT and/or development of GVHD.

Contacts

Public
Prinses Máxima Centrum voor Kinderoncologie

Heidelberglaan 25
Utrecht 3584 CS
NL

Scientific
Prinses Máxima Centrum voor Kinderoncologie

Heidelberglaan 25
Utrecht 3584 CS
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Babies and toddlers (28 days-23 months)
Newborns

Inclusion criteria

Patients treated by the PMC or LUMC;
Planned to receive systemic corticosteroids after HCT;
Informed consent form (ICF) signed prior to participation in the study;
A present central line to sample blood

Exclusion criteria

None in advance. However, according to expert opinion of the PI, any disease/circumstance that may influence the participation of the potential subject in a negative way, will be excluded from participation in this study

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-09-2020
Enrollment:	130
Type:	Actual

Ethics review

Approved WMO Date:	08-07-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	03-03-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-02-2023
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 21503
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL70886.041.19
Other	NL8703 (via ICTRP)