Optimizing of Ciclosporin monitoring, towards improved ciclosporine therapy in children after stem cell transplantation

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To define the relation between CsA exposure and occurrence of acute Graft-versus-Host disease. To investigate the relation between CsA exposure and other clinical outcome parameters (engraftment, relapse, treatment related toxicity and survival). To...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON36960

Source
ToetsingOnline

Brief title
AUC monitoring in CsA therapy

Condition

- Other condition

Synonym
Graft-versus-host disease, immuun reaction of transplant against the patients cells

Health condition

atients undergoing an allogeneic stem cell transplantation due to a malignant or non-malignant immuno-hematologic disease.

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Area under the curve (AUC), Ciclosporin, Pharmcokinetics

Outcome measures

Primary outcome

Acute GvHD, follow up of 100 days.

CsA exposure is defined as Area under the Curve over 12 hours.

Secondary outcome

CsA trough level

Stem cell engraftment

Toxicity (renal, liver, neurological)

Study description

Background summary

Ciclosporine a (CsA) is given to pediatric patients after their stem cell transplantation (SCT) to prevent the occurrence of Graft-versus-Host Disease (GVHD). Pharmacokinetic studies on CsA in different patient populations have provided evidence that CsA dosing can be optimized when guided by determination of CsA exposure (based on Area under the Curve (AUC) calculation). In the pediatric population undergoing allogeneic SCT, CsA therapy monitoring is still based in on trough levels. At this moment target AUC levels for CsA therapy in these patients are not known and the relation with trough levels is unresolved. In addition, the evidence for the currently applied target trough levels is limited.
We hypothesize that CsA therapy to prevent GVHD can be optimized by AUC guided dosing instead of dosing based on trough levels. Therefore, we will investigate

the association between CsA exposure and clinical outcome. Next to that, we will investigate the association between CsA exposure and CsA trough levels.

Study objective

To define the relation between CsA exposure and occurrence of acute Graft-versus-Host disease. To investigate the relation between CsA exposure and other clinical outcome parameters (engraftment, relapse, treatment related toxicity and survival).
To investigate the association between CsA exposure and trough levels and investigate the feasibility of CsA exposure monitoring using the limited sampling model in clinical practice.

Study design

This is a multicenter prospective observational study.

Study burden and risks

In the pediatric population undergoing allogeneic stem cell transplantation CsA therapy monitoring is still based in on trough levels. Earlier studies in solid organ transplantation in both pediatric and adult patients demonstrated that CsA dosing can be optimized when guided by CsA exposure. However, CsA exposure is not studied before in this patient population in relation to clinical outcome.
To minimize patient burden and study CsA exposure a limited sampling model was developed, resulting in a reliable prediction of AUC using only 2 blood samples. As these patients have a permanent venous access, we think the addition of one blood samples per week (in hospital) and at another 2 time points in the ambulant setting will not increase the burden of the patient significantly.

This study will not be directly beneficial for the pediatric population participating in the study. In the future, we will implement AUC guided monitoring of CsA in normal patient care, provided that we can determine an optimal AUC in relation to the occurrence of acute GVHD.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Pediatric patients of the stem cell transplantation program of the Willem-Alexander Children*s Hospital, LUMC or Wilhelmina Children*s hospital, UMCU undergoing allogeneic stem cell transplantation.
Patients starting with intravenous CsA as GVHD prophylaxis.

Exclusion criteria

Absence of central venous access from which the blood samples can be drawn.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-02-2013
Enrollment:	110
Type:	Actual

Ethics review

Approved WMO

Date:	08-11-2012
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL40992.058.12