Prospective Analysis of an individualized dosing Regimen of ATG (Thymoglobulin) in Children Undergoing HCT: redUcing Toxicity and improving Efficacy – a single arm phase II study

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Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON26849

Bron
Nationaal Trial Register

Verkorte titel
PARACHUTE-trial

Aandoening

Bone Marrow Transplantation
Stem cell transplantation
Thymoglobulin
ATG
Thymoglobuline
Beenmergtransplantatie
Stamceltransplantatie
Immuunreconstitutie
Immune Reconstitution

Ondersteuning

Primaire sponsor: UMC Utrecht
Overige ondersteuning: Sanofi Aventis, France
ZonMW, NWO, The Netherlands

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Incidence of CD4+ T-cell immune reconstitution, defined as a CD4+ T- cell count > 50 x 106/L in 2 consecutive measurements within 100 days.

Toelichting onderzoek

Achtergrond van het onderzoek

Thymoglobulin® was introduced to the conditioning regimen in hematopoietic cell transplantation (HCT) to prevent graft-versus-host-disease (GvHD) and graft failure. Side effects of Thymoglobulin® include delayed immune reconstitution (IR) of donor T-cells due to its long half-life and potential remaining circulating drug post-HCT resulting in an increased probability of viral reactivations/infections. The currently used dosing regimen for Thymoglobulin in children leads to markedly different exposures across the pediatric age range. Low post-HCT Thymoglobulin AUC is associated with a high chance on successful immune reconstitution, important for preventing viral reactivations and relapse. High pre-HCT exposure on the other hand led to a decrease in GvHD and rejection.We defined an optimal exposure based on historical data with which a PK-model was generated, and developed an individual dosing regimen for Thymoglobulin, aiming for improved IR and a reduction of GvHD and graft failure. The goal of this prospective study is to investigate the effects of an individualized PK/PD based dosing regimen for Thymoglobulin on immune reconstitution after pediatric HCT.

Doel van het onderzoek

Our hypothesis is that individualized dosing of Thymoglobulin will result in an improved immune reconstitution, without significantly increasing the risk on aGvHD. This may lead to an improved survival, both through reducing non-relapse mortality (GvHD, viral reactivations) as well as relapse mortality. As a final step in the validation process of our proposed individualized dosing strategy, this needs to be studied in in a prospective, phase II trial.

Onderzoeksopzet

Primary endpoints will be assessed at 100 days post-HCT, engraftment at 40 days post-HCT, other endpoints at 1 year follow up

Onderzoeksproduct en/of interventie

Patient will receive an individualized dose of Thymoglobulin according to a PK/PD derived dosing regimen, as opposed to a fixed standard dose of 10 mg/kg Thymoglobulin, the current standard of care.

Contactpersonen

Publiek

room KC.03.065.2

J.J. Boelens
Wilhelmina Kinderziekenhuis, Lundlaan 6

Utrecht 3584 EA
The Netherlands
0031-88-754003

Wetenschappelijk

room KC.03.065.2

J.J. Boelens
Wilhelmina Kinderziekenhuis, Lundlaan 6

Utrecht 3584 EA
The Netherlands
0031-88-754003

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- All patients eligible for a non-haplo-identical non-T-cell depleted HCT with Thymoglobulin as part of the conditioning regimen treated in the pediatric ward of the participating centers

- Any hematopoietic stem cell source

- First transplantation

- Age at time of transplantation (i.e. infusion of stem cells) < 18 years

- Signed written informed consent according to local law and regulations

- Lansky/Karnofsky ≥ 70%

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- Ex-vivo T-cell depleted grafts

- Other serotherapy in conditioning (e.g. Campath, or Campath in the bag)

- Received serotherapy within 3 months before this transplantation

- Pregnancy or breast-feeding or unwilling to use adequate contraceptive methods

- Sensibility to rabbit proteins or previous treatment with Thymoglobulin

- Acute or chronic infections, in which each form of immune suppression is contra-indicated

- Patients not planned to receive or having received at least 90% intentioned dose of Thymoglobulin

- Ejection fraction < 30%

- No complete morphological remission (CR-status) in bone marrow in case of malignancy

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd

Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-04-2015
Aantal proefpersonen:	53
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	27-01-2015
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 47267
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL4836
NTR-old	NTR4960
CCMO	NL51460.041.14
OMON	NL-OMON47267

Resultaten

Samenvatting resultaten
Admiraal et al, Clinical Pharmacokinetics 2014
Admiraal et al, Lancet Haematology 2015.