Modification of ocular graft-versus-host disease development by early local Cyclosporin A application in patients after donor stem cell transplant.

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Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON28561

Bron
Nationaal Trial Register

Verkorte titel
ocuGVHD CsA

Aandoening

Ocular GVHD
Preventive treatment
Topical Cyclosporine A

Ondersteuning

Primaire sponsor: UMC Utrecht
Heidelberglaan 100
3584 CX Utrecht
The Netherlands
Overige ondersteuning: Fischer stichting
SNOO

Uitzicht (LSBS, St. Blindenpenning, Gelderse blindenbelangen).

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

To investigate the potential efficacy of topical cyclosporine A 0.05% (Restasis) application in preventing ocular surface disease in ocular chronic GVHD in patients who have undergone donor stem cell transplantation an compare this to the effect of preventive treatment with Vidisic PVP Ophtiole eye drops.

Toelichting onderzoek

Achtergrond van het onderzoek

Background of the study:

Allogeneic stem cell transplantation (allo-SCT) is the only curative option for a number of hematological malignancies. This beneficial effect is in part due to a valuable graft-versus-tumor (GvT) effect mediated by donor cytotoxic T cells. The GvT effect however is closely associated with graft-versus-host disease (GvHD), which represents a major cause of morbidity and mortality of allo-SCT patients. Ocular manifestations of GvHD typically arise during chronic GvHD, in many cases together with the skin, mucosa, and serous membranes being affected. Recent improvements in the systemic management and the longer survival of the patients have led to the more frequent manifestations of the ocular problems.
The most common clinical manifestations of ocular GVHD result from involvement of the lacrimal gland and the conjunctiva. Lacrimal gland involvement can lead to aqueous tear deficiency resulting in severe keratoconjunctivitis sicca (KCS) which can significantly increase the morbidity of patients with chronic GVHD. In addition, the ocular manifestations of GvHD may include conjunctivitis and blepharitis, cicatricial lagophthalmos, corneal ulceration and melting; all of these characteristics are usually being indicated as ocular surface disease (OSD). Occasionally the disease progresses to the necrotizing stage complicated by corneal melting and sometimes even eyeball perforation. The high prevalence of ocular involvement and potentially severe ocular problems in GVHD patients necessitate close ophthalmic monitoring. The prevalence of ocular GvHD following allo-SCT was not systematically studied and only limited series on ocular GVHD were published so far. In a very recent study, where only patients with severe complaints were evaluated, major ocular complications as corneal ulceration occurred in 80 (13%) of 620 patients who underwent allo-SCT. Based on these above data, it appears that a systematic study on ocular GVHD is highly desirable.

Objective of the study:

The objective of this proposed prospective randomized double masked placebo controlled study is to investigate the safety and potential efficacy for the prevention or mitigation of ocular GvHD using local early medication with Cyclosporin A drops (Restasis) in patients who have undergone stem cell transplant for hematological malignancy or bone marrow failure disorder.

Study design:

Design: Prospective randomized masked study of at least 102 consecutive patients who will receive allo-SCT for hematologic malignancies.

In this study a complete medical history and full ophthalmologic examination will be performed prior to the allo-SCT. Patients will be stratified to intensity of conditioning regimen (myeloablative versus non-myeloablative) and randomized to one of the 2 treatment arms (lubricant or corticosteroid drops). Four week after allo-SCT (in the re-population phase) the treatment will be instituted either with lubricant drops or with topical cyclosporin if available in the Netherlands). Follow-up examinations will be performed at 3 and 6 months after transplant and whenever the patients will develop ocular complaints. The pre-transplant examination will include visual acuity assessment, corneal and conjunctival staining grading, Schirmer tear test measurement (with anesthesia) as well as slit lamp examination and fundoscopy and intraocular pressure (IOP) measurements. The follow-up examinations will include BCVA, corneal staining index, conjunctival staining index, Schirmer test results, tear break-up time and assessment of Meibomian gland dysfunction and IOP. Further we will register all medications required and any ocular complications. Photographic documentation of all patients with ocular abnormalities will be performed. The ocular GVHD develops in (at least) 50% of all persons 6 months after allo-SCT. We attempt to achieve a clinically relevant decrease of this development from 50% to at least 20%.The statistical analysis reveals that for this, we would need to include 51 patients in both arms of the protocol; the decrease from 50% to 15% requires 36 patients in each arm and the decrease to 10% requires 25 persons in each arm. The approval of medical ethical committee for this study will be obtained. This results of this study will clarify whether the preventive treatment with local cyclosporin might prevent of mitigate ocular GVHD. If topical cyclosporin will be available in the Netherlands at the time of the study, than topical cyclosporin will be used instead of corticosteroid drops since this drug is also effective on GVHD, but has less ocular side effects.

Study population:

Patients > 18 yrs who have undergone donor stem cell transplant for haematological malignancy or bone marrow failure disorder.

Exclusion criteria:

1. History of Sjögren’s syndrome;

2. Documented dry eye prior to stem cell transplantation / significant non-GVHD ocular problems;

3. History of non-compliance.

Intervention:

Cyclosporin group: Cyclosporin A 0.05% eye drops (Restasis) 2 times a day in each eye.

Vidisic group: Vidisic PVP Opthiole eye drops 2 times a day in each eye.

Primary study parameters/outcome of the study:

The main outcome measures will be the occurrence and severity of ocular GvHD.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

The patient will receive two questionnaires (OSDI and VFQ_25) following the informed consent and phone consult. The first visit to the outpatient department (OPD) of ophthalmology will be 1 month prior to SCT. The following visits will be at 3 month and 6 months after SCT. All the visits to the OPD of ophthalmology will be planned simultaneously with the patient’s visit to the haematology department for the follow-up of their SCT. At each OPD visit the previously mentioned questionnaires and ophthalmologic investigations will be performed.
All patients will start therapy with Cyclosporine A 0.05% eye drops 2 times a day in each eye or Vidisic PVP Opthiole eye drops 2 times a day in each eye starting 1 month after transplantation till 6 months after transplantation (5 months). Because this study is a randomised masked trial neither the patient nor the investigator knows which eye drop the patient administers. The use of Vidisic PVP Opthiole eye drops doesn’t involve any risk but can cause some physical discomfort due to blurring of vision or a burning sensation as well as the psychological discomfort of using eye drops 2 times a day during 5 months. Cyclosporine A 0.05% eye drops can cause burning, itching, redness and blurred vision.

Doel van het onderzoek

The objective of this proposed prospective randomized double masked placebo controlled

study is to investigate the safety and potential efficacy for the prevention or mitigation of ocular GvHD using local early medication with Cyclosporin A drops (Restasis) in patients who have undergone stem cell transplant for hematological malignancy or bone marrow failure disorder.

Onderzoeksopzet

The patient will receive two questionnaires (OSDI and VFQ_25) following the informed consent. The first visit to the outpatient department (OPD) of ophthalmology will be 1 day prior to SCT. The following visits will be at 3 months and 6 months after SCT. The first two visits are part of the regular healthcare and patients not included in this study will visit our OPD as well. All the visits to the OPD of ophthalmology will be planned simultaneously with the patient's visit to the haematology department for the follow-up of their SCT. At each OPD visit the previously mentioned questionnaires and ophthalmologic investigations will be performed.

All patients will start therapy with ocular drops according to randomization Cyclosporine A 0.05% (Restasis) 2 times a day in each eye or Vidisic PVP ophtiole eye drops 2 times a day in each eye starting 1 month after transplantation till 6 months after transplantation (5 months).

Onderzoeksproduct en/of interventie

Arm 1: Cyclosporine 0.05% eye drops (Restasis) 2 times a day in each eye (51 patients);

Arm 2: Vidisic PVP ophtiole eye drops 2 times a day in each eye (51 patients).

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Patients > 18 yrs who have undergone donor stem cell transplant for haematological malignancy or bone marrow failure disorder.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. History of Sjögren’s syndrome;

2. Documented dry eye prior to stem cell transplantation / significant non-GVHD ocular problems;

3. History of non-compliance.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Enkelblind
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-04-2010

Aantal proefpersonen:	102
Type:	Verwachte startdatum

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL2493
NTR-old	NTR2610
Ander register	CCMO : 2010-019502-16
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
Current insights into ocular graft-versus-host disease
Anjo Riemens, Liane te Boome, Saskia Imhof, Jurgen Kuball;
Aniki Rothova
Current Opinion in Ophthalmology 2010,
21:000–000.