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

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON28561

Source
Nationaal Trial Register

Brief title
ocuGVHD CsA

Health condition

Ocular GVHD
Preventive treatment
Topical Cyclosporine A

Sponsors and support

Primary sponsor: UMC Utrecht
Heidelberglaan 100
3584 CX Utrecht
The Netherlands
Source(s) of monetary or material Support: Fischer stichting
SNOO
Uitzicht (LSBS, St. Blindenpenning, Gelderse blindenbelangen).

Intervention

Outcome measures

Primary outcome

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.

Secondary outcome

1. Evaluate the safety and frequency of side effects of Cyclosporine A;

2. Evaluate the correlation of ocular GVHD symptoms in relation to GVHD symptoms in general.

Study description

Background summary

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.

Study objective

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

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).

Intervention

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).

Contacts

Public
P.O. Box 85 500
Anjo Riemens
Dept. of Ophtalmology, University Medical Center
Utrecht 3508 GA
The Netherlands
+31 (0)88 7559646
Scientific
P.O. Box 85 500
Anjo Riemens

Dept. of Ophtalmology, University Medical Center
Utrecht 3508 GA
The Netherlands
+31 (0)88 7559646

Eligibility criteria

Inclusion criteria

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.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2010

Enrollment:	102
Type:	Anticipated

Ethics review

Not applicable
Application type: Not applicable

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
NTR-new	NL2493
NTR-old	NTR2610
Other	CCMO : 2010-019502-16
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
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.