An open study to investigate the effect of 4 instead of 2 daily dosing mycophenolate mofetil (MMF) in renal transplant patients on diarrhea

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The main objective is to find out if dividing the daily oral dose prevents diarrhea without increasing risk of graft failure. Secondary objective is the quality of life and effect on intestinal permeability.

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

Summary

ID

NL-OMON30619

Source
ToetsingOnline

Brief title
4xMMF

Condition

- Other condition

Synonym
Renal transplantation

Health condition

transplantatie geneeskunde

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Diarrhea, dosis frequency, Mycophenolate mofetil, renal transplant patients

Outcome measures

Primary outcome

- Stool frequency and faeces weight

- Incidence of acute graft rejection (according to BANFF 1997 criteria)

Secondary outcome

- Quality of life as measured by the SF36 questionnaire

- Renal function as measured by serum creatinine and creatinine clearance

(Cockcroft-Gault formula)

- Intestinal permeability as measured by the intestinal permeability

lactulose-mannitol test

- Comparison of the 2 hours MMF-AUC (0, 30, 60, 90 and 120 min) between a 2 and

4 times daily schedule

- Faeces bacterial profile

- Incidence of adverse events

- Co-medication used during the study will be analyzed

Study description

Background summary

Mycophenolate mofetil (MMF or Cellcept®) is an immunosuppressive that is used for the prevention of acute rejection in renal transplantation. Its major side effect is diarrhea, which may lead to MMF dose reductions and discontinuations. Unfortunately this is associated with an increased risk of graft failure. Therefore we will investigate the effect of dividing the daily oral dose (4 times instead of 2) on diarrhea in renal transplant patients.

Study objective

The main objective is to find out if dividing the daily oral dose prevents diarrhea without increasing risk of graft failure. Secondary objective is the quality of life and effect on intestinal permeability.

Study design

An 18 weeks open crossover intervention study.
Patients will be screened (2 weeks). In the first study period (week 0-8) the daily oral dose is divided into 4 doses. After 8 weeks patients switch and receive MMF twice a day for another 8 weeks.

Intervention

The daily oral dose will be divided into 4 doses a day instead of the ususal 2 doses a day

Study burden and risks

Extra procedures:
During the study period (18 weeks) patients visit the hospital 6 times. Serum creatinine and MPA-AUC will be determined several times. Faeces and urine will be collected at the end of each period for investigation on bacterial profile and intestinal permeability respectively. Furthermore, patients have to fill out quality of life questionnaires and a diary for body weight and stool frequency.

Risks:
With every change in the immunosuppressive protocol there is a chance of an acute organ rejection. The chance of this, however, is considered small, since the total daily dose is unchanged. Moreover, such rejections are nearly always treatable with the standard therapies available (methylsolumedrol and ATG)

Benefits:
The severity of diarrhea may decrease without an increase in graft rejection, resulting in a measurable improved quality of life.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Male or female > 18 years old
Renal transplantation > 6 months with stable renal function (serum creatinine < 250 mumol/L)
Use of MMF (Cellcept®) 2 times daily
History of diarrhea (> 1 month >= 3 times a day loose/ watery stool in at least 75% of the cases)
Willing and capable to give written informed consent
Able to communicate and cooperate with the investigators

Exclusion criteria

Usage of morfinomimetics, anti-diarretics, laxans or other drugs that are known to induce diarrhea.
Recent use of antibiotics (< 4 weeks before study)
Gastro-intestinal infections (Yersinea, Campylobacter, Shigella, Salmonella, Clostridium difficile toxin, CMV)
Known gastro-intestinal diseases or recent major gastro-intestinal surgery

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-05-2008
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cellcept
Generic name:	Mycophenolate mofetil
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	02-03-2007
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	05-06-2007
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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
EudraCT	EUCTR2007-000033-19-NL
CCMO	NL15396.041.07