EXTENDED REPORT

Mycophenolate mofetil in the treatment of uveitis in children

D Doycheva, C Deuter, N Stuebiger, S Biester, M Zierhut

Br J Ophthalmol 2007;91:180–184. doi: 10.1136/bjo.2006.094698

See end of article for
authors' affiliations

Correspondence to:
M Zierhut, Eberhard-Karls-
University Tuebingen, Abt
Augenheilkunde I,
Schleichstr 12-15D,
Tubingen 72076, Germany;
manfred.zierhut@med.uni-
tuebingen.de

Accepted for publication
2 July 2006

Published Online First
6 July 2006

Background: Mycophenolate mofetil (MMF) is a new immunosuppressive agent that effectively controls the intraocular inflammation in adults.

Purpose: To assess the efficacy of MMF in uveitis in children and to analyse the possible side effects.

Participants and methods: A retrospective analysis was carried out on 17 children (32 eyes) with intraocular inflammation treated with MMF and followed up at the University Eye Hospital Tuebingen, Tuebingen, Germany, between 2000 and 2005. All children had chronic non-infectious uveitis and received MMF for at least 6 months. All patients were given steroids or other immunosuppressive agents before initiating treatment with MMF.

Results: 17 children (10 boys and 7 girls) with a mean age of 8 (range 2–13) years at the onset of uveitis were examined. The average duration of follow-up after initiation of MMF was 3 (range 2–5) years. A steroid-sparing effect was achieved in 88% of the patients. The oral prednisolone was successfully discontinued in 41% children and reduced to a daily dose of ≤ 5 mg in 47% of the children. 24% of the patients remained relapse-free during the treatment, but a reduction in the relapse rate was observed in all other patients except one. Visual acuity was increased or maintained in 13 children (76%). Mild side effects (headache, rash, gastrointestinal discomfort) occurred in 7 patients (41%) and were the cause of discontinuation of MMF in 1 patient.

Conclusion: The results of our study are encouraging and suggest that MMF is an effective agent also in the treatment for uveitis in children, with marked steroid-sparing potential and an acceptable side effect profile.

Uveitis in children is a potentially blinding disease associated with difficulties in diagnosis and treatment.^{1–3} Early and aggressive anti-inflammatory treatment is the best means to improve long-term outcomes from intraocular inflammation, but drug-related adverse reactions may be more troubling and less well tolerated by children.⁴ Corticosteroids, which are often the mainstay of treatment of non-infectious uveitis, cause considerable side effects, especially in children. Immunosuppressive drugs used as steroid-sparing agents also increase the susceptibility of children to infections. Organ toxicity, reversible bone marrow suppression and high rate of malignancies are other adverse effects of immunosuppressive treatment.^{4–5} Better alternative treatment with improved efficacy and fewer side effects is desirable.

Mycophenolate mofetil (MMF) is a relatively new immunosuppressive agent with a stronger cytostatic effect on lymphocytes than on other cell types.^{6–7} Owing to its selective action, the drug shows fewer and milder side effects than other immunosuppressive agents with similar immune potency.^{8–9}

Initially, MMF found widespread use in the prophylaxis of transplant rejection in organ transplantation.^{10–12} Since then, it has been used in the treatment of various autoimmune diseases.^{13–16} In ophthalmology, Kilmartin *et al.*¹⁷ and Larkin and Lightman¹⁸ were the first to publish data showing that MMF is useful in controlling ocular inflammation with minimum side effects.

In the paediatric population, MMF is used successfully in organ transplant recipients^{19–25} and in patients with autoimmune diseases.^{26–29} To our knowledge, no study has investigated the role of MMF in the treatment of children with intraocular inflammation. The purpose of this study was to assess the efficacy and the spectrum of side effects of MMF as a steroid-sparing agent in uveitis in children.

PARTICIPANTS AND METHODS

We retrospectively analysed the clinical records of all 18 children with intraocular inflammation who were treated with

MMF and followed up at the University Eye Hospital Tuebingen, Tuebingen, Germany, between 2000 and 2005. All children had chronic non-infectious uveitis. One child developed side effects—for example, hair loss—and the treatment was stopped after 2 months. All other 17 children received MMF for at least 6 months.

All patients were treated with steroids or other immunosuppressive agents before initiating treatment with MMF. The rationale for using MMF was a high frequency of sight-threatening recurrences of uveitis or intolerance to steroids or other immunosuppressive drugs, with severe adverse reactions.

The children's clinical status, blood cell counts, liver and renal function tests were checked by paediatricians every 4–6 weeks during the period of MMF treatment. At follow-up examinations, the patients were monitored closely and examined for drug-related side effects.

Anterior chamber and vitreous cells were graded as 0.5+, 1+, 2+, 3+ and 4+ according to the guidelines of the Standardization of Uveitis Nomenclature Working Group³⁰ and Nussenblatt *et al.*³¹ Improvement or worsening of activity of inflammation was assessed according to the Standardization of Uveitis Nomenclature Group's directions. As per these suggestions, the relapse rate is presented as frequency—the number of relapses in 1 year.

The grading of efficacy of the treatment was assessed according to the relapse rate before and during the MMF treatment as follows:

1. *Effective:* no relapse or at least two relapses less than before MMF treatment
2. *Mildly effective:* one relapse less than before MMF treatment
3. *No response:* no change in relapse rate
4. *Worsening:* more relapses than before after MMF treatment.

Abbreviation: MMF, mycophenolate mofetil

Change in visual acuity is given as change of lines in Snellen chart. The outcome measures were defined as reduction in relapse rate during the MMF treatment and improvement in visual acuity.

RESULTS

In all, 17 children (10 boys and 7 girls) were included in the study. The mean age of the patients at the onset of uveitis was 8 (range 2–13) years. The median duration of uveitis before treatment with MMF was 4.5 years (range 4 months to 11 years). The average duration of follow-up after initiation of MMF was 3 (range 2–5) years. Intermediate uveitis was the predominant clinical type, with a prevalence of 58.8% (10 children). In all, 6 children (35.3%) had anterior uveitis and 1 child (5.9%) had panuveitis. The most frequent identified aetiology was antinuclear antibody-positive uveitis, followed by juvenile idiopathic arthritis-associated uveitis, sarcoidosis, and tubulointerstitial nephritis and uveitis syndrome. Eleven children had idiopathic intraocular inflammation.

All children had been previously treated with oral prednisolone. Six children had received steroids in combination with one immunosuppressive agent, and three children in combination with two or three immunosuppressive agents or biologicals. At the beginning of MMF treatment, nine children had active intraocular inflammation.

The dose of MMF given was that recommended in paediatric renal transplant recipients—600 mg/m² twice daily. The average maintenance dose was 1 g daily (range 750 mg to 2 g daily). During the first week of treatment, the children received half the dose, which was subsequently increased to the desirable maintenance dose, given in two divided doses.

At the time of starting treatment with MMF, all patients were receiving corticosteroids. During the treatment with MMF, oral prednisolone was discontinued in 7 patients (41%); in 8 children (47%) it was reduced to a daily dosage of ≤ 5 mg. In 2 children, the doses of prednisolone were dropped to 7.5 and 10 mg daily, respectively. A combination of MMF, steroids and other immunosuppressive agents was required in only 5 of the 17 patients (29.4%). Adalimumab was given to two of the patients. Steroids were discontinued or the dosage was decreased to ≤ 5 mg daily in 15 patients (88%). MMF was discontinued in two children after 3 and 2 years (children numbers 3 and 15, respectively) of successful treatment. Table 1 shows details of treatment before and after starting MMF, and the period of follow-up.

According to the relapse rate, presented as the number of relapses in 1 year before and during the treatment, MMF was assessed as effective (grade 1) in 11 children and as mildly effective (grade 2) in 5. Only in one child was no change in relapse rate observed (grade 3). No child was found to have a worsening of the relapse rate (grade 4) after treatment with MMF. During the treatment period, 4 children (24%) were relapse-free; a reduction in the relapse rate was observed in all other children but one. In seven children the recurrence of uveitis was treated with a short-term increase in topical or systemic steroids, in one child with increase of MMF only, and in two children with increase in MMF and systemic prednisolone in parallel. In two children, control of inflammation was achieved by addition of adalimumab (children 16 and 17), and in another one (child 2) by addition of methotrexate. Table 2 summarises the relapse rate before and during treatment, and the efficacy of treatment regarding recurrences and side effects before and during treatment.

Visual acuity was increased or maintained in 13 children (76%) and decreased in 4 children (24%). Epiretinal membrane was the cause of visual impairment in 1 child (child 11). One child developed cataract (child 12) and two children had

progression of the glaucomatous optic disc damage (children 6 and 16). The successful treatment of macular oedema with azetazolidine in addition to immunosuppressive treatment was the main reason for improved vision.

During MMF treatment, improvement of inflammation as either a two-step decrease in the level or a decrease in inactive inflammation was observed in 14 patients. In 3 of 17 children, a one-step decrease in level of inflammation was detected. No worsening in the activity of uveitis was seen in our patients.

Several adverse events to corticosteroids and other immunosuppressive agents were detected before starting MMF. Steroid-related side effects were seen in 11 children (65%). The most frequent side effects were raised intraocular pressure, growth retardation, secondary Cushing's syndrome, and emotional lability. In two children treated with methotrexate, a reduction of liver function tests was observed. One child showed an anaphylactic reaction after infliximab infusion. Decreasing the dosage of prednisolone during MMF treatment yielded a considerable reduction in steroid-induced adverse effects.

The side effects to MMF were remarkably few; most children tolerated the treatment well. Four patients had transient headache at the time of starting MMF, but they continued treatment; one had gastrointestinal problems. Slightly decreased leucocyte count was found in one child, and two children developed rash; in one of them MMF was discontinued and not restarted on the parents' request.

DISCUSSION

The widest clinical experience with MMF in paediatric patients has been in renal allograft rejection.^{10–12 19 20} Several authors have reported the use of MMF in paediatric heart and liver transplant recipients.^{21–25} The drug has a steroid-sparing effect and low rate of side effects. MMF has also been used in the treatment of children with different autoimmune diseases.^{27–29}

A few studies have investigated the efficacy of MMF in treatment of intraocular inflammation in adults.^{17 18 32–36} Kilmartin *et al*¹⁷ evaluated nine patients with uveitis with previous ciclosporin resistance or toxicity. The authors concluded that MMF may improve visual acuity despite chronic disease and is effective as rescue treatment in refractory uveitis, particularly when treatment with ciclosporin has failed. In an open-label prospective study, Larkin and Lightman¹⁸ used MMF as a third agent in 11 patients with diminishing ocular inflammation. Of all patients studied, only one had transient gastrointestinal symptoms.

Our own group^{35 36} previously reported favourable results in 106 patients with uveitis treated with MMF either alone or in combination with prednisolone or one other systemic immunosuppressant.

In an open-label retrospective study of 14 patients with refractory uveitis treated with MMF for an average period of 33 months, Lau *et al*³⁷ showed that intraocular inflammation remained under control in 10 patients. Vision was improved in 7 eyes; it did not change in 14 eyes and was reduced in 7 eyes. In another retrospective study of 18 patients treated with MMF, Greiner *et al*³³ achieved resolution of inflammatory activity in 13 patients. Transient side effects included myalgia, tiredness and moderate headache.

Published data available on the use of MMF in childhood uveitis are limited. Only Baltatzis *et al*³⁴ reported on four children—three of these four patients with juvenile idiopathic arthritis-associated uveitis were successfully treated.

In 12 of our patients (22 eyes) the intraocular inflammation remained under control with MMF and steroids, and in three patients a second immunosuppressive agent was required. Tumour necrosis factor α antagonists were additionally necessary in only two children. During MMF treatment, 24%

Table 1 Treatment before and after starting mycophenolate mofetil, and period of follow-up

Patients	Diagnosis	Age at onset of uveitis (years)	Uveitis duration before starting MMF	Previous treatment besides steroids	MMF (g/day)	Steroids (mg/day)	Other IS	Duration of MMF treatment (years)	Follow-up (years)
1	AU, ANA positive	8	4 years	MTX, CsA, Aza	1.5	7.5	No	5.0	5.0
2	AU, ANA positive	6	4 years	CsA	1.0	5.0	MTX	3.5	3.5
3	IU, idiopathic	9	6 years	No	1.5	2.5	No	3.0, discount	3.5
4	IU, idiopathic	6	2 years	No	0.75	4.0	No	2.5	2.5
5	IU, idiopathic	10	1 year	MTX	2.0	1.0	No	2.5	2.5
6	AU, sarcoidosis	2	8 years	MTX	2.0	5.0	MTX	3.0	3.0
7	IU, idiopathic	11	2 years	No	1.5	Discont	No	3.0	3.0
8	AU, TINU syndrome	13	8 months	No	1.0	Discont	No	2.5	2.5
9	IU, idiopathic	11	4 months	No	1.5	Discont	No	2.2	2.2
10	Panuveitis, idiopathic	7	1 year	MTX	1.5	1.0	No	2.0	2.0
11	IU, idiopathic	5	7 years	No	1.5	Discont	No	2.2	2.2
12	AU, ANA positive	5	8 years	MTX	1.0	5.0	MTX	4.0	4.0
13	IU, idiopathic	13	4 years	No	2.0	5.0	No	3.5	3.5
14	IU, idiopathic	12	3.5 years	Sulfasalazine	2.0	Discont	No	2.0	2.0
15	IU, idiopathic	11	2 years	no	1.0	discont	No	2.0, discount	5.0
16	AU, JIA	6	10 years	MTX, CsA, infliximab	2.0	Discont	MTX discount, Adalim	3.0	3.0
17	IU, idiopathic	4	11 years	CsA, etanercept	1.5	10.0	CsA, Adalim	6 months	2.5

Adalim, Adalimumab; ANA, antinuclear antibody; AU, anterior uveitis; Aza, azathioprine; CsA, ciclosporin A; discount, discontinued; IS, immunosuppressants; IU, intermediate uveitis; JIA, juvenile idiopathic arthritis; MMF, mycophenolate mofetil; MTX, methotrexate; TINU syndrome, tubulointerstitial nephritis and uveitis syndrome.

Table 2 Relapse rate before and during treatment with mycophenolate mofetil, change in level of inflammation and in visual acuity, side effects

Patient	Diagnosis	Relapse rate before MMF treatment (/year)	Relapse rate after MMF treatment (/year)	Efficacy regarding relapse rate	Change in level of inflammation	Rate of visual acuity change (R/L)	Complications	Side effects before MMF treatment	Side effects during MMF treatment
1	AU, ANA positive	4	1	Effective	Improved	2/1	No	Raised IOP	Headache
2	AU, ANA positive	2.5	0.3	Effective	Improved	2/0	No	No	No
3	IU, idiopathic	1	0.3	Effective	Improved	0/3	No	Raised IOP, growth retardation	No
4	IU, idiopathic	1	1	No response	No change	1/3	No	No	Headache
5	IU, idiopathic	3	1.5	Moderate	No change	0/0	No	Growth retardation, reduction of liver tests	No
6	AU, sarcoidosis	1.5	1.0	Moderate	Improved	3/-3	Secondary glaucoma	No	No
7	IU, idiopathic	1.5	0.6	Moderate	Improved	6/0	No	Secondary Cushing, acne	Headache
8	AU, TINU syndrome	2	No relapses	Effective	Improved	4/2	No	No	No
9	IU, idiopathic	2	0.5	Effective	Improved	0/6	No	No	No
10	Panuveitis, idiopathic	2	No relapses	Effective	Improved	2/2	No	Raised IOP, reduction of liver tests	Rash
11	IU, idiopathic	2	0.5	Effective	Improved	0/-1	Epi-retinal membrane	Obesity, emotional lability	Headache, gastrointestinal discomfort
12	AU, ANA positive	2	1	Moderate	Improved	-6/-5	Cataract	Raised IOP, secondary Cushing	No
13	IU, idiopathic	2	0.3	Effective	Improved	0/6	No	Raised IOP	No
14	IU, idiopathic	2.5	0.5	Effective	Improved	0/4	No	Emotional lability	No
15	IU, idiopathic	1.5	No relapses	Effective	Improved	1/0	No	No	Leucopenia
16	AU, JIA	2	1	Moderate	No change	4/-1	Secondary glaucoma	Secondary Cushing, anaphylactic reaction	No
17	IU, idiopathic	2	No relapses	Effective	Improved	0/0	No	Growth retardation	Rash

ANA, antinuclear antibody; AU, anterior uveitis; IOP, intraocular pressure; IU, intermediate uveitis; JIA, juvenile idiopathic arthritis; L, left; MMF, mycophenolate mofetil; R, right; TINU syndrome, tubulointerstitial nephritis and uveitis syndrome.

of the patients were relapse-free and the relapse rate decreased in all the remaining patients except one. According to the number of recurrences, MMF was evaluated as effective in 11 children and mildly effective in 5 children. No change in relapse rate during treatment was found in only one child. The improvement in vision or the prevention of visual impairment in 76% of the patients and the effective control of inflammation suggest that MMF is a useful and safe agent in treatment of uveitis in children.

One of the most important goals in using new immunosuppressive agents, especially in children, is to minimise exposure to corticosteroids and to reduce steroid levels. In this series, a steroid-sparing effect was achieved in 88% of the patients. We successfully discontinued the prednisolone in 41% of the children and reduced it to a daily dose of ≤ 5 mg in an additional 47%. Two patients received steroids in doses of 7.5 and 10 mg daily, respectively. Our results are in accordance with the data obtained in adults. Baltatzis *et al*³⁴ reported a steroid-sparing effect in 54% of the patients. In another study on adults,³³ steroids were discontinued in 22% and reduced to a daily dose of < 5 mg in 55% of all patients.

Almost half of the children (8 of 17 children) received no second-line treatment in addition to the steroids, and MMF was used as a first steroid-sparing agent. In 5 of these 8 children (62%), the steroids could be discontinued completely. This suggests that MMF may have a high potential of preferred treatment.

Interestingly, effective treatment with MMF was observed only in 1 of 4 patients (25%) with ANA-associated anterior uveitis. In the children with idiopathic intermediate uveitis, the rate of success was higher than in those with anterior uveitis. Decrease in relapse rate and improvement in level of inflammation and visual acuity after MMF treatment was found in 6 of 10 patients (60%) with idiopathic intermediate uveitis.

The average dose of MMF for treatment of uveitis in adults is 2 g daily (range 1–3 g/day). There is no reported effective dose in children with intraocular inflammation. MMF in paediatric organ transplant recipients is given in fixed doses, based on either body weight²¹ or body surface area.^{19–20–38} In our patients, we gave the drug in doses based on body surface area according to the recommended dose in children with renal transplantation—600 mg/m² twice daily. In clinical practice, a fixed daily dose is used without monitoring the blood levels. Doses are adjusted according to gastrointestinal side effects and blood counts. David-Neto *et al*¹⁹ and Ghio *et al*³⁹ recommended the simple adjustment of MMF to be replaced by mycophenolic acid monitoring. Dipchand *et al*²¹ reported an effective average dose of 40 (+/– 14) mg/kg of MMF in children. The optimal dosage is yet to be determined.

During MMF treatment, we observed drug-related adverse reactions in 7 children (41%). The side effects of MMF in our patients were mild and common, and were the cause of discontinuance of MMF in only one child. As a result of the marked reduction in the dosage of systemic prednisolone, a dramatic decrease in the steroid-related adverse effects was observed compared with the treatment given before MMF.

The reported tolerance of MMF by children in the published literature is similar to our results.^{20–23–26–29} The most frequent and noteworthy complaints leading to dose reduction or discontinuation have been gastrointestinal problems, including nausea, vomiting and diarrhoea, leucopenia and increase in opportunistic infections. Dipchand *et al*²¹ showed 30% incidence of side effects (gastrointestinal discomfort, diarrhoea and leucopenia) in paediatric heart transplant recipients treated with other immunosuppressive agents in addition to MMF. Novak *et al*²⁹ reported a low rate of side effects in 21 children

with nephritic syndrome who received MMF. The drug had been discontinued only in one patient owing to varicella infection.

CONCLUSION

Our results are encouraging and suggest that MMF is effective in the treatment of uveitis in children. It has a marked steroid-sparing potential and an acceptable side effect profile. Controlled clinical trials are required to assess the efficacy of MMF, the appropriate dosing regimens and the rate of side effects in children with intraocular inflammation.

Authors' affiliations

D Doycheva, C Deuter, N Stuebiger, S Biester, M Zierhut, University Eye Hospital Tuebingen, Tuebingen, Germany

Competing interests: None.

REFERENCES

- De Boer J, Wulffraat N, Rothova A. Visual loss in uveitis of childhood. *Br J Ophthalmol* 2003;**87**:879–84.
- Edelsten C, Reddy A, Stanford M, *et al*. Visual loss associated with pediatric uveitis in English primary and referral centers. *Am J Ophthalmol* 2003;**135**:676–80.
- Rosenbeg KD, Feuer WJ, Davis JL. Ocular complications of pediatric uveitis. *Ophthalmology* 2004;**111**:2299–306.
- Holland GH, Stiehm ER. Special considerations in the evaluation and management of uveitis in children. *Am J Ophthalmol* 2003;**135**:867–78.
- Jabs DA, Rosenbaum JT, Foster CS, *et al*. Guidelines for the use of immunosuppressive drugs in patients with intraocular inflammatory disorders: recommendations of an expert panel. *Am J Ophthalmol* 2000;**130**:492–513.
- Allison AC. Mechanisms of action of mycophenolate mofetil. *Lupus* 2005;**14**(Suppl 1):S2–8.
- Allison AC, Kowalski WJ, Muller CJ, *et al*. Mycophenolic acid and brequinar, inhibitors of purine and pyrimidine synthesis, block the glycosylation of adhesion molecules. *Transplant Proc* 1993;**25**(Suppl 2):67–70.
- Lipsky JJ. Mycophenolate mofetil. *Lancet* 1996;**348**:1357–9.
- Allison AC, Eugui EM. Immunosuppressive and other effects of mycophenolic acid and an ester prodrug, mycophenolate mofetil. *Immunol Rev* 1993;**136**:5–28.
- European Mycophenolate Mofetil Cooperative Study Group. Placebo-controlled study of mycophenolate mofetil combined with cyclosporine and corticosteroids for prevention of acute rejection. *Lancet* 1995;**345**:1321–5.
- Sollinger HW. US Renal Transplant Mycophenolate Mofetil Study Group. Mycophenolate mofetil for the prevention of acute rejection in primary cadaveric renal allograft recipients. *Transplantation* 1995;**60**:225–32.
- Tricontinental Mycophenolate Mofetil Renal Transplantation Study Group. A blinded, randomized clinical trial of mycophenolate mofetil for the prevention of acute rejection in cadaveric renal transplantation. *Transplantation* 1996;**61**:1029–37.
- Pisani CN, Karim Y, Cuadrado MJ. Mycophenolate mofetil and systemic lupus erythematosus: an overview. *Lupus* 2005;**14**(Suppl 1):S9–11.
- Vermersch P, Stojkovic T, de Seze J. Mycophenolate mofetil and neurological diseases. *Lupus* 2005;**14**(Suppl 1):S42–5.
- D'Cruz DP. Mycophenolate mofetil in systemic vasculitis. *Lupus* 2005;**14**(Suppl 1):S55–7.
- Hartmann M, Enk A. Mycophenolate mofetil and skin diseases. *Lupus* 2005;**14**(Suppl 1):S58–63.
- Kilmartin DJ, Forrester JV, Dick AD. Rescue therapy with mycophenolate mofetil in refractory uveitis. *Lancet* 1998;**352**:35–6.
- Larkin G, Lightman S. Mycophenolate mofetil a useful immunosuppressive in inflammatory eye disease. *Ophthalmology* 1999;**106**:370–4.
- David-Neto E, Araujo LMP, Sumita NM, *et al*. Mycophenolic acid pharmacokinetics in stable pediatric renal transplantation. *Pediatr Nephrol* 2003;**18**:266–72.
- Smith JM, Nemeth TL, McDonald RA. Current immunosuppressive agents in pediatric renal transplantation: efficacy, side-effects and utilization. *Pediatr Transplant* 2004;**8**:445–53.
- Dipchand AI, Benson L, McCrindle BW, *et al*. Mycophenolate mofetil in pediatric heart transplant recipients: a single-center experience. *Pediatr Transplant* 2001;**5**:112–18.
- Nobili V. Mycophenolate mofetil in pediatric liver transplant patients with renal dysfunction: preliminary data. *Pediatr Transplant* 2003;**7**:454–7.
- Evans HM, McKiernan PJ, Kelly DA. Mycophenolate mofetil for renal dysfunction after pediatric liver transplantation. *Transplantation* 2005;**79**:1575–80.
- van Mourik ID, Kelly DA. Immunosuppressive drugs in pediatric liver transplantation. *Paediatr Drugs* 2001;**3**:43–60.
- Boyer O, Le Bidois J, Dechaux M, *et al*. Improvement of renal function in pediatric heart transplant recipients treated with low-dose calcineurin inhibitor and mycophenolate mofetil. *Transplantation* 2005;**79**:1405–10.
- Filler G, Hansen M, LeBlanc C, *et al*. Pharmacokinetics of mycophenolate mofetil for autoimmune disease in children. *Pediatr Nephrol* 2003;**18**:445–9.

- 27 **Rao VK**, Dugan F, Dale JK, *et al*. Use of mycophenolate mofetil for chronic, refractory immune cytopenias in children with autoimmune lymphoproliferative syndrome. *Br J Haematol* 2005;**129**:534–8.
- 28 **Moudgil A**, Bagga A, Jordan SC. Mycophenolate mofetil therapy in frequently relapsing steroid-dependent and steroid-resistant nephritic syndrome of childhood: current status and future directions. *Pediatr Nephrol* 2005;**20**:1376–81.
- 29 **Novac I**, Frank R, Vento S, *et al*. Efficacy of mycophenolate mofetil in pediatric patients with steroid-dependent nephrotic syndrome. *Pediatr Nephrol* 2005;**20**:1265–8.
- 30 **The Standardization of Uveitis Nomenclature (SUN) Working Group**. Standardization of uveitis nomenclature for reporting clinical data. Results of the first international workshop. *Am J Ophthalmol* 2005;**140**:509–16.
- 31 **Nussenblatt RB**, Palestine AG, Chan CC, *et al*. Standardization of vitreal inflammatory activity in intermediate and posterior uveitis. *Ophthalmology* 1985;**92**:467–71.
- 32 **Zierhut M**, Stübiger N, Aboalchamat W, *et al*. Immunosuppressive treatment with mycophenolate mofetil in the therapy of uveitis. *Ophthalmologie* 2001;**98**:647–51.
- 33 **Greiner K**, Varikkara M, Santiago C, *et al*. Efficiency of mycophenolate mofetil in the treatment of intermediate and posterior uveitis. *Ophthalmologie* 2002;**99**:691–4.
- 34 **Baltatzis S**, Tufail F, Yu EN, *et al*. Mycophenolate mofetil as an immunomodulatory agent in the treatment of chronic ocular inflammatory disorders. *Ophthalmology* 2003;**110**:1061–5.
- 35 **Zierhut M**, Stübiger N, Siepmann K, *et al*. MMF and eye disease. *Lupus* 2005;**14**(Suppl 1):S50–4.
- 36 **Siepmann K**, Huber M, Stübiger N, *et al*. Mycophenolate mofetil is a highly effective and safe immunosuppressive agent for the treatment of uveitis. A retrospective analysis of 106 patients. *Graefes Arch Clin Exp Ophthalmol* 2006;**244**:788–4.
- 37 **Lau CH**, Comer M, Lightman S. Long-term efficacy of mycophenolate mofetil in the control of severe intraocular inflammation. *Clin Exp Ophthalmol* 2003;**31**:487–91.
- 38 **Filler G**, Foster J, Berard R, *et al*. Age-dependency of mycophenolate mofetil dosing in combination with tacrolimus after pediatric renal transplantation. *Transplant Proc* 2004;**36**:1327–31.
- 39 **Ghio L**, Ferarresso M, Vigano SM, *et al*. Mycophenolate mofetil pharmacokinetic monitoring in pediatric kidney transplant recipients. *Transplant Proc* 2005;**37**:856–8.