



# Mycophenolate Mofetil for Treatment of Chronic Rejection in Liver Allograft Under Tacrolimus

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**T**ACROLIMUS IS KNOWN to halt or even reverse the process of chronic rejection in liver transplantation under cyclosporin A (CsA).<sup>1</sup> The introduction of tacrolimus has led to a reduced rate of chronic rejection after primary liver transplantation. Chronic rejection still occurs in patients whose primary diagnosis is HCV, HBV, PBC, PSC, or autoimmune disease or in whom adequate baseline immunosuppression is not maintained for medical reasons or reasons of noncompliance. Some patients respond to optimization of baseline immunosuppression, but in others chronic rejection leads to graft failure or death despite these measures.<sup>2</sup> There is no satisfactory treatment for this group of patients.

The aim of our study is to examine the role of mycophenolate mofetil (MMF) in chronic rejection after liver transplantation under tacrolimus-based immunosuppression.

## MATERIALS AND METHODS

Eight patients who underwent liver transplantation under tacrolimus and steroid-based immunosuppression had an episode of biopsy-proven chronic rejection as defined by Banff's criteria<sup>3</sup> and received MMF at our institution between 1994 and 1998. Four male and four females, mean age 51 years ( $\pm 10.3$  years [SD], absolute range 38 to 69 years). Mean time to an episode of chronic rejection was 69 months ( $\pm 34$  months). Etiology of liver failure leading to initial transplant consisted of ethanol induced ( $n = 3$ ), HCV ( $n = 3$ ), Budd Chiari ( $n = 1$ ), and autoimmune ( $n = 1$ ). All patients were started on 1 g of MMF BID and the dose was adjusted to patient tolerance (range: 1 to 2 g/d). The patients were followed for a mean of  $48.5 \pm 14.2$  months (range 26 to 80).

## RESULTS

### Survival

Six of eight patients survived 5 years after chronic rejection, for an overall 5 year survival rate of 75%. Patient #1 had improved transaminases but died from aspergillus pneumonia 15 months after the initiation of MMF and 55 months after liver transplant. Patient #5 also had a biochemical

**Table 1. Liver Biochemistries Before and After MMF**

Mean	Bilirubin (mg/dL)	ALT (u/L)	AST (u/L)	GGTP (u/L)
Before MMF	1.73	151.20	106.20	970.10
After MMF	1.02	32.49	57.48	311.38

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGTP, gamma glutamyltransferase.

response but died at home from uncertain causes at 40 months post-MMF and 59 months posttransplant. No one required retransplantation. Patient and graft survival at 5 years was 71%.

### Biochemical Response

All patients showed improvement in transaminases. The mean total bilirubin, AST, ALT, and GGTP before MMF and at follow-up time points are shown in Table 1.

## CONCLUSION

MMF was found to be effective in controlling ongoing chronic rejection in liver allografts under tacrolimus-based immune suppression. A daily dose of 2 mg of MMF was better tolerated with tacrolimus than with CsA as primary treatment.

## REFERENCES

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