

# Postliver transplantation immunosuppression: The song does *not* remain the same

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## ARTICLE

McAlister VC, Peltekian KM, Malatjalian DA, Colohan S, MacDonald S, Bitter-Suermann H, MacDonald AS. Orthotopic liver transplantation using low-dose tacrolimus and sirolimus. *Liver Transplantation* 2001;7:701-708.

## ARTICLE SUMMARY

Sirolimus (SRL) exerts its T-cell antiproliferative activity by suppressing the action of the cytokines interleukin (IL)-2, IL-4, IL-7 and IL-15. In two large randomized trials, SRL reduced the incidence of renal allograft rejection by approximately 50% (1,2). In the present single-arm study, 56 liver transplant recipients were administered low dose tacrolimus (target trough 5 ng/mL), SRL (target trough 7 ng/mL) and tapering doses of steroids. After a mean follow-up of 23 months (range six to 35 months), patient and graft survival rates were 93% and 91%, respectively. Histologically, mild acute rejection occurred in 14%, and 9% (five patients) experienced SRL hepatotoxicity. Cytomegalovirus infection occurred in 7%, and no patient developed lymphoproliferative disease. Significant renal dysfunction did not occur, and only two patients developed dyslipidemia.

## COMMENTARY

The development of cyclosporine (3) in the early 1980s allowed liver transplantation to make the transition from an experimental procedure with poor outcomes to an accepted medical-surgical treatment for end-stage liver disease. In the past decade, tacrolimus (4), like cyclosporine, a calcineurin inhibitor (CNI), has also demonstrated graft-saving efficacy and is likewise commonly used by many centres. Although these CNIs have allowed excellent graft survival with manageable acute graft rejection, as more liver transplant recipients survive long term, it is clear that CNI toxicity, notably chronic renal failure (5) is becoming a greater issue. The experience of McAlister et al with regard to SRL and low dose tacrolimus demonstrates that excellent survival and rates of acute rejection can be achieved with minimal cost to the kidney. For the transplant hepatologist, SRL joins the list of newer immunosuppressive agents, including mycophenolate mofetil (6) and the IL-2 receptor antibodies (7), which are renally 'soft'. More important, it is clear that the rigid 'one size fits all' approach to immunosuppressive protocols of the past is no longer appropriate; an individualized approach that is 'tailor made' to the specific patient's needs is now possible. The end points of future immunosuppressive trials must not focus solely on graft survival and rejection but should look at minimizing the effects

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of the antirejection regimens, thereby improving the recipient's global well-being. The transplant community achieved allograft success a long time ago, now it is time to maximize the 'quality' of that success.

## REFERENCES

1. Kahan BD. Efficacy of sirolimus compared with azathioprine for reduction of acute renal allograft rejection: a randomised multicentre study. The Rapamune US Study Group. *Lancet* 2000;356:194-02.
  2. MacDonald AS. A worldwide, phase III, randomized, controlled, safety and efficacy study of a sirolimus/cyclosporine regimen for prevention of acute rejection in recipients of primary mismatched renal allografts. *Transplantation* 2001;71:271-80.
  3. Starzl TE, Klintmalm GB, Porter KA, Iwatsuki S, Schroter GP. Liver transplantation with the use of cyclosporine A and prednisone. *N Engl J Med* 1981;305:266-9.
  4. US Multicenter FK506 Liver Study Group. A comparison of tacrolimus (FK506) and cyclosporine for immunosuppression in liver transplantation. *N Engl J Med* 1994;331:1154-5.
  5. Fisher NC, Nightingale PG, Gunson BK, Lipkin GW, Neuberger JM. Chronic renal failure following liver transplantation: a retrospective analysis. *Transplantation* 1998;66:59-66.
  6. Wiesner R, Rabkin J, Klintmalm G, et al. A randomized double-blind comparative study of mycophenolate mofetil and azathioprine in combination with cyclosporine and corticosteroids in primary liver transplant recipients. *Liver Transpl* 2001;7:442-50.
  7. Eckhoff D, McGuire B, Sellars M, et al. The safety and efficacy of a two dose daclizumab (Zenapax) induction therapy in liver transplant recipients. *Transplantation* 2000;15:1867-72.
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