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.

ARTICLE

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-sav ing 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