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Tacrolimus: In Heart Transplant Recipients

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Tacrolimus has become the agent of choice for immunosuppression in the majority of heart transplant recipients and is approved in Japan, the US and Europe. Much work has been done to investigate the pharmacodynamic properties of tacrolimus and its primary mode of action seems to be well described, even though there is ongoing controversy about the significance of apoptosis of T cells or the generation of regulatory T cells. Similarly, the pharmacokinetic profile of tacrolimus is well described although necessarily new aspects of pharmacokinetics, particularly with regard to a new modified-release formulation (Prograf® MR4)[1], will have to be added on an ongoing basis.

Initially, tacrolimus was successfully evaluated as rescue therapy for treatment-resistant rejection episodes after heart transplantation. Subsequent clinical investigations for primary immunosuppression after heart transplantation have proven this drug to be highly effective in the prevention of rejection and to be at least equivalent (smaller studies), if not superior (larger studies; own experience), to ciclosporin in immunosuppressive potency. Tacrolimus is usually given in combination with other immunosuppressive drugs (azathioprine, mycophenolate mofetil [MMF] or sirolimus and corticosteroids) and some centres prefer to administer the compound in combination with antibody induction therapy. Experience from our own group has shown that both the tacrolimus plus MMF and the tacrolimus plus sirolimus combinations are highly effective and that it is important to monitor plasma concentrations of mycophenolic acid when combined with MMF. Using either of these combinations allows all patients to be completely weaned off corticosteroids as early as 6 months after transplantation.

Although many centres prefer to start tacrolimus therapy via the oral route, our own experience provides evidence that the initial intravenous administration of tacrolimus is a very safe and effective procedure. Long-term studies comparing tacrolimus with ciclosporin are still few. However, there is some evidence suggesting that tacrolimus has the potential to reduce chronic heart allograft vasculopathy and, despite its effects on glucose metabolism, is associated with a favourable safety profile. Most investigations indicate that tacrolimus-treated patients have a lower risk of hypertension and dyslipidaemia compared with ciclosporin recipients. ▲

1 The use of trade names is for product identification purposes only and does not imply endorsement.