

Tacrolimus Once-Daily Formulation in the Prophylaxis of Transplant Rejection in Renal or Liver Allograft Recipients

A Viewpoint by Sander Florman

Department of Surgery, Tulane School of Medicine, New Orleans, Louisiana, USA

The introduction of tacrolimus, a calcineurin inhibitor isolated from *Streptomyces tsukubaensis*, in the early 1990s led to significantly improved results in solid organ transplantation. Standard, twice-daily dose administration of tacrolimus is now the mainstay of liver and kidney transplant immunosuppression. Medication noncompliance after transplantation, however, is a critical factor that contributes to acute rejection and directly impacts on graft survival. It has been demonstrated that daily dose reduction is an important means of improving medication compliance.^[1,2]

Tacrolimus once-daily (OD) formulation (Advagraf®)¹ is administered in the morning with a similar efficacy and safety profile to that of standard tacrolimus. Pharmacokinetic studies have demonstrated that the steady-state exposure of tacrolimus OD is similar to that of standard, twice-daily

tacrolimus. There is good exposure : trough-concentration correlation with tacrolimus OD. Furthermore, tacrolimus OD is associated with a lower peak concentration, although the clinical significance of this remains to be determined.

The conversion studies have demonstrated equivalence regardless of recipient gender and/or the presence of diabetes mellitus. Conversion from twice-daily tacrolimus to once-daily tacrolimus has been demonstrated to be safe using a milligram-for-milligram (i.e. 1 : 1) conversion and has also been remarkable for less intrasubject variability in tacrolimus exposure following conversion.

Tacrolimus OD should allow for improved compliance with good tolerability and efficacy that is equivalent to standard, twice-daily tacrolimus in kidney and liver transplantation. It is appropriate for *de novo* transplants as well as for maintenance immunosuppression. ▲

References

1. Weng FL, Israni AK, Joffe MM, et al. Race and electronically measured adherence to immunosuppressive medications after deceased donor renal transplantation. *J Am Soc Nephrol* 2005; 16: 1839-48
2. Eisen SA, Miller DK, Woodward RS. The effect of prescribed daily dose frequency on patient medication compliance. *Arch Intern Med* 1990 Sep; 150 (9): 1881-4

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