Foreword

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A large international multicentre study in kidney transplantation was conducted in 1996. This study showed the newly introduced agent mycophenolate mofetil (MMF) to be superior to azathioprine for the prevention of acute rejection in kidney transplant patients [1]. At that time, data comparing tacrolimus with the old (oil-based) formulation of cyclosporin were also available in kidney transplantation, but there were some concerns about tacrolimus having a diabetogenic effect. However, a preliminary study investigating the use of tacrolimus in pancreatic transplantation, which was published in the same year by Gruessner et al., showed that pancreatic graft survival at 6 months post-transplant was higher with tacrolimus (79%) than in a historical group of simultaneous pancreas-kidney (SPK) recipients treated with the oil-based formulation of cyclosporin (65%; \(P = 0.04\)) [2]. During the same era, the new microemulsion (ME) formulation of cyclosporin had been introduced into clinical practice.

Against this backdrop, the Euro-SPK Study Group was formed as a vehicle for combining expertise from different SPK transplantation centres in Europe and Israel. In view of the fact that this procedure was becoming increasingly adopted as an alternative to insulin therapy for type 1 diabetic patients with end-stage renal disease (ESRD), the group undertook the first ever randomized, prospective study comparing tacrolimus- with cyclosporin-ME-based immunosuppression in this patient population. Both immunosuppressive agents were used in combination with MMF and a short course of corticosteroids.

The protocol planned for corticosteroid cessation at 6 months post-transplantation and for the use of antibody induction therapy with rabbit anti-thymocyte globulin.

The interim results for the Euro-SPK 001 study were encouraging and have been published recently [3]. The 1-year incidence of biopsy-proven acute rejection of the kidney or pancreas was lower with tacrolimus (27.2%) than with cyclosporin-ME (38.2%; \(P = 0.09\)). Pancreatic graft survival at 1 year was significantly higher with tacrolimus (91.3%) than with cyclosporin-ME (74.5%; \(P = 0.0014\)), and kidney graft survival was similar in the two groups. The interim analysis also showed that 34 patients switched treatment from cyclosporin-ME to tacrolimus, whereas only six patients receiving tacrolimus required alternative therapy. Therefore, these preliminary findings provide initial evidence to support the use of tacrolimus in patients undergoing SPK transplantation.

This supplement presents the 3-year data from the same study, giving detailed analyses comparing tacrolimus with cyclosporin-ME in terms of a variety of outcome measures and interactions, including rejection rate, graft function, metabolic parameters, corticosteroid withdrawal, human leukocyte antigen (HLA) compatibility, surgical complications and cytomegalovirus infection.

The benefits of SPK transplantation are well defined: improved patient survival, freedom from dialysis and normalization of glucose control. The procedure also reduces the risk of long-term diabetic complications, e.g. cardiac disease, neuropathy and retinopathy, which tend to progress if diabetic patients with ESRD receive a kidney transplant alone [4]. Until now, however, SPK transplantation in patients with end-stage type 1 diabetes nephropathy has been a limited procedure in Europe compared with the USA [5], and the number of transplants has remained stable over time [6]. It is hoped that on the basis of the encouraging 3-year Euro-SPK 001 study data presented in this supplement, more centres in Europe will adopt SPK transplantation. Additionally, the 3-year data provide strong support for the long-term use of the
cornerstone immunosuppressant tacrolimus in SPK transplant patients.

Conflict of interest statement. None declared.

References


5. Gruessner AC, Sutherland DER. Pancreas transplant outcomes for United States (US) and non-US cases as reported to the United Network for Organ Sharing (UNOS) and the International Pancreas Transplant Registry (IPTR) as of October 2002. In: Cecka JM, Terasaki PI, eds. *Clin Transplant*. UCLA Immunogenetics Center, Los Angeles, CA; 2002: 41–77