

Surveillance Registry of Sirolimus Use in Recipients of Kidney Allografts From Expanded Criteria Donors

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ABSTRACT

Background. The use of expanded criteria donor (ECD) kidneys has increased the overall availability of renal transplants. This study assessed the use of sirolimus in patients receiving Argentina-ECD kidneys.

Methods. This observational, open-label, 1-arm, prospective, longitudinal pilot study was conducted at 8 transplant centers in Argentina. Adults receiving kidney transplants (without pancreas) from ECDs were eligible if they were converted to sirolimus 1 to 36 months' posttransplantation, with sirolimus becoming base therapy within 1 month after conversion. Patients were followed up for 1 year. Outcomes included reasons for conversion, acute rejection, patient and graft survival, graft status, and safety.

Results. The intention-to-treat population included 52 patients (mean age, 48.7 years). Calcineurin inhibitor nephropathy (40%) and chronic allograft nephropathy (25%) were the most frequent reasons for conversion. Two acute rejections occurred during follow-up, but no patients experienced graft loss. One patient died during follow-up, and 3 patients died within 1 month of the last sirolimus dose. Levels of serum creatinine and creatinine clearance remained stable from baseline to week 52/53. Mean proteinuria measured in a subset of patients was 0.2 ± 0.2 g/24 hours before conversion and increased to 0.6 ± 1.2 g/24 hours at week 24/25 and 0.5 ± 0.6 g/24 hours at week 52/53. Adverse events were consistent with those in previous conversion trials; the most common were infections and infestations (54%).

Conclusions. This pilot study illustrates the potential benefits of sirolimus in recipients of ECD kidneys in Argentina. Larger, randomized controlled trials are needed to confirm these findings and to clarify the long-term benefits of sirolimus in this patient population.

THE SHORTAGE of kidney donors remains a major limitation for patients awaiting kidney transplantation and has prompted many transplant centers to use expanded criteria donor (ECD) kidneys [1]. This approach has increased the availability of renal transplantation for patients with end-stage renal disease and has reduced the time spent on waiting lists for patients who are willing to accept ECD kidneys. As defined by the United Network for Organ Sharing (UNOS), ECD refers to deceased donors aged ≥ 60 years with no comorbidities and to those aged 50 to 59 years with 2 of 3 high-risk conditions (terminal serum creatinine level

>1.5 mg/dL, death due to cerebrovascular accident, or history of hypertension) [2]. The definition of ECD used in this study

This study was sponsored by Pfizer Inc.

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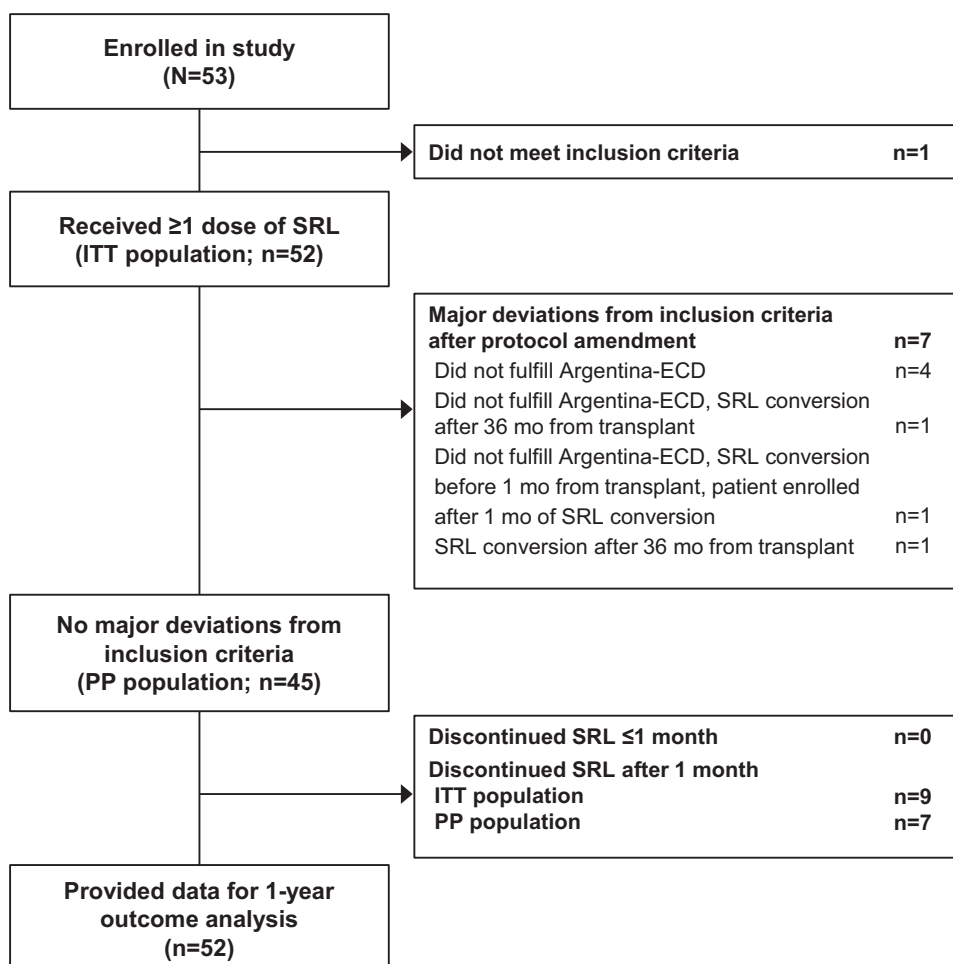


Fig 1. Patient disposition. ECD, expanded criteria donor; ITT, intention-to-treat; PP, per-protocol; SRL, sirolimus.

in Argentina (Argentina-ECD) includes UNOS criteria but also takes into account other conditions associated with suboptimal nephron mass, such as deceased donors with cold ischemia times >24 hours; deceased donors aged <50 years with a history of hypertension and/or serum creatinine level >1.5 mg/dL; and living donors aged ≥60 years with a history of mild hypertension. In Argentina, ~31% of kidneys from deceased donors over the last 5 years were ECD organs (Liliana Bisignano, MD, Director of Instituto Nacional Central Unico Coordinador de Ablacion e Implante [INCUCAI], personal communication, June 2014).

It is well recognized that both donor and recipient characteristics influence graft and patient outcomes. ECD kidneys are generally associated with poorer outcomes compared with kidneys from standard criteria donors [3,4]. In 1 study in Argentina, graft survival was 41% in renal transplant recipients when using the more liberal ECD criteria compared with 90% in standard donor kidney recipients ($P < .0003$) [5]. Upon multivariate analysis, ECD was the only donor-related factor to be independently associated with poorer graft survival.

Calcineurin inhibitors (CNIs), such as cyclosporine and tacrolimus, are effective in reducing acute graft rejection, but patients may be weaned from them within months after transplantation because of concerns regarding nephrotoxicity and other possible side effects [6]. Sirolimus is an immunosuppressive agent that is effective in preventing acute rejection and in preserving renal function after CNI withdrawal [7–9]. The present observational pilot study was designed to evaluate the use of sirolimus as base therapy in patients receiving Argentina-ECD kidneys, including reasons why sirolimus was used and its impact on outcomes.

MATERIALS AND METHODS

Patients

This study included patients aged ≥18 years who received a renal transplant without a pancreas transplant from an Argentina-ECD (as previously described) and who were converted to sirolimus at 1 to 36 months after transplant, with sirolimus becoming base therapy within 1 month after conversion. Patients participating in other clinical trials during the last 6 months and pregnant or lactating women were excluded.

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