Living-Related Donor Renal Transplantation in HIV+ Recipients using Alemtuzumab Preconditioning and Steroid-Free Tacrolimus Monotherapy: A Single Center Preliminary Experience

Henkie P. Tan, David J. Kaczorowski, Amit Basu, Akhtar Khan, Jerry McCauley, Amadeo Marcos, John J. Fung, Thomas E. Starzl, and Ron Shapiro

Background. End-stage renal disease (ESRD) is an increasing problem in patients infected with the human immunodeficiency virus (HIV). The use of highly active antiretroviral therapy (HAART) has decreased the morbidity associated with HIV and has prompted renewed interest in renal transplantation.

Methods. We performed four cases of deceased donor renal transplantation in HIV+ recipients and three cases where laparoscopic live donor nephrectomy (LLDN) was utilized to obtain the kidney for transplantation into living-related HIV+ recipients. In the four deceased donor cases, conventional tacrolimus-based immunosuppression, without antibody induction was used. In the three living-related cases, the immunosuppressive regimen was based on two principles: recipient pretreatment and minimal posttransplant immunosuppression. Alemtuzumab 30 mg (Campath 1-H) was used for preconditioning followed by low-dose tacrolimus monotherapy.

Results. Of the four deceased donor cases, one patient continues to have good graft function, and another is not yet on dialysis but has significant graft dysfunction. Rejection was observed in three patients (75%). Infectious complications occurred in one patient (25%), all non-acquired immunodeficiency syndrome (AIDS) defining. In the three living-related cases, all had good graft function, and none have experienced acute rejection. HIV viral loads remain undetectable. CD4 counts are slowly recovering. No infectious or surgical complications occurred. There were no deaths in either group.

Conclusions. These data suggest that living-related donor renal transplantation with steroid-free tacrolimus monotherapy in a "tolerogenic" regimen can be efficacious. However, long-term follow-up is needed to confirm this observation.

Keywords: Living-related renal transplantation, HIV, Campath, Steroid-free immunosuppression.

(Transplantation 2004;78: 1683–1688)

There are an estimated 40 million people infected with human immunodeficiency virus (HIV) around the world, with an incidence of 5 million new cases in 2003 (1). End-stage renal disease (ESRD) is an increasingly common problem in this growing patient population. Furthermore, the survival of patients infected with HIV who are on chronic hemodialysis is poor (2). Until recently, HIV-infected patients have generally not been considered candidates for renal transplantation (3). Before the introduction of highly active antiretroviral therapy (HAART), the substantially elevated morbidity and mortality associated with HIV infection was considered a contraindication to transplantation in most centers. The use of HAART has markedly decreased the rate of opportunistic infection and the overall mortality (4, 5). This has prompted renewed interest in solid organ transplantation in this population.

Despite improvements in survival with the use of HAART, there is still an increase in morbidity and mortality associated with HIV infection, and it has been difficult to justify the use of scarce deceased donor organs for transplantation into these patients (6). The utilization of living-related donor organs represents a way of providing organs for patients infected with HIV without further depleting the already short supply of deceased donor organs. Since its introduction in 1995, laparoscopic live donor nephrectomy (LLDN) has been shown to have a number of advantages over the traditional open operation (7). Patients experience less postoperative pain, shorter hospital stays, and shorter recovery times before returning to work (8, 9).

In addition, because of the elevated risk of opportunistic infection and the risk of progression to AIDS, subjectsing patients infected with HIV to pharmacologic immunosuppression has raised some concerns about the safety of renal transplantation in these patients. The avoidance of posttransplant over-immunosuppression is thought to permit the induction of partial tolerance (10). Recent data demonstrate that recipient pretreatment with rabbit anti-thymocyte globulin (Thymoglobulin), a T-cell depleting agent, followed by minimal use of posttransplant immunosuppression, permits a dramatic ability to wean immunosuppression (10, 11). More recently, preconditioning with alemtuzumab (Campath-1H, Millennium Pharmaceuticals, Cambridge, MA), a humanized anti-CD52 monoclonal antibody (12, 13), has been used instead of Thymoglobulin (14), with excellent early outcomes. A

1 The Thomas E. Starzl Transplantation Institute, University of Pittsburgh Medical Center, Pittsburgh, PA.
2 Address correspondence to: Henkie P. Tan, M.D., Ph.D., Thomas E. Starzl Transplantation Institute, University of Pittsburgh Medical Center, UPMC Montefiore, Suite NE 758.1. 3459 Fifth Avenue, Pittsburgh, PA 15213. E-mail: tanhp@upmc.edu.
Received 24 July 2004. Accepted 17 August 2004.
Copyright © 2004 by Lippincott Williams & Wilkins
ISSN 0041-1337/04/7811-1683
DOI: 10.1097/01.TP.0000145880.38548.0D

Transplantation • Volume 78, Number 11, December 15, 2004 1683
similar approach may be of benefit in HIV+ patients by permitting the weaning of maintenance immunosuppression.

Here we present a total of seven consecutive cases of HIV+ patients who underwent renal transplantation at the University of Pittsburgh Medical Center from 1998 to the present. All seven patients had undetectable viral loads and CD4 counts over 200 cells/mm³ before transplantation. Four deceased donor recipients and three cases where LLDN was utilized to obtain the kidney for transplantation into living-related (sibling) recipients infected with HIV are described.

MATERIALS AND METHODS

Clinical data were collected through a detailed computer-assisted chart review of the University of Pittsburgh Medical Center Archive and Retrieval (MARS) and the Electronic Data Interface for Transplantation (EDIT) systems of the Thomas E. Starzl Transplantation Institute. The data collection was approved by the University of Pittsburgh Institutional Review Board (IRB). The immunosuppressive regimen utilized in the living donor recipients was approved by the Innovative Practices Committee and The Pharmacy & Therapeutics Committee. As this regimen represents the standard of care in our program for the last 3 years, the IRB has ruled that it does not require IRB approval. All living donors and recipients provided informed consent, in addition to a separate (IRB-approved) informed consent for immune monitoring studies not routinely obtained in our conventional practice. All three living donors were specifically counseled by our psychologists/psychiatrists. All three living donor recipients had their primary residence outside the state of Pennsylvania and were referred to us through recommendations of their physicians. No other potential living donor recipients were contacted during this time period. Four HIV+ consecutive recipients of deceased donor grafts between 1998 and the present were identified.

Data on the recipients of living-related donor grafts were collected prospectively. Demographic, laboratory, and other data collected included age, race, gender, indication for transplantation, creatinine clearance, creatinine, CD4 counts before and after transplantation, HIV viral loads before and after transplantation, and tacrolimus levels. Complications in each group were also noted.

Immunosuppression for the deceased donor recipients was a function of the immunosuppressive practices of the era and utilized a tacrolimus-based regimen without antibody induction. For recipients of living-related donor organs, the immunosuppressive regimen utilized pretreatment with alemtuzumab 30 mg intravenously (IV) premedicated by 1 gm of IV methylprednisolone, diphenhydramine 50 mg IV, famotidine 20 mg IV, and acetaminophen 650 mg orally (PO), and another 1 gm of IV methylprednisolone before reperfusion, followed by tacrolimus monotherapy to achieve a level of 10 ng/mL for the first 100 days posttransplant, with subsequent tacrolimus dose weaning. The use of tacrolimus monotherapy (starting with an initial two times per day (BID) dosing to obtain an initial level of 10 ng/mL) is the standard of care for all renal transplantation recipients, unless contraindicated, at the University of Pittsburgh Medical Center for the last 2 years. All patients were taking HAART therapy before transplantation. HAART regimens were restarted for each patient after the resumption of oral intake postoperatively and managed by a dedicated HIV infectious disease specialist at UPMC and by each patient's local academic infectious disease physician after discharge.

RESULTS

Deceased Donor Renal Transplant Recipients

Between 1998 and 2004, four consecutive HIV+ patients received deceased donor renal transplants. The mean follow-up is 49±14 months. All of the patients were male, with a mean age of 45±11 years (range 32–58). Two patients were African-American, and two were Caucasian. All (100%) are alive at most recent follow-up. Only one of the four patients (25%) continues to have good graft function (creatinine 1.7 mg/dL), and another patient has not yet returned to dialysis but has a creatinine of 4 mg/dL. Medical noncompliance was a contributing factor to graft failure in the other two patients.

CD4 counts and HIV viral loads were available for all four patients. Three of these four (75%) experienced decreases in their CD4 counts and one of these four patients (25%) experienced an increase in viral load. One patient developed plantar fasciitis and cellulitis of both lower extremities.

One patient developed a periallograft hematoma requiring transfusion after a biopsy. Three of the four patients (75%) had at least one episode of acute cellular rejection, and one experienced only one episode of borderline rejection. One patient developed a basal cell carcinoma, which was excised. No other complications were reported. Individual recipient and donor demographics are detailed in Tables 1 and 2.

Living-Related Renal Transplant Recipients

Case #1

A 44-year-old Caucasian hemodialysis-dependent man with HIV presented for evaluation for renal transplantation because of ESRD secondary to type 1 diabetes mellitus in July 2002. His medical history was notable for hypothyroidism, hypertension, in addition to diabetic neuropathy and retinopathy. He contracted HIV in 1985 from a male sexual partner. At the time of his pretransplant evaluation, his CD4 count was 692 cells/mm³, and his viral load was undetectable. His serum creatinine was 4.5 mg/dL.

In September of 2003, the patient's healthy 46-year-old donor brother underwent a left LLDN without complication. The donor serum creatinine was 1.0 mg/dL, and creatinine clearance was 93 mL/min. Donor demographics are summarized in Table 2. The warm ischemic time was 4.5 min. The kidney, which had a single renal artery, a single renal vein, and a single ureter, was subsequently used for transplantation without complication. The donor's hospital course was uneventful, and he was subsequently discharged home on postoperative day 3 with a creatinine of 1.6 mg/dL. No complications have been reported to date.

The recipient received 30 mg of IV alemtuzumab intraperoperatively before revascularization. His postoperative course was uncomplicated and he was discharged home on postoperative day 5. His antiviral regimen is listed in Table 3. Approximately 1 month after transplant his CD4 count was 15 cells/mm³ and is currently 147 cells/mm³. His viral load...
TABLE 1. Demographic data on HIV-infected recipients of deceased donor renal transplants at the University of Pittsburgh between 1998 and 2004

<table>
<thead>
<tr>
<th>Recipient</th>
<th>Age</th>
<th>Race</th>
<th>Indication</th>
<th>Maintenance</th>
<th>Cr (lowest)</th>
<th>Anti-retrovirals</th>
<th>CD4 pre-Tx</th>
<th>CD4 post-Tx</th>
<th>Viral load copies/mL</th>
<th>Complications</th>
<th>Follow-up months</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>58</td>
<td>C</td>
<td>PKD</td>
<td>Tacrolimus</td>
<td>1.6</td>
<td>Lamivudine, stavudine, nevirapine</td>
<td>&gt;500</td>
<td>482</td>
<td>&lt;50</td>
<td>Delayed graft function, Periarterial hematoma following biopsy, ACR, plantar fasciitis, cellulitis</td>
<td>39</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
<td>AA</td>
<td>HTN, DM</td>
<td>Tacrolimus</td>
<td>1.7</td>
<td>Lamivudine, zidovudine, zidovudine, stavudine</td>
<td>1,054</td>
<td>172</td>
<td>&lt;50</td>
<td>Delayed graft function, multiple episodes of ACR, chronic allograft nephropathy, dialysis dependent</td>
<td>51</td>
</tr>
<tr>
<td>3</td>
<td>32</td>
<td>AA</td>
<td>HTN, HIVAN</td>
<td>Tacrolimus</td>
<td>1.3</td>
<td>Lamivudine, zidovudine, stavudine, efavirenz</td>
<td>391</td>
<td>98</td>
<td>5,774</td>
<td>Multiple episodes of ACR, severe chronic rejection</td>
<td>39</td>
</tr>
<tr>
<td>4</td>
<td>46</td>
<td>C</td>
<td>PKD</td>
<td>Tacrolimus</td>
<td>1.3</td>
<td>Nevirapine, lamivudine, stavudine</td>
<td>411</td>
<td>944</td>
<td>&lt;50</td>
<td>Basal cell carcinoma, s/p excision</td>
<td>69</td>
</tr>
</tbody>
</table>

* This patient was also infected with hepatitis C.
* On dialysis.

C, Caucasian; AA, African-American; PKD, polycystic kidney disease; FSGS, focal and segmental glomerulosclerosis; HTN, hypertension; DM, diabetes mellitus; HIVAN, human immunodeficiency associated nephropathy; Ct, creatinine; Tx, transplant; NA, not available; ACR, acute cellular rejection; CMV, cytomegalovirus.

TABLE 2. Demographic features of deceased donors and grafts for HIV-infected recipients

<table>
<thead>
<tr>
<th>Donor</th>
<th>Donor age</th>
<th>Kidney</th>
<th>Anatomy</th>
<th>Cold ischemic time</th>
<th>Immediate graft function</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>37</td>
<td>Left</td>
<td>Single artery, vein and ureter</td>
<td>15 hr, 3 min</td>
<td>No</td>
<td>High risk donor (IVDA)</td>
</tr>
<tr>
<td>2</td>
<td>NA</td>
<td>Right</td>
<td>Single artery, vein and ureter</td>
<td>33 hr, 10 min</td>
<td>No</td>
<td>Hepatitis C positive donor</td>
</tr>
<tr>
<td>3</td>
<td>22</td>
<td>Right</td>
<td>Two renal arteries, single vein and ureter</td>
<td>24 hr, 11 min</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>Left</td>
<td>Single artery, vein and ureter</td>
<td>19 hr, 46 min</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

IVDA, intravenous drug abuse; NA, not available.

remains undetectable. His current immunosuppressive regimen consists of 0.1 mg of tacrolimus every 4 days (he takes a protease inhibitor) with most recent tacrolimus level of 3.7 ng/mL, gradually weaned from an initial posttransplant level of 10.0 ng/mL. His most recent serum creatinine is 1.6 mg/dL. He was found to have two episodes of tacrolimus toxicity by biopsy for an elevated creatinine. He has not had any complications, episodes of rejection, or opportunistic infections.

In November 2003, the patient’s 32-year-old sister who had sickle-cell trait but was otherwise healthy, elected to undergo a left LDLN without complication. The warm ischemia time was 5.5 min. The donor was discharged home on postoperative day 2 with a creatinine of 1.1 mg/dL after an unremarkable postoperative hospital stay. She has not had any complications to date.

The recipient received 30 mg of alemtuzumab intraoperatively. Her postoperative course was uneventful and she was subsequently discharged home on postoperative day 5 with a creatinine of 1.0 mg/dL. Her most recent CD4 count is 53 cells/mm³. Her viral load has remained undetectable. Her current antiviral regimen is detailed in Table 3. She had tried multiple other regimens, some of which included protease inhibitors, but she was unable to tolerate them because of side effects. She has had no complications, episodes of rejection, or opportunistic infections to date.

Case #2

A 40-year-old African-American woman presented for evaluation for renal transplantation in May 2003. She developed ESRD secondary to hypertensive nephropathy and had been hemodialysis dependent since 1998. She contracted HIV from heterosexual contact. Her past medical history was notable for preeclampsia and cervical dysplasia, for which she underwent ablative therapy. Her CD4 count was 304 cells/mm³. Her viral load was 140 copies/mL at the time of her initial evaluation but was undetectable at the time of her transplant. She had no history of opportunistic infections.


**TABLE 3.** Demographic data on HIV+ living-related kidney recipients

<table>
<thead>
<tr>
<th>Recipient</th>
<th>Age</th>
<th>Race</th>
<th>Sex</th>
<th>Indication</th>
<th>FK506 level (mg/dL)</th>
<th>Maintenance</th>
<th>Anti-retrovirals</th>
<th>CD4 pre-Tx</th>
<th>CD4 post-Tx</th>
<th>Complications</th>
<th>Duration of follow-up* (days)</th>
<th>HLA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>44</td>
<td>C</td>
<td>M</td>
<td>DM</td>
<td>FK506 0.1 mg PO q 3d</td>
<td>3.7</td>
<td>1.6</td>
<td>Lamivudine, abacavir, efavirenz</td>
<td>692</td>
<td>147</td>
<td>Tacrolimus toxicity by bx</td>
<td>325</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>AA</td>
<td>F</td>
<td>HTN</td>
<td>FK506 16 mg PO qod</td>
<td>3.0</td>
<td>0.9</td>
<td>Lamivudine, zidovudine, efavirenz</td>
<td>304</td>
<td>53</td>
<td>None</td>
<td>262</td>
</tr>
<tr>
<td>3</td>
<td>58</td>
<td>C</td>
<td>M</td>
<td>Re flux nephropathy</td>
<td>FK506 2 mg PO bid</td>
<td>7.0</td>
<td>1.6</td>
<td>Lamivudine, zidovudine, efavirenz</td>
<td>1,843</td>
<td>39</td>
<td>Tacrolimus toxicity by bx</td>
<td>152</td>
</tr>
</tbody>
</table>


Case #3

In September 2002, a 58-year-old man presented for evaluation for renal transplantation for ESRD secondary to reflux nephropathy, for which he had already undergone corrective surgery. He was started on peritoneal dialysis shortly after his evaluation. He was diagnosed with HIV approximately 5 years before his evaluation, which he contracted through a homosexual contact. His medical history was also notable for insulin-dependent diabetes mellitus, hypertension, and biliary pancreatitis, for which he previously underwent cholecystectomy. Before transplantation, he also had basal cell cancer of his face and squamous cell cancer of his neck, which were both successfully excised. His CD4 count was 1,843 cells/mm³ before transplantation, and his viral load was undetectable.

In February 2004, his healthy 56-year-old sister elected to undergo an uncomplicated left LLDN. Her creatinine was 0.6 mg/dL at the time. She was found to have two renal arteries. One of the renal arteries supplying the upper pole was approximately 1 mm in diameter and was ligated. Otherwise, the kidney had one vein and one ureter. The warm ischemic time was approximately 5 min. The donor was subsequently discharged home on postoperative day 3 with a creatinine of 0.9 mg/dL. She has had no complications to date.

The recipient received 30 mg alemtuzumab before revascularization. The recipient’s peri- and postoperative course was uneventful and he was discharged home on postoperative day 4 with a creatinine of 1.0 mg/dL. His immunosuppressive regimen currently consists of tacrolimus 4 mg once daily. His most recent tacrolimus level was 7.0 ng/mL. On postoperative day 14, his creatinine rose to 1.3 mg/dL and was 1.6 mg/dL on postoperative day 21. It has subsequently remained stable at 1.6 mg/dL. On multiple biopsies, there has been no evidence of acute cellular rejection. There was some subcapsular fibrous tissue with focal nonspecific mixed inflammation. There was also tubular vacuolization compatible with tacrolimus toxicity in spite of initial posttransplant levels of about 10 ng/mL. Otherwise, he has had no infectious or surgical complications and is doing well.

**DISCUSSION**

The survival of patients with HIV infection and ESRD receiving hemodialysis has improved compared with the uniformly dismal outcomes in the 1980s. Ifudu and colleagues found that, with 68-months follow-up, 50% (17/34) of patients with both ESRD and HIV infection were deceased, comparable with the mortality of patients (65/131) with ESRD alone (15). However, when the data were adjusted for age, patients with both ESRD and HIV infection had a 97% higher risk of death than did their counterparts with ESRD alone.

Recent data demonstrate that recipient pretreatment with Thymoglobulin, a T-cell depleting agent followed by minimal use of posttransplant immunosuppression, permits a dramatic ability to wean immunosuppression (10, 11, 14), and similar findings have been demonstrated using alemtuzumab preconditioning (13). The exact mechanism remains to be elucidated and we are in the process of elucidating this high frequency of profound in vitro hyporesponsiveness induced by alemtuzumab preconditioning (16). It is also known that lymphopenia is followed by spontaneous homeostatic expansion of the remaining T-cell pool size. Recently, Dummer and colleagues demonstrated that T-cell homeostatic proliferation elicits effective antitumor autoimmunity.

**TABLE 4.** Characteristics of donors undergoing LLDN for transplantation into HIV+ recipients

<table>
<thead>
<tr>
<th>Donor</th>
<th>Age</th>
<th>Sex</th>
<th>Race</th>
<th>Kidney donated</th>
<th>Cr prior to LLDN</th>
<th>Cr post-LLDN</th>
<th>Days hospitalized</th>
<th>Complications</th>
<th>HLA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>46</td>
<td>M</td>
<td>C</td>
<td>Left</td>
<td>1.0</td>
<td>1.6</td>
<td>3</td>
<td>None</td>
<td>A3,24, B8,35, DR16,11</td>
</tr>
<tr>
<td>2</td>
<td>32</td>
<td>F</td>
<td>AA</td>
<td>Left</td>
<td>0.7</td>
<td>1.1</td>
<td>2</td>
<td>None</td>
<td>A1,74, B58,72, DR8,11</td>
</tr>
<tr>
<td>3</td>
<td>56</td>
<td>F</td>
<td>C</td>
<td>Left</td>
<td>0.6</td>
<td>0.9</td>
<td>3</td>
<td>None</td>
<td>A2,--, B35,60, DR1,17</td>
</tr>
</tbody>
</table>

M, male; F, female; C, Caucasian; AA, African-American; Cr, creatinine; LLDN, laparoscopic live donor nephrectomy.
(17). It can be speculated that "lost" or "absent" immunity to experimental tumors results during recovery from the kind of T-cell depletion that is achieved with alemtuzumab.

Transplantation of solid organs into patients with HIV before the introduction of HAART yielded variable results. A number of reports described cases with varying degrees of success. In 1990, Tzakis and colleagues (18) performed a retrospective analysis of 25 solid organ transplant recipients at the University of Pittsburgh between 1981 and 1988, with a mean follow-up of 2.75 years (range 0.7–6.6 years). Five of the 25 patients were recipients of kidney transplants. The other organs were liver (n = 10) or heart (n = 5). Four out of the five kidney transplant recipients were alive at follow-up. Overall, the time to the development of AIDS appeared to be shortened after receiving an organ transplant and immunosuppression, but the difference was not statistically significant.

Erice and colleagues from the University of Minnesota in 1991 reported five cases and reviewed the literature (19). They included a total of 11 recipients of kidney transplants that were HIV+ at the time of transplant. They found that six of eight (75%) of these patients had functioning grafts after a mean follow-up of over 30 months. Eight of the patients had no progression of HIV or HIV-related diseases, but three of the patients developed AIDS and died within 2 years of transplant. Another patient died of sepsis that was thought to be unrelated to HIV approximately 2 months after transplant.

In 1993, a group from Germany reported four cases of patients that were infected with HIV through renal transplantation from HIV+ donors (20). Although they experienced several infectious complications and multiple episodes of rejection, none of the patients in their series developed AIDS. In addition to reporting these four cases, they reviewed case reports of 53 patients in the literature. Interestingly, they found that the cumulative incidence of AIDS was significantly lower in HIV-infected transplant recipients that had an immunosuppressive regimen that included cyclosporine.

A historical cohort analysis using data from the United States Renal Data System (USRDS) on solitary cadaveric renal transplant recipients between 1987 and 1997 was performed to determine the impact of HIV infection on graft and patient survival (21). Compared with the national USRDS transplant population, the HIV+ patients had better HLA matching and younger donors. However, both patient and 3-year graft survival were reduced in HIV+ patients (83% patient, 53% graft) compared with the USRDS population (88% patient, 73% graft).

Since the introduction of HAART, results have been more encouraging. A recent pilot trial reported 100% survival, all with functioning grafts, at a mean follow-up of 480 days in 10 patients undergoing renal transplantation (22). No adverse effect of HIV on graft function was observed in this study. While CD4 counts generally dropped transiently in all patients immediately after transplantation, they soon returned to normal levels. However, in all patients treated with Thymoglobulin, CD4 counts dropped below 220 and have been slow to recover. Rejection occurred in 5 of 10 (50%) kidney transplant recipients, and 3 of the 5 required Thymoglobulin to treat the rejection. No AIDS defining infections occurred in this series. However, one patient developed Staphylococcus aureus endocarditis, and another developed Pseudomonas aeruginosa pneumonia and sepsis after treatment with Thymoglobulin. There were also two cases of S. aureus wound infections and one case of influenza B pneumonia. With a longer mean follow-up of 23 months, the same investigators found unexpectedly high incidence of rejection in 67% of HIV+ recipients of renal transplants using a cyclosporine, mycophenolate mofetil, and steroid maintenance immunosuppression protocol (23).

In the recipients of deceased donor organs that we have reported here, the incidence of rejection was also high (75%) using conventional tacrolimus-based immunosuppression without antibody induction. Chronic allograft nephropathy was also a significant problem. These observations, coupled with the occurrence of multiple infectious complications in these patients, suggest that further investigation into novel approaches to renal transplantation in HIV+ recipients was warranted.

In contrast to these results, all three of the patients presented here who received living-related donor grafts under a tolerogenic immunosuppressive regimen are doing well with functioning grafts to date, albeit with a short follow-up. As expected, because of pretreatment with alemtuzumab, each of the patients has experienced a drop in CD4 count, but they appear to be recovering. Importantly, although the follow-up is short, we have not observed any infectious complications or graft rejection in this group receiving posttransplant steroid-free tacrolimus monotherapy. In addition, HIV viral loads have remained undetectable. These initial results are encouraging. None of the donors have had any surgical complications after undergoing LLDN. While long-term follow-up will be needed, the data presented here suggest that LLDN is an effective means for providing organs for patients with ESRD who are infected with HIV who otherwise would be on a potentially controversial deceased donor waiting list and that a "tolerogenic" regimen involving pretreatment with alemtuzumab and posttransplant immunosuppression with low-dose tacrolimus monotherapy seems to be safe and effective for the prevention of graft rejection. We believe that our immunosuppression protocol will also benefit the HIV+ recipients who will receive deceased donor organs.

ACKNOWLEDGMENTS
We would like to thank Dr. Margaret Ragni for reviewing this manuscript and for her help in caring for the HIV recipients.

REFERENCES