REVIEW ARTICLE

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An update on immunosuppression for the HIV-positive kidney transplant recipient

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ABSTRACT

The outcome of human immunodeficiency virus (HIV)-positive patients has improved dramatically with the advent of combined antiretroviral therapy. The mortality rate for HIV-positive patients with chronic kidney disease stage 5 is now similar to those without HIV infection, making kidney transplantation an increasingly considered alternative treatment for end-stage renal disease in this population. Knowledge of the pharmacokinetics of antiretroviral medications and potential drug-drug interactions between antiretroviral and immunosuppressive medications are critical to the success of transplantation in this setting. The aim of this article is to present the state of the art kidney transplant therapy in HIV-positive patients.

Key-Words:
Antiretroviral therapy; HIV; immunosuppression; kidney transplantation.

INTRODUCTION

Human immunodeficiency virus (HIV) infection is no longer an absolute contraindication for transplantation[1]. Since the introduction of effective combined antiretroviral regimens which promote immunological recovery and suppression of viral replication, the outcome of HIV patients has improved dramatically. Several studies demonstrate that the mortality rate for HIV-positive patients with end-stage renal disease (ESRD) is now similar to those without HIV infection[2,3]. Given this significant improvement in HIV patients' life expectancy, kidney transplantation has been increasingly considered as an alternative treatment for ESRD in this population[4].

In recent years, more than 200 renal transplants have been performed in HIV-infected patients worldwide[1]. According to the Portuguese Society of Nephrology the prevalence of HIV-positive patients on haemodialysis in Portugal in 2010 was close to 1.2% of all dialysis patients or, approximately, 120 patients[5]. There are no specific registries of transplantation in HIV-positive patients in Portugal, but as of today, five kidney transplants have been performed in four centres nationwide, according to a personal inquiry to all transplant units.

All nephrologists are likely to take care of HIV-positive patients with kidney disease and therefore need to be acquainted with the pharmacokinetics of antiretroviral medications and proper dosing of these drugs at different stages of chronic kidney disease (CKD). Furthermore, awareness of drug interactions between antiretroviral and immunosuppressive medications is of paramount importance for the success of transplantation in these individuals. Close monitoring of drug levels is also critical due to the robust interactions that can be observed[6].

KIDNEY TRANSPLANTATION IN THE PRE-CART ERA

Before the advent of combined antiretroviral therapy (cART), reports on kidney transplantation in HIV-positive patients were limited to either isolated case reports or to a small number of patients[4] because of the potential risks of immunosuppression in the context of unleashed HIV infection[7]. One of the first reports, released in the early '90s, showed a 36% mortality rate and a graft survival of only 54.9% at 30 months[4].

The largest review of kidney transplantation in HIV patients over the pre-cART period was obtained from the United States Renal Data System (USRDS) and analysed kidney transplantations performed between 1987 and 1997. The results showed both a worse five-year patient survival (71% versus 78%) and kidney graft survival (44% versus 61%) when HIV-positive recipients of kidney allografts were compared to seronegative individuals. In multivariate analysis, HIV infection was listed as an independent risk factor for mortality, as well as for graft loss, in kidney transplant recipients from deceased donors[8].

KIDNEY TRANSPLANTATION IN THE POST-CART ERA

After the advent of cART in 1996, life expectancy in HIV-infected patients changed significantly, with a marked decrease in morbidity and mortality rates[4]. In addition to being effective in treating established HIV-associated nephropathy (HIVAN), cART may also potentially decrease the actual incidence of *novo* HIVAN[9,10]. However, after several years of cART therapy, some patients eventually progress to ESRD with the mechanisms remaining to be elucidated[11]. It is important to keep in mind that several components of cART, with particular emphasis on the protease inhibitors, may impact on cardiovascular and metabolic risk factors which cause or accelerate kidney disease.

A recent analysis of the USRDS confirmed that the mortality in HIV patients receiving deceased kidneys in the cART era had improved dramatically, although black patients tended to be underrepresented[12]. Most transplant groups from Europe and North America considered the following criteria for including HIV-infected patients on the transplant waiting list: clinical (no AIDS-defining diseases), immunological (CD_4 T-cell count above 200 cells/μl), virological (undetectable HIV viral load in plasma, *i.e.* < 50 copies/ml for at least 6 months) and social (appropriate degree of stability with no active consumption of drugs or alcohol and adherence to proposed therapies)[1].

Current therapeutic HIV guidelines recommend the initiation of cART in individuals presenting with less than 350 CD_4 T-cells/μl or with concurrent morbidities, namely HIVAN[13].

Contemporary treatment of HIV infection involves the combination of at least three fully active drugs from the currently available classes of antiretroviral medications: nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), entry inhibitors and integrase inhibitors. The current antiretroviral regimens considered to *naïve* patients are based on a combination of two NRTIs and a boosted PI, an NNRTI or an integrase inhibitor[13,14].

Some antiretroviral medications need to be adjusted to kidney function, namely NRTIs (Table I). For patients with CKD, dose adjustments are not necessary for NNRTIs (delavirdine, efavirenz, etravirine, nevirapine); PIs (atazanavir, darunavir, fosamprenavir, indinavir, lopinavir/ritonavir, nelfinavir, ritonavir, saquinavir, tipranavir); C-C chemokine receptor type 5 (CCR5) antagonists (maraviroc); fusion inhibitors (enfurvitide); or integrase inhibitors (raltegravir)[13].

Despite the fact that tenofovir has been associated with nephrotoxicity, a large observational study in Africa failed to detect worsening of kidney function in patients treated with this NRTI. In this study, almost all cases of deterioration of kidney function were attributed to well-established causes other than this drug[15]. It is important to mention that tenofovir is particularly attractive in regions with high prevalence of hepatitis B, due to the dual effect against both viruses. Nevertheless, due to the potential to increase serum creatinine at least in some patients, alternative therapies such as abacavir may be preferable to treat kidney allograft recipients as other toxic, immunologic and haemodynamic factors may affect kidney function in this specific group of patients and tenofovir's effect may be a confounding factor.

Table I

Antiretroviral dosing recommendations in HIV infected adults according to creatinine clearance (adapted from[11])

Antiretroviral drug	Dosage according to creatinine clearance
Nucleoside reverse-transcriptase inhibitors	
Zidovudine	≥ 15 mL/min: 300 mg po bid ‹ 15 mL/min: 100mg q6-8h
Lamivudine	≥ 50 mL/min: 150 mg po bid / 300 mg po qd 30-49 mL/min: 150 mg po qd 15-29 mL/min: 150 mg first dose, then 100 mg po qd 5-14 mL/min: 150 mg first dose, then 50 mg po qd ‹ 5 mL/min: 50 mg po first dose, then 25 mg po qd
Abacavir	No adjustment: 300 mg po bid / 600mg po qd
Stavudine immediate release	›50 mL/min: 40 mg po bid 26-50 mL/min: 20 mg po bid ≤25 mL/min: 20 mg po qd
Didanosine buffered tablets	≥60 mL/min: 200mg po bid 30-59 mL/min: 200 mg po qd 10-29 mL/min: 150 mg po qd ≤10 mL/min: 100 mg po qd
Zalcitabine	≥40 mL/min 0,75 mg po tid 10-40 mL/min: 0,75 mg po q12h ‹10 mL/min: 0,75 mg po q24h
Emtricitabine	≥50 mL/min: 200 mg po qd 30-49 mL/min: 200mg q48h 15-29 mL/min: 200mg po q72h ‹15 mL/min: 200mg po q96h
Emtricitabine / tenofovir	≥50 mL7min: 200mg/300mg po qd 30-49 mL/min: one tab po 48h ‹30 mL/min: unknown, should not use combination tablet
Tenofovir	≥50 mL/min: 300 mg po qd 30-49 mL/min: 300mg po q48h 10-29 mL/min: 300mg po q72h
Non-nucleoside reverse-transcriptase inhibitors	
Nevirapine	No adjustment: 200 mg po bid
Efavirenz	No adjustment:600 mg po qd
Delavirdine	No adjustment:400 mg po tid
Protease inhibitors	
Indinavir	No adjustment: 800mg po tid
Saquinavir soft gel	No adjustment:1200mg po tid
Nelfinavir	No adjustment: 1250mg po bid
Amprenavir	No adjustment:1200 mg po bid
Fosampenavir	No adjustment:1400mg po qd / 700mg po bid
Ritonavir	No adjustment:600 mg po bid
Lopinavir/ritonavir	No adjustment:400mg / 100mg po bid
Atazanavir	No adjustment:400 mg po qd
CCR5 antagonists	
Maraviroc	No adjustment: 150 – 600 mg bid *
Entry/fusion inhibitors	
Enfurvitide	≥ 35 mL/min: 90 mg sc bid ‹35 mL/min: unknown, use with caution
Integrase inhibitors	
Raltegravir	No adjustment:400 mg po bid

* the dosage depends on concomitant medications interfering with CYP3A4

IMMUNOSUPPRESSION AFTER KIDNEY TRANSPLANTATION IN HIV-POSITIVE PATIENTS

With the dramatic reductions in HIV-associated morbidity and mortality observed since the availability of cART, the safety of immunosuppression in this population has become the more pressing concern. Surprisingly, immunosuppression may have a beneficial impact on patients with HIV infection by reducing the pool of activated T-cell targets for new infection, decreasing the immune activation characteristic of HIV pathogenesis, inhibiting HIV replication, and/or interacting synergistically with antiretroviral agents[7].

A critical point for transplantation is the selection of the optimal immunosuppression protocol to prevent rejection, which requires the modulation of the immune system in a group of patients displaying an immunological dysfunction, and therefore more prone to opportunistic infections, but, on the other hand, with an intact and probably even enhanced potential for allorecognition[16,17].

1 – Induction therapy

In the initial clinical trials of organ transplantation in HIV-positive patients, immunosuppressive regimens focused on maintenance therapy with agents with known antiretroviral qualities. This therapy consisted of a combination of steroids, a calcineurin inhibitor (CNI) and mycofenolate mofetil (MMF). However, organ recipients with HIV infection can mount an alloimmune response and HIV-positive renal transplant recipients have a higher rejection rate than their counterparts without HIV[17]. The reason for such high rejection rates is unclear, although dysregulation of the immune system or insufficient immunosuppression are two possible causes[2].

For this reason, induction therapy with interleukin-2 receptor inhibitor (basiliximab) was successfully introduced[2,18]. Most transplant centres are reluctant to use lymphocyte depleting agents for induction (thymoglobulin, alemtuzumab) as these agents severely deplete CD_4 T-cells for several months. Nevertheless, these potent agents have successfully reversed aggressive rejection in several HIV-positive kidney transplant recipients[19].

2 – Maintenance therapy

In a recent meta-analysis of twelve published case series[16], maintenance immunosuppression therapy in HIV-positive kidney transplant recipients consisted most commonly of triple therapy with a CNI (ciclosporin as the most frequently used), MMF and steroids.

Some studies have demonstrated that some of the immunosuppressive drugs used in transplantation, such as CNI, sirolimus and mycophenolic acid, exhibit an antiretroviral action[4] (Table II).

Corticosteroids- Izzedine *et al.* showed that prednisolone increases CD_4 T-cell lymphocyte population[20]. Another study showed that prednisolone acts by suppressing HIV viral load and inhibiting CCL2,

Table II

Effects of immunosuppressive drugs on antiretroviral activity

Immunosuppressive drug	Potential effects
Thymoglobulin	• decrease in CD_4 T-cell counts
Corticosteroids	• increase CD_4 T-cell lymphocyte population • suppress HIV viral load and inhibit cytokine CCL2
Azathioprine	• increase viral replication
Mycophenolate mofetil / Mycophenolic acid	• antiretroviral activity (inhibition of virus lifecycle) • synergistic activity with reverse transcriptase inhibitors
Ciclosporin / Tacrolimus	• selective inhibition of infected cell growth
Sirolimus	• suppression of T-cell activation • suppression of antigen presenting cell function • disruption of infective virion replication • prevention of HIV virus entry and replication into the cells?

a proinflammatory cytokine induced by HIV infection[19].

Antimetabolic agents- Azathioprine use has been associated with increased viral replication, while the opposite seems to happen with the use of mycophenolic acid or its prodrug MMF[20]. Its virostatic action is thought to result from the depletion of guanoside nucleosides, which are necessary for the virus lifecycle and subsequent synergistic activity with NRTIs, namely abacavir, didanosine and tenofovir. However, it negatively affects the action of zidovudine and stavudine[21].

Calcineurin inhibitors- Ciclosporin and tacrolimus have well-documented antiretroviral effects through selective inhibition of infected cell growth. These agents interfere with HIV pathogenic protein functions, which ultimately results in the reduction of virus formation[2]. CNIs can however cause glucose intolerance, which can be exacerbated by concomitant administration of some antiretroviral agents.

Mamalian target of rapamycin (mTOR) inhibitors- Similarly to CNIs, sirolimus, a macrolid antibiotic produced by the fungus *Streptomyces hygroscopicus*, also exerts some antiretroviral activity through suppression of T-cell activation, suppression of professional antigen presenting cell function and disruption of infective virion replication. Sirolimus decreases the expression of CCR5 on monocytes and lymphocytes, thus potentially preventing the HIV virus from entering these cells and replicating[22]. This receptor may be a common link between HIV infection and allorecognition, as lower transplant rejection rates are observed in individuals expressing genetic deficiency (a 32 base pair deletion) at the CCR5 or following CCR5 blockade[23]. This concept is consistent with the possibility that CCR5 antagonists such as maraviroc may have a role in prolonging graft survival in solid organ and bone marrow transplantation, raising also the possibility that sirolimus may be a reasonable option to treat the HIV-positive renal transplant recipient[22].

3 – Rejection therapy

There are no current recommendations on how to treat rejection episodes in HIV-positive kidney transplant recipients[24]. The use of antilymphocyte polyclonal antibodies is controversial and many authors recommend restricting this therapy for patients with a very high immunological risk for rejection[19,25]. Thymoglobulin, an agent frequently used to manage acute rejection, may be associated with marked CD_4 T-cell count depletion[4]. Several studies have reported significant decreases in CD_4 T-cell counts in HIV-infected recipients related to the use of thymoglobulin[3,25]. In a study published by Stock *et al.* [3], the median change in the CD_4 T-cell count from baseline to one year was greater in patients who received induction therapy with thymoglobulin compared to those who did not (-239 versus -135 cells per mm^3). However, these changes were transient and the median change in CD_4 T-cell count from baseline to 3 years was not significantly different between these groups (-57 and -52 cells per mm^3, respectively). In addition, another study[25] failed to detect an increased risk of opportunistic infections and progression to AIDS or death related to the use of lymphocyte depleting agents.

DRUG INTERACTIONS BETWEEN IMMUNOSUPPRESSIVE AGENTS AND CART

Pharmacokinetic interaction between antiretrovirals and immunosuppressants is the most intricate issue in organ transplantation of HIV-positive patients. The administration of a complex immunosuppressive regimen in combination with antiretroviral therapy can result in an altered exposure to immunosuppressants and may be associated with rejection[1].

In most centres, allograft recipients with HIV infection receive the same cART regimens they received before transplantation[2]. Early studies demonstrate that with this strategy, HIV-infected patients do not progress to AIDS[17,18,26]. Initial experience also suggests that these recipients can tolerate cART withdrawal for several weeks without changes in viral load and CD_4 T-cell count[26,27]. Nevertheless, potential drug-drug interactions should be taken into consideration when selecting an antiretroviral regimen (Table III).

Most drug interactions with antiretroviral drugs are mediated through inhibition or induction of hepatic drug metabolism[13]. The most notable drug

Table III

Drug interactions between antiretroviral agents and immunosuppressive drugs (adapted from[1])

	NRTIs	NNRTIs	Protease inhibitors	CCR5 antagonists	Integrase inhibitors
Methylprednisolone	drug-drug interaction unlikely	may increase the metabolism of corticosteroids and decrease blood levels	may decrease the metabolism of corticosteroids and increase blood levels	drug-drug interaction unlikely	drug-drug interaction unlikely
Azathioprine	no drug-drug interactions have been described				
Mycophenolate mofetil / Mycophenolic acid	interaction cannot be ruled out with abacavir and zidovudine	drug-drug interaction unlikely	atazanavir may increase MMF blood levels; ritonavir, tipranavir and nelfinavir may decrease MMF blood levels	drug-drug interaction unlikely	drug-drug interaction unlikely
Calcineurin Inhibitors (Tacrolimus /Ciclosporin)	drug-drug interaction unlikely	may increase the metabolism of CNI and decrease blood CNI levels; therapeutic drug monitoring is recommended	risk of increased CNI levels/ toxicity; markedly lower doses may be required	drug-drug interaction unlikely	drug-drug interaction unlikely
mTOR inhibitors (Sirolimus/Everolimus)	drug-drug interaction unlikely	may increase the metabolism of mTOR and decrease blood mTOR levels; therapeutic drug monitoring is recommended	risk of increased mTOR levels/ toxicity; markedly lower doses may be required	drug-drug interaction unlikely	drug-drug interaction unlikely

Mycophenolate mofetil (MMF); mamalian target of rapamycin (mTOR); nucleoside reverse transcriptase inhibitors (NRTIs); non-nucleoside reverse transcriptase inhibitors (NNRTIs); C-C chemokine receptor type 5 (CCR5)

interaction occurs between antiretroviral medications and immunosuppressive agents that induce or inhibit the P-glycoprotein (P-gp) efflux transporters and CYP450 3A (CYP3A4) metabolising enzymes found in the gut and liver. These interactions can lead to unexpected increases or decreases in drug plasma levels, and result in toxic side effects, organ rejection or HIV disease breakthrough[2].

All PIs and NNRTIs are metabolised in the liver by the CYP3A4 isoenzyme. Some examples of other drugs include medications that are commonly prescribed for non-HIV medical conditions, such as lipid-lowering agents (e.g. statins), benzodiazepines, calcium channel blockers (e.g. diltiazem), immunosuppressants (e.g., CNIs and mTOR inhibitors), anticonvulsants, rifamycins, erectile dysfunction agents (e.g., sildenafil), ergot derivatives, azole antifungals, macrolides, oral contraceptives and methadone[13]. The use of a CYP3A4 substrate that has a narrow margin of safety in the presence of a potent CYP3A4 inhibitor may lead to markedly prolonged elimination half-life and toxic drug accumulation. Avoidance of concomitant use or dose reduction of the affected drug, with close monitoring for dose-related toxicities, may be warranted[13]. Three frequently used groups of drugs are very robust blockers of CYP3A4: diltiazem, imidazolic antifungals (such as ketoconazol) and macrolides (erythromycin, clarithromycin). It is also relevant to mention that among antiretroviral drugs, ritonavir is specifically used as a booster, meaning that this less expensive PI is specifically used to block CYP 3A4 to allow lower doses of newer, more expensive PIs (such as atazanavir or darunavir) to reach therapeutic levels. As CNIs and mTOR inhibitors are metabolised by the same enzymatic system, it is rather predictable that drug levels may become astronomical if doses are not substantially reduced. However, there is a concern that in order to achieve reasonable pre-dose levels, total exposure may be reduced, increasing the risk of rejection[3].

On the other hand, the use of NNRTIs with a potential to induce CYP3A4, such as efavirenz, may lead to suboptimal immunosuppressive drug concentrations, although with a smaller magnitude than with the use of more potent inducers such as rifampin, phenobarbital, phenytoin or *Hypericum perforatum* tea or plant extract (St John's wort). These drug combinations should be avoided if alternative agents can be used. If this is not possible, close monitoring of plasma HIV RNA, with or without antiretroviral dosage adjustment and therapeutic drug monitoring, may be warranted[13].

Unlike PIs and NNRTIs, NRTIs do not undergo hepatic transformation through the CYP metabolic

pathway. Some, however, do have other routes of hepatic metabolism[13]. The integrase inhibitor raltegravir has high antiretroviral efficacy and no significant interactions with immunosuppressive agents because of its lack of effect on CYP3A4 and has been successfully used in some cases[1]. Pretransplant conversion to a cART regimen using raltegravir rather than boosted PI will significantly reduce the potential for interactions and ease postransplant management. However, these regimens in Portugal are on average EUR 2,600 more expensive yearly than a comparable boosted PI-based regimen: abacavir/lamivudine/atazanavir/ritonavir EUR 30.64/day versus abacavir/lamivudine/raltegravir EUR 37.93/day for average doses (prices from September 2011; data provided by Dr João Rijo, Pharmaceutical Department, Centro Hospitalar de Lisboa Ocidental). Maraviroc-based regimens, likewise free of CYP 3A4 interactions and with the abovementioned attractive immunomodulatory potential, pose similar pharmacoeconomic constraints.

The CYP450 system and P-gp are also involved in the metabolism and elimination of glucocorticosteroids, CNIs and mTOR inhibitors[28]:

– **Glucocorticoids** are substrates of CYP3A4 and P-gp. PI inhibit metabolism of glucocorticoids, increasing their plasma concentration and clinical effects, so doses may need to be reduced accordingly[20,29]. Glucocorticoids may also be inducers of CYP3A4, reducing plasma levels of co-administered PI[6].

Patients on glucocorticoids steroids often take ranitidine or proton inhibitors, which can reduce intestinal absorption of the PI atazanavir (very dependent on a low gastric pH) and, therefore, its plasma concentration. This undesirable side effect does not occur with the PI ritonavir[2].

– **MMF and azathioprine** are not metabolised by the CYP450 system or transported by P-gp, so interactions with cART medications are less of an issue[6] and they are considered safe immunosuppressants in HIV-positive patients, although only MMF displays antiretroviral activity. However, diarrhoea, a well-known MMF side effect, may hinder the use of MMF in clinical practice, since it can be added to the diarrhoeal effects of antiretroviral drugs and the disease itself in these patients[4].

– **CNIs and mTOR inhibitors** are substrates and inhibitors of CYP3A4 and P-gp. Administration of these drugs with PIs (namely ritonavir) has the potential to delay elimination and markedly increase blood concentrations of both drugs[30,31]. Bioavailability is also increased. On average, only 25% of the standard dose of ciclosporin is required if administered concomitantly with PIs[32].

As there is a great deal of interindividual variability in patients on NNRTIs, therapeutic concentrations of immunosuppressants such as CNIs and mTOR inhibitors should be monitored routinely, with dosage adjustments made as necessary[6]. Efavirenz can markedly induce CYP3A4 activity, increasing drug metabolism and leading to decreased plasma drug levels[2].

There is evidence that high sirolimus blood levels associated with ciclosporin contribute to the thrombotic microangiopathy pathogenesis, a proven risk factor for thrombotic microangiopathy development in HIV-positive patients[4]. Cases of haemolytic-uraemic syndrome associated with sirolimus have been reported, possibly resulting from reduced VEGF (related with vascular endothelium viability maintenance) expression induced by sirolimus[33].

It is important to pay special attention to other antimicrobiological prophylaxis needs common to other kidney transplant recipients, but which are particularly relevant to HIV-positive individuals. These include *Pneumocystis jirovecii* prevention with cotrimoxazol or atovaquone and cytomegalovirus with valganciclovir. Attention must also be placed on coinfection with polyomavirus, Epstein-Barr virus, *Toxoplasma gondii* or human herpes virus-8 (HHV-8). Noteworthy is the elevated potential of HHV-8 to induce Kaposi's sarcoma in this susceptible population[32].

SPECIAL SITUATION: PATIENTS WITH HIV-2 INFECTION

Unlike what is observed in HIV-1, standard care in HIV-2 management relies mainly on data from small cohort studies and case series, theoretical assertions, and parallels with HIV-1 therapeutics. HIV-2 infection occurs mainly in West Africa and among here Guinea-Bissau has one of the highest rates of HIV-2 infection[35].

HIV-2 transmission routes are the same as those for HIV-1, but HIV-2 virus has a lower infectivity[36].

As recently described by Ferreira *et al.*, renal disease is not frequent in HIV-2-infected patients, and, when present, is probably not directly associated with HIV infection[37].

In comparison to HIV-1, more patients with HIV-2 infection present as long-term nonprogressors or slow progressors. Although this could be used to argue for a later CD_4 T-cell driven initiation of cART, it has been demonstrated that immunological recovery on therapy could be slower in HIV-2 than HIV-1 patients[38] and excessive delay in initiating cART may carry negative long-term immunological consequences[39]. Clinical trials of cART in HIV-2 are scarce compared to the ones available to HIV-1, possibly related to low prevalence and geographic distribution constraints[39].

Antiretroviral susceptibility can differ significantly between HIV-1 and HIV-2, such as that HIV-2 is intrinsically resistant to two of the major classes of antiretroviral drugs: NNRTIs and fusion inhibitors. Considering the class of PI, indinavir, saquinavir, lopinavir and darunavir are the most efficient molecules in HIV-2 supression[21].

The authors recently reported a successful case of kidney transplantation in an HIV-2 positive patient, the first described in the literature[40].

CONCLUSIONS

Unlike cardiac and hepatic transplantation for which there is no other alternative to life support, patients with ESRD have dialysis as an alternative renal replacement therapy. This fact must always be weighed in the individual assessment of potential risks and benefits. Note that some HIV-positive patients have been stable on dialysis for over 10 years, showing steady health state. Conversely, there is no long-term experience in HIV-positive kidney transplant recipients. However, kidney transplantation is already an option for selected HIV-infected patients. Further studies are required to identify the optimal choice of immunosuppressive therapy in this group of patients.

Conflict of interest statement. None declared.

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