# Antiretroviral Interactions With Transplant Medications

| | Cyclosporine (Neoral®) | Tacrolimus (Prograf®, Advagraf®) and Sirolimus (Rapamune®) | Mycophenolate Mofetil (CellCept®) |
|---|---|---|---|
| **Pharmacokinetic characteristics** | >90% metabolized (substrate and inhibitor of CYP3A4; also inhibits P-glycoprotein[1]) | >90% metabolized (substrate of CYP3A4) substrate and inhibitor of P-glycoprotein | MPA, the active metabolite is a substrate of glucuronyl transferase |
| ***CCR5 Inhibitor*** | | | |
| **Maraviroc** Substrate of CYP3A4 and p-glycoprotein. | Significant changes in CsA concentrations not expected. | Case report of an HIV-positive liver transplant recipient who initiated maraviroc 300 mg BID and tenofovir/ emtricitabine post-transplant, after being stabilized on tacrolimus 2 mg BID, MMF 500 mg BID and prednisone 10 mg once daily. Tacrolimus exposures ↑ 21% when coadministered with maraviroc compared to baseline, with both tacrolimus trough concentrations and maraviroc concentrations remaining within therapeutic range.[2] | |
| ***Integrase Inhibitors*** | | | |
| **Dolutegravir** Metabolized by UGT1A1 with some contribution from 3A4. | Significant pharmacokinetic interaction not expected. | Significant pharmacokinetic interaction not expected. | Significant pharmacokinetic interaction not expected. |
| **Elvitegravir** Metabolized by 3A4, UGT1A1/3; moderate 2C9 inducer.<br><br>Boosted with cobicistat, an inhibitor of 3A4, 2D6 and p-glycoprotein | Potential for ↑ immunosuppressant concentrations. Therapeutic monitoring of immunosuppressant is recommended.[3] | Potential for ↑ immunosuppressant concentrations. Therapeutic monitoring of immunosuppressant is recommended.[3] | Potential for ↑ immunosuppressant concentrations. Therapeutic monitoring of immunosuppressant is recommended.[3] |
| **Raltegravir** Metabolized by UGT1A1. | Case report of an HIV-positive liver transplant recipient who received cyclosporine and raltegravir post-transplant. Cyclosporine concentrations were measured regularly and remained therapeutic. Pre- and post dose raltegravir levels were measured at weeks 4 and 8, and were comparable with published data. The authors concluded that raltegravir and cyclosporin may be coadministered without dose adjustment.[4] | Raltegravir may avoid interactions with certain immunosuppressives as it is primarily metabolized via glucuronidation and not by CYP3A4.<br><br>Case report of the successful use of raltegravir/3TC/abacavir and sirolimus in a 49 year old HIV/HCV+ patient who underwent liver transplantation. The patient was switched to this regimen after a series of medication modifications. Pt had developed renal insufficiency with hyperpotasemia and | The pharmacokinetics of raltegravir 400 mg BID and mycophenolic acid were prospectively determined in 6 HIV-infected solid-organ transplant recipients. Raltegravir kinetics were not significantly different from historical controls, and MPA metabolism was not significantly altered by raltegravir.[9] |

| | Cyclosporine (Neoral®) | Tacrolimus (Prograf®, Advagraf®) and Sirolimus (Rapamune®) | Mycophenolate Mofetil (CellCept®) |
|---|---|---|---|
| | In 13 HIV-infected transplant patients (n=8 liver, n=5 kidney) who received raltegravir + 2 NRTIs, median raltegravir Ctrough was 507 ng/mL (range 176-890) and target Ctrough of tacrolimus or cyclosporine were achieved with standard doses. After a median follow-up of 9 months (range: 6-14), all patients were alive with satisfactory graft function.[5] | metabolic acidosis due to increased tacrolimus levels (> 25 ng/ml) related to atazanavir use.[6]<br><br>In 13 HIV-infected transplant patients (n=8 liver, n=5 kidney) who received raltegravir + 2 NRTIs, median raltegravir Ctrough was 507 ng/mL (range 176-890) and target Ctrough of tacrolimus or cyclosporine were achieved with standard doses. After a median follow-up of 9 months (range: 6-14), all patients were alive with satisfactory graft function.[5]<br><br>In a case series of 11 HIV-positive solid organ transplant (10 liver, 1 renal) patients who received raltegravir/2 NRTI therapy (plus enfuvirtide, n=2) and tacrolimus (91%), median CD4 increased to 380 cells/mm3 and VL remained <50 copies/mL after a median follow-up of 57 weeks. No patients discontinued raltegravir, and no toxicity or interactions with tacrolimus were noted.[7]<br><br>Two HIV-positive patients began raltegravir-based cART while on tacrolimus 1 or 2 mg twice daily (1 for liver transplantation and 1 for Crohn's disease); no tacrolimus dose | |

| | Cyclosporine (Neoral®) | Tacrolimus (Prograf®, Advagraf®) and Sirolimus (Rapamune®) | Mycophenolate Mofetil (CellCept®) |
|---|---|---|---|
| | | adjustment was needed and tacrolimus blood levels were not altered.[8] | |
| ***Protease inhibitors*** | | | |
| **Amprenavir/ fosamprenavir** Primarily metabolized by CYP3A4. Inhibitor of CYP3A4 (similar potency as indinavir and nelfinavir)[10]; also induces CYP3A4[11]. | May ↑/↓ CsA concentrations via CYP3A4 inhibition or induction | May ↑/↓ tacrolimus concentrations via CYP3A4 inhibition or induction. In a case series of HIV-positive patients undergoing liver transplantation, tacrolimus levels were markedly ↑ in the presence of PI-based HAART regimens (LPV/r, APV, and NFV).[12]<br><br>In a separate report, a 61-year old patient on fosamprenavir/ritonavir was started on 0.5 mg QD tacrolimus post-renal transplant; target tacrolimus concentrations were reached within 2 days and tacrolimus was discontinued due to high (37 ng/mL) levels. Target levels were subsequently achieved with tacrolimus 0.5 mg every 4 days.[13]<br><br>In four HIV-infected liver transplant patients who switched from nelfinavir to fosamprenavir, mean tacrolimus Ctrough ↓ significantly from 6.9 to 3.2 ng/mL before vs. after the switch. Tacrolimus dose increase was needed, from an average of 0.29 mg/day to 0.48 mg/day (p=0.046) to attain the desired target of 8.7 +/- 2.3 ng/mL. These findings suggest that | |

| | Cyclosporine (Neoral®) | Tacrolimus (Prograf®, Advagraf®) and Sirolimus (Rapamune®) | Mycophenolate Mofetil (CellCept®) |
|---|---|---|---|
| | | fosamprenavir may be less potent than nelfinavir in inhibiting tacrolimus clearance.[14]<br><br>A retrospective analysis of HIV-positive patients receiving tacrolimus with various cART regimens was conducted. Three liver transplant patients were on ritonavir-boosted PI therapy (1 on saquinavir 1000 mg BID plus lopinavir 400/ritonavir 100 mg BID, 1 on **fosamprenavir 700/100 mg BID**, 1 on darunavir 600/ritonavir 100 mg BID), and received tacrolimus doses of 0.06, 0.03, and 0.08 mg daily, with median tacrolimus levels of 6.6, 3.0 and 7.9 ng/mL, respectively. Two other patients began raltegravir-based cART while on tacrolimus 1 or 2 mg twice daily; no tacrolimus dose adjustment was needed and tacrolimus blood levels were not altered.[8]<br><br>Monitor tacrolimus levels. | |
| **Atazanavir**<br>Primarily metabolized by CYP3A4; also inhibits CYP3A. | May ↑ CsA concentrations via CYP3A4 inhibition | May ↑ tacrolimus concentrations via CYP3A4 inhibition.<br><br>A case report describes a 53-year old HIV-positive, African-American man who received a renal transplant and was placed on mycophenolate mofetil and tacrolimus along | |

| | Cyclosporine (Neoral®) | Tacrolimus (Prograf®, Advagraf®) and Sirolimus (Rapamune®) | Mycophenolate Mofetil (CellCept®) |
|---|---|---|---|
| | | with concomitant **unboosted atazanavir**, abacavir and lamivudine. The patient initially received tacrolimus 0.5 mg on day 2 post-transplant, but serum tacrolimus levels became subtherapeutic by 6 hours, so tacrolimus dosing was changed to 1 mg every 8 hours, and subsequently to 1.5 mg every 12 hours to maintain therapeutic levels and optimize patient convenience.[15]<br><br>Monitor tacrolimus levels, renal & hepatic function and serum electrolytes. | |
| **Darunavir**<br>Primarily metabolized by CYP3A4; also inhibits CYP3A. | May ↑ CsA concentrations via CYP3A4 inhibition. | May ↑ tacrolimus concentrations via CYP3A4 and/or P-gp inhibition. Case report of a patient with HIV-associated focal segmental glomerulosclerosis who underwent a kidney cadaveric transplantation and was started on a regimen including darunavir/ritonavir. This resulted in a marked increased in tacrolimus trough levels to 106.7 ng/ml (target range 6-7 ng/ml). A decrease in tacrolimus dosage to a single dose of 0.5 mg/week (3.5% of the usual dose) enabled maintenance of stable tacrolimus trough levels. Addition of maraviroc 150 mg BID three months later did not impact renal function or | |

| | Cyclosporine (Neoral®) | Tacrolimus (Prograf®, Advagraf®) and Sirolimus (Rapamune®) | Mycophenolate Mofetil (CellCept®) |
|---|---|---|---|
| | | tacrolimus concentrations.[16]<br><br>A retrospective analysis of HIV-positive patients receiving tacrolimus with various cART regimens was conducted. Three liver transplant patients were on ritonavir-boosted PI therapy (1 on saquinavir 1000 mg BID plus lopinavir 400/ritonavir 100 mg BID, 1 on fosamprenavir 700/100 mg BID, 1 on **darunavir 600/ritonavir 100 mg BID),** and received tacrolimus doses of 0.06, 0.03, and 0.08 mg daily, with median tacrolimus levels of 6.6, 3.0 and 7.9 ng/mL, respectively. Two other patients began raltegravir-based cART while on tacrolimus 1 or 2 mg twice daily; no tacrolimus dose adjustment was needed and tacrolimus blood levels were not altered.[8] | |
| **Indinavir**<br>Primarily metabolized by CYP3A4; also an inhibitor of CYP3A4.[17] | May ↑ CsA concentrations via CYP3A4 inhibition.<br><br>In liver transplant patient (n=1), prolonged $t_{1/2}$ of CsA observed with concomitant IDV/r regimen; daily doses of CsA ↓ 5-20% to maintain serum CsA trough levels.[18] | May ↑ tacrolimus concentrations via CYP3A4 inhibition. In a case series of HIV-positive patients undergoing liver transplantation, tacrolimus levels were markedly ↑ in the presence of PI-based HAART regimens (LPV/r, APV, and NFV)[12] and IDV, NFV[19] Monitor tacrolimus levels. | In a small case series (n=6) of HIV+ subjects receiving ddI, 3TC, abacavir, indinavir 800/ ritonavir 100 mg BID and nevirapine 200 mg BID, there was no significant change in indinavir concentrations in the presence of chronic MMF administration.[20] |
| **Lopinavir/ritonavir**<br>Lopinavir is primarily metabolized by | In liver transplant patients (n=2), prolonged $t_{1/2}$ of CsA | May ↑ tacrolimus concentrations via CYP3A4 inhibition. | - may ↓ MMF via GT induction |

| | Cyclosporine (Neoral®) | Tacrolimus (Prograf®, Advagraf®) and Sirolimus (Rapamune®) | Mycophenolate Mofetil (CellCept®) |
|---|---|---|---|
| CYP3A4. Kaletra inhibits CYP3A4, 2D6 (to lesser extent). At clinically relevant concentrations, Kaletra does not inhibit CYP2C9, 2C19, 2E1, 2B6 or 1A2. Induces glucuronyl transferases and possibly CYP1A2[21], CYP2C19 and 2C9.[22] | observed with concomitant LPV/r; daily doses of CsA ↓ 5-20% to maintain serum CsA trough levels.[18] | In a case series of HIV-positive patients undergoing liver transplantation, tacrolimus levels were markedly ↑ in the presence of PI-based HAART regimens (LPV/r, APV, and NFV).[12]<br><br>When a **LPV/r** based regimen was added to tacrolimus regimen (range 1-6mg BID; target steady state conc: 5-10ng/ml) in 7 HCV-HIV coinfected liver transplant patients, the tacrolimus dose was reduced by 99% (to 0.5 - 1.5mg every 7- 25 days) to maintain target tacrolimus concentrations. Concentrations of LPV were within the ranges published for patients with normal liver function tests.[23]<br><br>Similarly, a 41-year old patient on lopinavir/ritonavir was started on 1 mg QD tacrolimus post-renal transplant; target tacrolimus concentrations were reached within 12 hours and the patient was maintained on a dose of 0.5 mg tacrolimus every 8 days.[24]<br><br>A retrospective analysis of HIV-positive patients receiving tacrolimus with various cART regimens was conducted. Three liver transplant patients | |

| | Cyclosporine (Neoral®) | Tacrolimus (Prograf®, Advagraf®) and Sirolimus (Rapamune®) | Mycophenolate Mofetil (CellCept®) |
|---|---|---|---|
| | | were on ritonavir-boosted PI therapy (1 on **saquinavir 1000 mg BID plus lopinavir 400/ritonavir 100 mg BID**, 1 on fosamprenavir 700/100 mg BID, 1 on darunavir 600/ritonavir 100 mg BID), and received tacrolimus doses of 0.06, 0.03, and 0.08 mg daily, with median tacrolimus levels of 6.6, 3.0 and 7.9 ng/mL, respectively. Two other patients began raltegravir-based cART while on tacrolimus 1 or 2 mg twice daily; no tacrolimus dose adjustment was needed and tacrolimus blood levels were not altered.[8]<br><br>Monitor tacrolimus levels. | |
| **Nelfinavir**<br>Primarily metabolized by CYP3A4; minor pathways include CYP2C19, CYP2D6, others. Inhibitor of CYP3A4.[25] | May ↑ CsA concentrations via CYP3A4 inhibition | Case reports of patients undergoing liver transplantation who received nelfinavir; in each instance, tacrolimus concentration rose to toxic levels, and patient developed severe, prolonged tacrolimus toxicity.[26]<br>Significant ↓ in nelfinavir dosages (up to >95% ↓) were required.[26, 27]<br>In a case series of HIV-positive patients undergoing liver transplantation, tacrolimus levels were markedly ↑ in the presence of PI-based HAART regimens (LPV/r, APV, and NFV)[12] and IDV, NFV.[19]<br><br>In a separate case | - may decrease MMF via GT induction |

| | Cyclosporine (Neoral®) | Tacrolimus (Prograf®, Advagraf®) and Sirolimus (Rapamune®) | Mycophenolate Mofetil (CellCept®) |
|---|---|---|---|
| | | series, 2 HIV-infected liver transplant recipients on NFV + 2 NRTIs experienced ↑ tacrolimus half-life; therapeutic tacrolimus levels were maintained with a 75-93% decrease in the daily dose of tacrolimus. Low NFV concentrations were seen in 1 patient (details not provided).[23]<br><br>Monitor tacrolimus levels. | |
| **Ritonavir**<br>Potent inhibitor of CYP enzymes in following order: 3A>2D6>2C9>2C19>>2A6>2E1. Induces glucuronyl transferases and CYP1A2. [17] May also induce CYP2C9, 2C19. | Low dose ritonavir (as booster) shown to ↑ $t_{1/2}$ of CsA in liver-transplant patients (n=3); daily doses of CsA ↓ 5-20% to maintain serum CsA trough levels.[18] | Case report of HCV/HIV patient who underwent liver transplantation; patient received saquinavir, ritonavir, and nelfinavir at various times with tacrolimus. In each instance, tacrolimus concentration rose to toxic levels, and patient developed severe, prolonged tacrolimus toxicity.[27]<br>Monitor tacrolimus concentrations and adjust dosage accordingly. | - may decrease MMF via GT induction |
| **Saquinavir**<br>Primarily metabolized by CYP3A4. Weak inhibitor of CYP3A4.[17] | Case report of an HIV-positive renal transplant patient whose cyclosporine levels tripled 3 days after initiation of SQV; postulated mechanism was competition for CYP3A metabolism and P-glycoprotein drug transport by SQV.[28] | Case report of HCV/HIV patient who underwent liver transplantation; patient received saquinavir, ritonavir, and nelfinavir at various times with tacrolimus. In each instance, tacrolimus concentration rose to toxic levels, and patient developed severe, prolonged tacrolimus toxicity.[27]<br><br>A retrospective analysis of HIV-positive patients receiving tacrolimus with various cART regimens | |

| | Cyclosporine (Neoral®) | Tacrolimus (Prograf®, Advagraf®) and Sirolimus (Rapamune®) | Mycophenolate Mofetil (CellCept®) |
|---|---|---|---|
| | | was conducted. Three liver transplant patients were on ritonavir-boosted PI therapy (1 on **saquinavir 1000 mg BID plus lopinavir 400/ritonavir 100 mg BID**, 1 on fosamprenavir 700/100 mg BID, 1 on darunavir 600/ritonavir 100 mg BID), and received tacrolimus doses of 0.06, 0.03, and 0.08 mg daily, with median tacrolimus levels of 6.6, 3.0 and 7.9 ng/mL, respectively. Two other patients began raltegravir-based cART while on tacrolimus 1 or 2 mg twice daily; no tacrolimus dose adjustment was needed and tacrolimus blood levels were not altered.[8]<br><br>Monitor tacrolimus concentrations and adjust dosage accordingly. | |
| ***NNRTIs*** | | | |
| **Efavirenz** induces CYP3A4 and inhibits 2C9, 2C19, and 3A4 isoezymes[3] | In a renal transplant patient on stable CsA who initiated an efavirenz-containing regimen, CsA concentrations ↓ 54% after 5 days and declined by a total of 75% after 1 month.[29] | In a case series of HIV-positive patients undergoing liver transplantation, tacrolimus levels were markedly ↓ in the presence of EFV-based HAART regimens.[12]<br><br>When an **EFV** based regimen was added to tacrolimus in 4 HCV-HIV coinfected liver transplant patients, very little change in tacrolimus dosing was required.[23] Concentrations of EFV were within the ranges published for patients | |

| | Cyclosporine (Neoral®) | Tacrolimus (Prograf®, Advagraf®) and Sirolimus (Rapamune®) | Mycophenolate Mofetil (CellCept®) |
|---|---|---|---|
| | | with normal liver function tests. Monitor tacrolimus concentrations and adjust dosage accordingly. | |
| **Nevirapine** Potent inducer of CYP3A4 and 2B6 enzymes.[2] | May ↓ CsA concentrations via CYP3A induction | May ↓ tacrolimus concentrations via CYP3A induction. In a case series of HIV-positive patients undergoing liver transplantation, no changes in tacrolimus levels were observed in patients on nevirapine, Trizivir,or tenofovir.[12] | In a small case series (n=6) of HIV+ subjects receiving ddI, 3TC, abacavir, indinavir 800/ ritonavir 100 mg BID and nevirapine 200 mg BID, NVP clearance ↑ 27% in the presence of chronic MMF administration. Clinical significance unclear.[20] |
| ***NRTIs*** | | | |
| **Tenofovir** | | In a case series of HIV-positive patients undergoing liver transplantation, no changes in tacrolimus levels were observed in patients on nevirapine, Trizivir,or tenofovir.[12]<br><br>When **TDF/3TC/ddI** were added to tacrolimus in 1 HCV-HIV coinfected liver transplant patient, very little change in tacrolimus dosing was required.[23] | |
| **Zidovudine** | | In a case series of HIV-positive patients undergoing liver transplantation, no changes in tacrolimus levels were observed in patients on nevirapine, Trizivir,or tenofovir.[12] | Zidovudine - both are substrates of glucuronyl transferase; competitive inhibition may result in ↑AZT or MPA |

References:


1. Novartis Pharmaceuticals. Neoral Product Monograph. April 26, 2010.

2. Dufty NE, Gilleran G, Hawkins D, et al. Pharmacokinetic interaction of maraviroc with tacrolimus in a patient coinfected with HIV and hepatitis B virus following hepatic transplant due to hepatocellular carcinoma. J Antimicrob Chemother 2013;68(4):972-4.

3. Gilead Sciences Inc. Stribild (elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate) Prescribing Information. Foster City, CA August, 2012.

4. Di Baggio A, Rosso R, Siccardi M, et al. Lack of interaction between raltegravir and cyclosporin in an HIV-infected liver transplant recipient. J Antimicrob Chemother 2009;64(4):874-5.

5. Tricot L, Teicher E, Peytavin G, et al. Safety and efficacy of raltegravir in HIV-infected transplant patients cotreated with immunosuppressive drugs. Am J Transplant 2009;9(8):1946-52.

6. Moreno A, Barcena R, Querada C, et al. Safe use of raltegravir and sirolimus in an HIV-infected patient with renal impairment after orthotopic liver transplant. AIDS 2008;22(4):547-8.

7. Moreno-Zamora A, Pérez-Elías MJ, Casado JL, et al. Safety (specially renal) and antiretroviral activity or raltegravir-based HAART in HIV-subjects after solid organ transplantation [abstract]. XVIII International AIDS Conference, July 18-23, 2010, Vienna, Austria.

8. Bickel M, Anadol E, Vogel M, et al. Daily dosing of tacrolimus in patients treated with HIV-1 therapy containing a ritonavir-boosted protease inhibitor or raltegravir. J Antimicrob Chemother 2010;65(5):999-1004.

9. Miro J, Manzardo C, Brunet M, et al. Combination of RAL + 3TC or FTC + ABV or TDF is safe, effective, and prevents pharmacokinetic interactions with immunosuppressive drugs in HIV-1-infected solid organ transplant recipients [abstract 644]. 18th Conference on Retroviruses and Opportunistic Infections, Feb 27-Mar 2, 2011, Boston, USA.

10. GlaxoSmithKline. Agenerase (amprenavir) Agenerase Capsules & Oral Solution Product Monograph. Mississauga June 28, 2004.

11. ViiV Healthcare ULC. Telzir (fosamprenavir) Prescribing Information. Montreal, QC January 24, 2011.

12. Neff G, Tzakes A, Safdar K, et al. Liver transplantation in HIV, complex pharmacokinetic interactions between tacrolimus and highly active antiretroviral therapy [abstract 8.4]. 4th International Workshop on Clinical Pharmacology of HIV Therapy, March 27-29, 2003, Cannes, France.

13. Barau C, Blouin P, Creput C, et al. Effect of coadministered HIV-protease inhibitors on tacrolimus and sirolimus blood concentrations in a kidney transplant recipient. Fundam Clin Pharmacol 2009;23(4):423-5.

14. Pea F, Tavio M, Pavan F, et al. Drop in trough blood concentrations of tacrolimus after switching from nelfinavir to fosamprenavir in four HIV-infected liver transplant patients. Antivir Ther 2008;13(5):739-42.

15. Tsapepas DS, Webber AB, Aull MJ, et al. Managing the atazanavir-tacrolimus drug interaction in a renal transplant recipient. Am J Health Syst Pharm 2011;68(2):134-42.

16. Mertz D, Battegay M, Marzolini C, et al. Drug-drug interaction in a kidney transplant recipient receiving HIV salvage therapy and tacrolimus. Am J Kidney Dis 2009;54(1):e1-4.

17. Eagling VA, Back DJ, Barry MG. Differential inhibition of cytochrome P450 isoforms by the protease inhibitors, ritonavir, saquinavir and indinavir. British Journal of Clinical Pharmacology 1997;44(2):190-4.

18. Vogel M, Voight E, Wasmuth JC, et al. Drug to drug interactions between ritonavir and

cyclosporine A in liver-transplanted HIV-infected patients [abstract 4.7]. 5th International Workshop on Clinical Pharmacology of HIV Therapy, April 1-3, 2004, Rome, Italy.

19. Jain AK, Venkataramanan R, Shapiro R, et al. The interaction between antiretroviral agents and tacrolimus in liver and kidney transplant patients. Liver Transplantation 2002;8(9):841-5.

20. Martorell J, Brunet M, García F, et al. Mycophenolate mofetil lowers plasma nevirapine concentrations but has no effect on intracellular triphosphate concentrations [abstract 539]. 10th Conference on Retroviruses and Opportunistic Infections, February 10-14, 2003, Boston, MA.

21. AbbVie Corporation. Kaletra (lopinavir/ritonavir) Prescribing Information. Saint Laurent, Canada November 1, 2012.

22. Yeh R, Gaver V, Park JJ, et al. Lopinavir/ritonavir induces CYP2C9 and 2C19 activity, as measured by warfarin and omeprazole biomarkers in healthy human volunteers [abstract 4.1]. 5th International Workshop on Clinical Pharmacology of HIV Therapy, April 1-3, 2004, Rome, Italy.

23. Teicher E, Vincent I, Bonhomme-Faivre L, et al. Effect of highly active antiretroviral therapy on tacrolimus pharmacokinetics in hepatitis C virus and HIV co-infected liver transplant recipients in the ANRS HC-08 study. Clin Pharmacokinet 2007;46(11):941-52.

24. Barrail-Tran A, Furlan V, Blouin P, et al. Effect of coadministered protease inhibitor regimen on tacrolimus blood concentration in 3 kidney transplanted HIV-infected patients [abstract 58]. 8th International Workshop on Clinical Pharmacology of HIV Therapy, April 16-18, 2007, Budapest, Hungary.

25. Lee CA, Liang BH, Wu EY, et al. Prediction of nelfinavir mesylate (VIRACEPT) clinical drug interactions based on in vitro human P450 metabolism studies. 4th National Conference on Retroviruses and Opportunistic Infections, January 22-26, 1997, Washington DC.

26. Schvarcz R, Rudbeck G, Soderdahl G, et al. Interaction between nelfinavir and tacrolimus after orthoptic liver transplantation in a patient coinfected with HIV and hepatitis C virus (HCV). Transplantation 2000;69(10):2194-5.

27. Sheikh AM, Wolf DC, Lebovics E, et al. Concomitant human immunodeficiency virus protease inhibitor therapy markedly reduces tacrolimus metabolism and increases blood levels. Transplantation 1999 July 27;68(2):307-9.

28. Brinkman K, Huysmans F, Burger DM. Pharmacokinetic interaction between saquinavir and cyclosporine [letter]. Annals of Internal Medicine 1998;129:915-6.

29. Tseng A, Nguyen ME, Cardella C, et al. Probable interaction between efavirenz and cyclosporine. AIDS 2002 February 15;16(3):505-06.