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Poster 687: Short-term plasma HIV-1 RNA viral load and immunological changes following temporary discontinuation of HAART after liver transplantation (OLT) in HIV-1–infected recipients

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Background: Discontinuation of HAART in chronic HIV-1 infection is accompanied by a rapid rise in plasma HIV-1 RNA viral load (pVL) and a decrease in CD4+ T-cell counts. However, pVL and immunological dynamics following transitory cessation of HAART after OLT in HIV-1–infected patients on immunosuppressive therapy has not been well characterized. The aim of this study is to describe the short-term (4 weeks) dynamics of pVL and CD4/CD8 subset changes after discontinuation of HAART.

Methods: We included 25 consecutive HCV/HIV-coinfected patients who underwent OLT between 2002-2006 and had on HAART a pVL below detection levels (BDL, <50 copies/mL) at OLT, who transiently discontinued cART and restarted it at least 7 days later. Plasma HIV-1 RNA viral load and T cell subsets were determined before after cART discontinuation. Data were obtained from the FIPSE OLT-HIV-05-GESIDA 45-05 database.

Results: Ten patients were off cART at 6-9 days of OLT, 11 after 10-17 days and 4 after 28 days. The 25 cases had been on cART for a median (IQR) of 4.80 (1.04-8.56) years. Median (IQR) pre-HAART pVL was 4.63 (3.29; 5.03) log 10 copies/mL. cART based on efavirenz, a protease inhibitor or other combinations at OLT was taken in 8, 7 and 10 cases, respectively. Median (IQR) CD4+ and CD8+ T-cell counts before discontinuation were 321 (200-408) and 487 (297;724) cells/mm3, respectively. A cyclosporine A (CsA)–based immunosuppressive regimen was started in 40% patients and a tacrolimus-based regimen in 60%. A rebound in pVL was detected at 6-17 days in 6 out of 24 patients (25%; 95% CI 12%;45%). Only one of the patients on CsA had a pVL rebound at 2 weeks (*P*=.18). pVL rebound was higher than 10,000 copies/mL at 6-9, 10-17 and 28 days in only 1, 1 and none case, respectively. Median CD4+ T-cell counts at 6-9, 10-17 and 28 days were 231 (104;342), 229 (88;356) and 316 (241;608), respectively (*P*<.05 at 6-9 and 10-17 days in comparison with baseline). Plasma VL returned to undetectable levels following reintroduction of cART in all cases

Conclusions: pVL remained BDL or rebounded at a very low level of viremia in most HCV-HIV OLT recipients after 2-4 weeks off HAART, probably due to the reduction in the T-cell immune activation induced by OLT immunosuppressive therapy.

BACKGROUND

Discontinuation of combined antiretroviral therapy (cART) in chronic HIV-1 infection (CHI) is accompanied by a rapid rise in plasma HIV-1 RNA viral load (pVL) and a decrease in CD4+ T-cell counts (*Garcia F et al. AIDS. 1999; 13:F79-F86*). However, pVL and immunological dynamics following temporary discontinuation of cART after OLT in HIV-1–infected patients on immunosuppressive therapy has not been well characterized.

OBJECTIVE

The aim of this study is to describe the short-term (4 weeks) dynamics of pVL and CD4/CD8 subset changes after temporary discontinuation of cART.

PATIENTS & METHODS

- We included 25 HCV/HIV-coinfected patients on cART who underwent OLT between 2002-2006 and had a pVL below detection levels (<50 copies/mL) at OLT, and who temporarily discontinued cART (at least 7 days).
- Plasma HIV-1 RNA viral load and T-cell subsets were determined before resumption of cART (at 1, 2 or 4 weeks).
- Clinical, virological, and immunological data were obtained from the FIPSE OLT-HIV-05-GESIDA 45-05 database.
- pVL rebound was compared with a historical cohort of 8 patients with CHI who stopped cART after 1 year of effective treatment (*Garcia F. AIDS. 1999;13:F79-F86*).

STATISTICAL ANALYSIS

- Continuous variables were assessed using the *t* test for normally distributed data or the Mann-Whitney U test for non-normally distributed data. Categorical variables were compared using the Fisher exact test.
- The analysis was performed using SAS version 9.1.3 software (SAS Institute, Cary, NC, USA) and the level of significance was established at 0.05 (two-tailed).

Patient Characteristics (I)

	OLT N=25	CHI* N=8
Male gender	76%	75%
Age (yr)**	42 (40; 45)	33 (30; 41)
HCV coinfection	100%	38%
HIV-risk factors		
- IDU	87%	12%
- Other	13%	88%
Immunosuppressive regimen		
- Cyclosporine A-based regimen	40%	NA
- Tacrolimus-based regimen	60%	NA

•Data from Garcia F et al., AIDS 1999;13:F79-F86. All patients were treated with a ritonavir-boosted PI-based regimen; ** Median (IQR); NA=not applicable.

Patient Characteristics (II)

	OLT N=25	CHI* N=8
pVL pre-cART	4.63 (3.29; 5.03)**	4.44 (4.32; 5.16)
cART duration (yr)	4.80 (1.04; 8.56)	All 1 yr
CD4 before D/C	321 (200; 408)	841 (677; 881)
CD8 before D/C	487 (297; 724)	1039 (724; 1488)
pVL< 50 c/mL before D/C	100%	100%
When cART was restarted		
- After 6-9 days	10 (40%)	-
- After 10-17 days	11 (44%)	6 (75%)
- After 28 days	4 (16%)	1 (12.5%)

* Data from Garcia F et al. AIDS 1999;13:F79-F86; ** Median (IQR).

cART Before and After OLT (I)

	Before N=25	After N=25
Antiretroviral regimen		
- Efavirenz-based cART	8 (32%)	14 (56%)
- Nevirapine-based cART	3 (12%)	1 (4%)
- PI-based cART	7 (28%)	8 (32%)
- Only NUCs	4 (16%)	-
- Other regimens	3 (12%)*	2 (8%)**

* T20+SQV+3TC — T20+TDF+FPV — DDI+EFV+SQV/r
** T20+SQV+3TC — LPV/r+EFV

cART Before and After OLT (II)

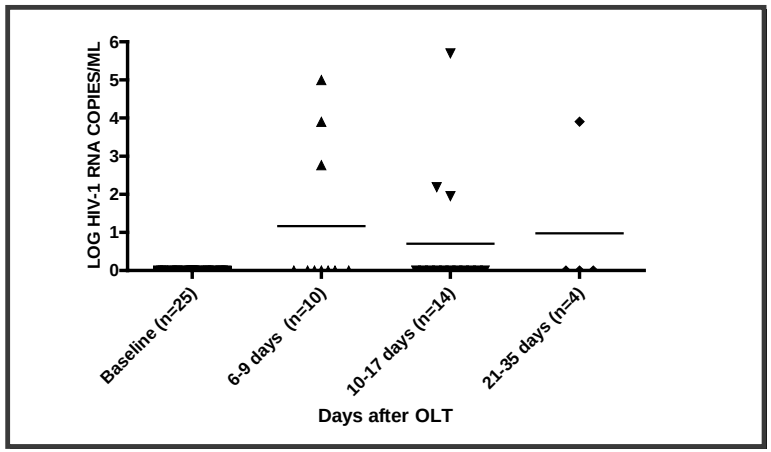
- Plasma HIV-1 RNA viral load rebound (>200 cp/mL) after 6-17 days of cART discontinuation was detected in 6 out of 24 patients (25%; 95% confidence interval, 12%-45%). Only one had a VL rebound >500,000 cp/mL.
- Median (IQR) time for restarting cART after OLT was 16 (13; 28) days.
- Twelve patients (48%) received the same cART regimen.
- All patients reached a plasma HIV-1 RNA viral load below detectable levels following reintroduction of cART.

Plasma HIV-1 RNA Viral Load Rebound After OLT

	OLT	CHI*
pVL >200 c/mL after cART D/C		
After 6-9 days**	3/10 (30%)	5/8 (62%)
After 10-17 days**	3/14 (21%)	7/8 (88%)
After 28 days	1/4 (25%)	NA
pVL rebound >4 $\log_{10}$/mL		
After 6-9 days	1/10 (1%)	-
After 10-17 days	1/14 (7%)	-
After 28 days	0/4 (--)	-

* Data from Garcia F et al. AIDS 1999;13:F79-F86; NA=not applicable.

Plasma HIV-1 RNA Viral Rebound After OLT



Predictors of Plasma VL Rebound > 200 cp./mL

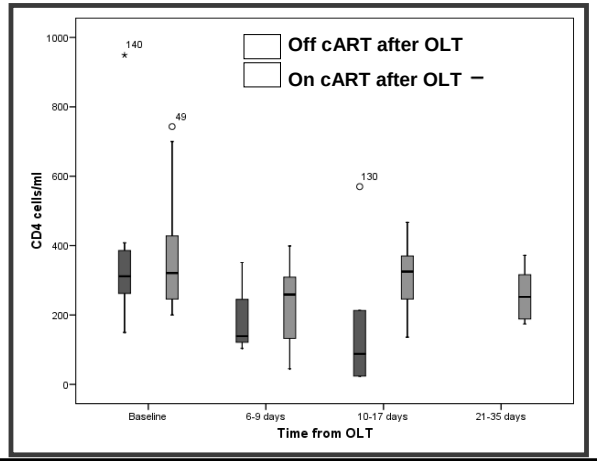
Variable	No. +ve/Total (%)	*P* value
Immunosuppressive regimen		
- Cyclosporine A–based regimen	1/10 (10%)	
- Tacrolimus-based regimen	6/15 (40%)	0.18
Antiretroviral regimen		
- NNRTI-based cART	2/12 (17%)	
- Non–NNRTI-based cART	5/13 (38%)	0.39
Length of cART before OLT		
- ≤ 5 years	2/12 (17%)	
- > 5 years	5/13 (38%)	0.39
CD4+ T-cell count before OLT		
- ≤ 350 cells/mm^3	3/14 (21%)	
- > 350 cells/mm^3	4/11 (36%)	0.66
Peak VL before starting cART		
- ≤ 4.5 log10 c/mL	3/10 (30%)	
- > 4.5 log10 c/mL	1/8 (12.5%)	0.58

Evolution of CD4 and CD8 in Patients With/out cART Discontinuation After OLT (≤ 4 Weeks)

	D/C N=25	No D/C N=46
CD4+ T-cell counts		
- Before OLT	321 (200; 408)	274 (150; 396)
- 6-9 days	231 (104; 342)*	147 (132; 180)
- 10-17 days	229 (88; 356)*	280 (192; 325)
- 21-35 days	316 (241; 608)	312 (132; 418)
CD8+ T-cell counts		
- Before OLT	487 (297; 724)	467 (293; 571)
- 6-9 days	189 (144; 250)*	198 (117; 275)
- 10-17 days	324 (208; 444)*	403 (266; 513)
- 21-35 days	483 (361; 923)	345 (270; 597)

* *P*<.05 at 6-9 and 10-17 days in comparison with baseline.

Evolution of CD4 and CD8 Counts in Patients With/out cART Discontinuation After OLT (≤ 4 Weeks)



CONCLUSIONS

- Plasma HIV-RNA viral load remained below detectable levels or rebounded at a very low level of viremia in most HCV/HIV-coinfected OLT recipients after 2-4 weeks off cART in comparison with chronically HIV-infected patients who stopped effective cART.
- pVL returned to undetectable levels following reintroduction of cART in all cases, suggesting that no mutations associated with antiretroviral resistance had been selected.
- This low level of viremia was probably due to the reduction in the T-cell immune activation induced by immunosuppressive therapy.

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Our patients.