

# Switching stavudine to tenofovir and protease inhibitor to efavirenz results in a favorable clinical outcome in HIV-infected children

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**1. INTRODUCTION:** PI-based therapies require complex regimens with high pill burden and dosing schedule constraint. These features may decrease adherence in HIV-infected children and adolescents. PI and NRTIs therapy, especially stavudine (d4T), have been associated with morphologic changes and metabolic abnormalities that could increase the risk of cardiovascular disease. These side effects are particularly worrisome in HIV-infected children and adolescent due to long-term expected survival.

**2. SUBJECTS AND METHODS:** We planned a 96-week prospective trial to evaluate the impact on virologic, immunologic, metabolic and body composition parameters of replacing PI with EFV and d4T with tenofovir (TDF) in HIV-infected children and adolescents who had been receiving an HAART regimen containing lamivudine (3TC) + d4T + 1PI. Current report describes the virologic, immunologic and metabolic parameters observed after 48 weeks of the new antiretroviral regimen. Entry criteria were: HIV-RNA < 50 copies/ml for the 48 weeks prior to enrollment in the study, absence of an active acquired immunodeficiency syndrome (AIDS)-defining condition in the preceding 48 weeks and no prior treatment with EFV and TDF. Twenty-seven patients were randomized to switch d4T to TDF and PI to EFV at study entry (n=14) or at week 24 (n=13). All of the patients maintained 3TC. EFV was administered once daily, at weight-dependent doses, as recommended by the manufacturer. TDF was administered once daily at body surface area-dependent doses (150 mg for 0,5-0,84 m<sup>2</sup>; 225 mg for 0,84-1,29 m<sup>2</sup>; 300 mg for ≥ 1,3 m<sup>2</sup>). Children were well matched for demographic, clinical characteristics and HIV disease markers, duration of previous exposure to AZT and duration of current exposure to HAART (Table 1).

Clinical evaluation, viral load and CD4+ cells count were obtained at study entry and at weeks 4, 12, 24, 36 and 48. Fasting blood samples were drawn at study entry, weeks 12, 24, 36 and 48 for measurements of total cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides and at study entry, weeks 24 and 48 for measurements of creatinine and pH

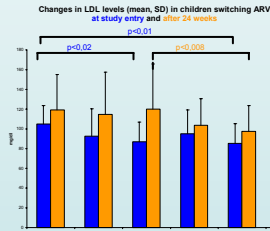
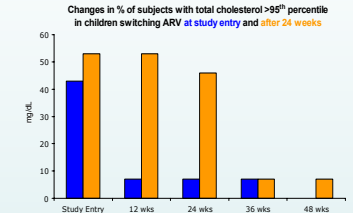
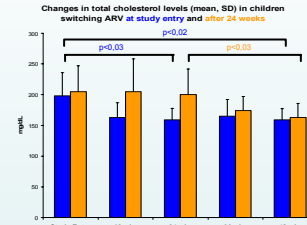


Table 1: baseline characteristic in children switching ARV at study entry and after 24 weeks

	N	AGE (years)	CDC class A/B+C	Previous AZT exposure (mos)	d4T+3TC+PI exposure (mos)	CD4+ cells/μL	Children with HIV-RNA <50 copies/ml
Switch at study entry	14	12.7 (6.0-17.4)	6/8	32.7 (30.1)	67.9 (7.29)	884.0 (305.1)	14/14
Switch after 24 weeks	13	12.1 (6.4-17.5)	5/8	31.7 (33)	72.6 (7.5)	809.6 (285.4)	13/13

### 3. RESULTS:

Table 2: immunologic and virologic parameters in children switching ARV at study entry and after 24 weeks

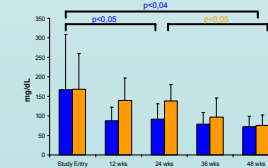
Time	CD4+ cells/μL mean (SD)	Children with HIV RNA <50 Copies/ml
Study entry	884.9 (305.1)	14
	809.6 (258.4)	13
12 weeks	1009.9 (288.3)	14
	919.1 (280.3)	13
24 weeks	788.6 (301.2)	14
	785.4 (279.9)	13
36 weeks	687.2 (283.5)	14
	706.1 (317.5)	13
48 weeks	848 (305.6)	14
	753.7 (286.9)	13

Table 3: renal parameters in children switching ARV at study entry and after 24 weeks

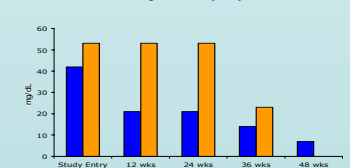
Variable	Study entry	24 weeks	48 weeks
Serum phosphorus (mg/dL)	4.3 (0.4)	4.6 (0.6)	4.5 (0.7)
Serum phosphorus <5th percentile for age	4.5 (0.7)	4.7 (0.9)	4.5 (0.9)
Serum creatinine (mg/dL)	0.6 (0.1)	0.6 (0.2)	0.7 (0.1)
Calculated creatinine clearance* (ml/min)	135.8 (20.4)	138.3 (30.9)	126.9 (18.3)
Glucosuria (>70 mg/dL)	0	0	0
Urine α1-microglobulin/creatinine	0.010 (0.005)	0.015 (0.009)	0.011 (0.006)
Urine albumin/creatinine	0.012 (0.008)	0.011 (0.007)	0.011 (0.007)
	0.010 (0.011)	0.012 (0.016)	0.014 (0.023)
	0.009 (0.010)	0.007 (0.006)	0.007 (0.005)

Data are as mean (SD)  
\* Using Schwartz formula

Changes in Triglycerides levels (mean, SD) in children switching ARV at study entry and after 24 weeks



Changes in % Triglycerides > 95th percentile in children switching ARV at study entry and after 24 weeks



**4. CONCLUSIONS:** The replacement of PI by EFV and of d4T by TDF in HIV-infected children who had been receiving an HAART regimen containing lamivudine (3TC) + d4T + 1PI and who had long lasting viral suppression provides continued virological suppression, stable CD4+ response, significant improvement of lipid profile and reversion of lipid abnormalities. Overall the new antiretroviral regimen was well tolerated and not associated with signs of renal dysfunction.