BONE MASS REMAINS HIGHER AMONG CHILDREN ON EFAVIRENZ VS. LOPINAVIR/RITONAVIR

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BACKGROUND

- In a study of virologically suppressed South African children living with HIV (HIV+) who were randomized to remain on a lopinavir/ritonavir (LPV/r)-based antiretroviral therapy (ART) regimen had lower bone mass compared to HIV+ children randomized to switch to efavirenz (EFV) and to controls without HIV (HIV-)
- Two years additional follow-up data were collected to assess the trend of bone mass and the associations among bone mass, bone turnover markers and immune activation/inflammation markers

METHODS

- 220 HIV+ and 220 HIV- children living in Johannesburg, South Africa were enrolled
- Measurements were collected at baseline, 12 months (N=414, 94.1%) and 24 months (N=407, 92.5%)
- Height, weight, physical activity, ART regimen, virologic and immunologic status and Whole body (WB) and Lumbar Spine (LS) dual-energy X-ray absorptiometry (DXA) scans were collected at three visits
- Bone mineral content (BMC) Z-scores adjusted for age, sex, race and height were calculated by reference norms from the Bone Mineral Density in Childhood Study
- C-telopeptide of type I collagen (CTx): a bone resorption marker and procollagen type I N-terminal propeptide (P1NP): a bone formation marker, were collected at baseline and 24 months
- Immune activation/Inflammation markers: IL-6, TNFα, soluble CD14 (ng/ml) and high-sensitivity C-reactive protein (hsCRP, mg/dl) were collected at baseline and 24 months
- ART regimen comparisons were limited to those on consistent regimen for all study visits (EFV: N=107; LPV/r: N=95)

RESULTS

Characteristics

- Male: 51.8%; Mean Age at baseline: 6.7 years
- 27.7% HIV+ vs. 8.6% HIV- stunted at baseline (p<0.01)
- Faster pubertal development (%Tanner Stage ≥ 2) among HIV- than HIV+ at 24 months (21% vs. 8.6%, p<0.01)
- Viral load: 94% < 400 copies/ml; 74% < 40 copies/ml

Children living with well-controlled HIV on EFV had consistent bone accrual benefit and lower pro-inflammatory cytokine profiles compared with those on LPV/r.

Figure 1: WB and LS BMC (grams), BMC Z-scores and BMD (grams/cm^2): HIV+ vs. HIV-

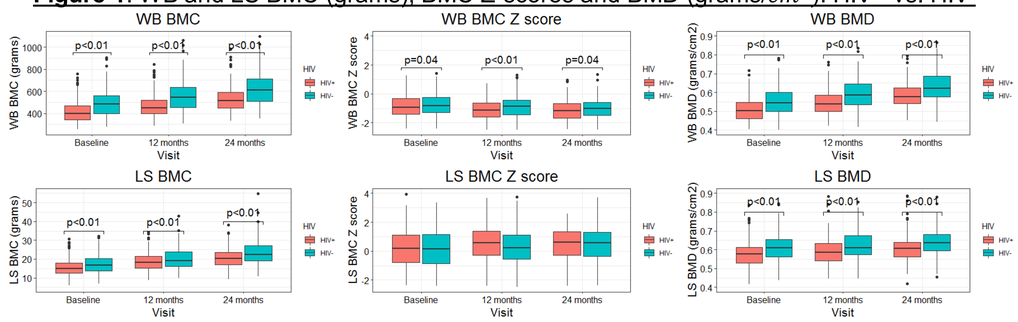

Figure 2: Mean annualized percentage change of WB BMC and BMD: HIV+ vs. HIV-; EFV vs. LPV/r

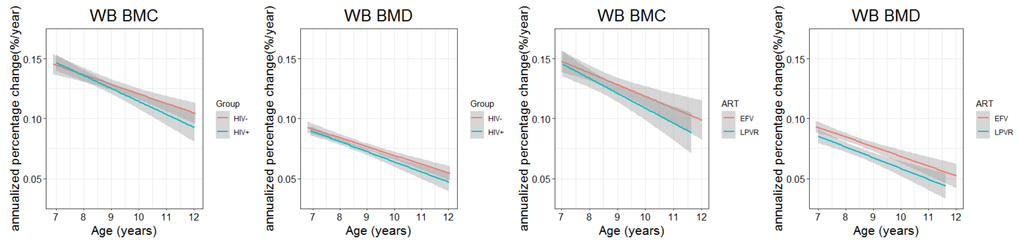

Table 1: Bone turnover markers and Inflammation markers comparisons:

	Visit	EFV (B0 & B24: N=107)	LPV/r (B0 & B24: N=95)	HIV- (B0:N=180; B24: N=202)	EFV vs. LPV/r: P	EFV vs. HIV-: P	LPV/r vs. HIV-: P
P1NP (ng/ml)	B0	594.7 (188.7)	588.9 (178.3)	634.4 (172.8)	0.83	0.07	**0.04**
Mean (SD)	B24	685.4 (202.7)	652.9 (178.4)	760.0 (265.3)	0.24	**<0.01**	**<0.01**
CTx (ng/ml)	B0	1.74 (0.63)	1.76 (0.64)	2.05 (0.69)	0.86	**<0.01**	**<0.01**
Mean (SD)	B24	1.88 (0.62)	1.79 (0.73)	2.09 (0.76)	0.38	**0.01**	**<0.01**
IL-6 (pg/ml)	B0	0.80 (0.54, 1.31)	0.96 (0.61, 1.61)	0.88 (0.54, 1.56)	**0.04**	0.08	0.96
Median (IQR)	B24	1.03 (0.68, 1.80)	1.56 (0.89, 2.19)	1.12 (0.77, 1.86)	**0.01**	0.39	0.49
TNFα (pg/ml)	B0	1.59 (1.24, 2.18)	2.13 (1.73, 2.75)	2.36 (1.93, 2.89)	**<0.01**	**<0.01**	0.45
Median (IQR)	B24	1.68 (1.45, 1.96)	1.91 (1.63, 2.33)	2.13 (1.82, 2.45)	**<0.01**	**<0.01**	0.09

HIV+ vs. HIV-

- Bone formation by mean P1NP (B0: 584±183 vs. 634±173, p<0.01; B24: 666±192 vs. 760±265, p<0.01) and bone resorption by mean CTx (B0: 1.72±0.63 vs. 2.05±0.69, p<0.01; B24: 1.84±0.68 vs. 2.09±0.76, p<0.01) were consistently lower among HIV+ than HIV-
- WB BMD annualized percentage change (APC, %/year) was positively correlated with APC of P1NP (β = 0.02±0.01, p<0.01) and CTx (β = 0.01±0.01, p<0.01) adjusted for age, sex and HIV status
- Median TNFα (B0: 1.87 vs. 2.36, p<0.01; B24: 1.76 vs. 2.13, p<0.01) was lower whereas soluble CD14 (B0: 1324 vs. 1103, p<0.01; B24: 1981 vs. 1311, p<0.01) and hsCRP (B0: 0.77 vs. 0.38, p<0.01; B24: 0.58 vs. 0.30, p<0.01) remained higher among HIV+ than HIV-
- WB BMC APC was negatively associated with soluble CD14 APC (β = -0.02±0.01, p = 0.03) adjusted for age, sex and HIV status

EFV vs. LPV/r

- Mean WB BMC Z-scores were significantly higher among children on EFV compared with those on LPV/r (B0: -0.77±0.77 vs. -1.14±0.78, p<0.01; B12: -0.94±0.74 vs. -1.34±0.70, p<0.01; B24: -1.01±0.76 vs. -1.40±0.69, p<0.01)
- Mean APC of WB BMD for HIV+ on EFV was higher than those on LPV/r (0.08±0.02 vs. 0.07±0.02, p<0.01), even adjusted for age, sex, BMI and baseline Vitamin D deficiency status

CONCLUSIONS

- South African children living with HIV consistently had lower bone mass, lower bone formation and resorption, compared with controls
- Bone mass remained higher in HIV+ children on EFV compared to those on LPV/r
- Among HIV+ children initiated and well-controlled on potent ART regimen from early in life, bone formation and resorption were coupled but overall lower compared with HIV- children
- HIV+ children on EFV had lower pro-inflammatory cytokine profiles compared to those on LPV/r
- The results support our previous recommendations to switch children with sustained viral suppression on first line regimen with LPV/r to EFV

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