



# Bone turnover markers evolution after treatment initiation with Truvada and Efavirenz in comparison to Truvada and Raltegravir -



## Another glimpse to osteoporosis in HIV

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### Introduction

In the era of efficient antiretroviral medications, when life expectancy of people living with HIV (PLWH) is almost comparable to HIV negative individuals, one of the most important role of HIV physicians is managing age related co-morbidities that are more prevalent in PLWH. Osteoporosis is 3.7 times more prevalent in PLWH in comparisons to the general population and result in 60% higher rate of osteoporotic fractures. Multiple risk factors have been identified as related for this excessive rate as smoking, malnutrition, recreational drugs, HCV and HBV co-infection, and antiretroviral therapy, the later was proved to result in 2.38 fold increase of risk for osteopenia and osteoporosis. Previous studies investigated multiple HAART regimens most of the are not relevant to the current used antiretroviral therapy. Additionally the main endpoint was bone density measurement by DEXA scan that does not explain the mechanisms of this phenomenon among PLWH. The correlation between different medications and bone loss has been studied in the past, and Tenofovir/FTC and protease inhibitors are the most “Bone eater”.

The rapid introduction of new medications and advances in diagnostic methods of bone loss using bone turnover markers combined with new anti-osteoporosis medications that are more mechanistic specific, call for reassessment of ART induced osteoporosis in PLWH.

### Aims

The aims of our study were to compare the impact of two commonly used different antiretroviral regimens (Truvada and Efavirenz Vs. Truvada and Raltegravir) on bone turnover markers representing bone absorption and bone production and to assess the dynamics of these two markers in the two different ART regimens.

### Methods

We retrospectively measured the levels of two bone turnover markers – CTX and P1NP, in the serum of three groups of PLWH, two treatment groups (TDF+FTC+RAL, TDF+FTC+EFV) and untreated control group. We enrolled 15 male patients to each group and examined stored frozen serum from 4 time points to each patient– before initiation of treatment (time=0), after 1,6 and 12 months. For the control group only 3 samples of 6 months apart were available. We have compared the results to CD4 levels and Viral Loads.

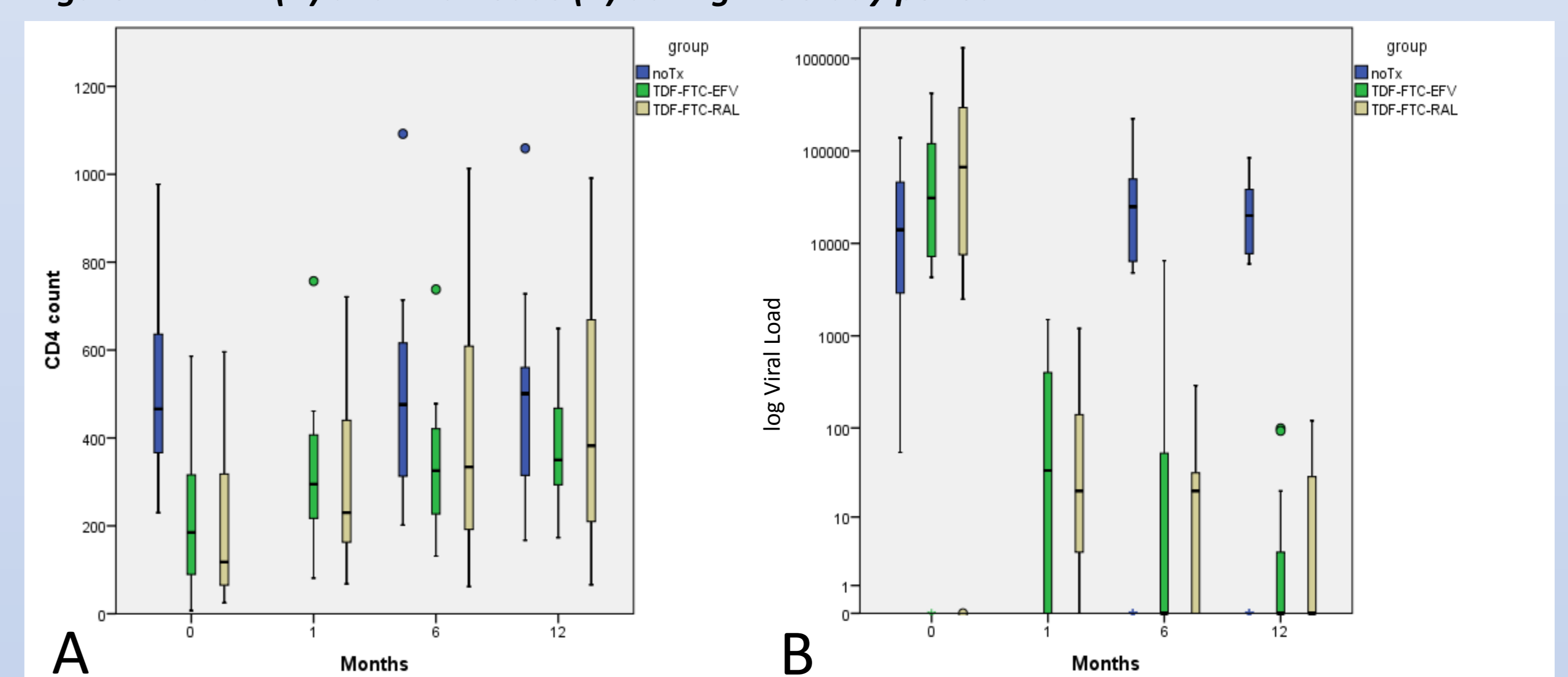
### Results

Table 1 – patients characteristics

	TDF+FTC+RAL (N=15)	TDF+FTC+EFV (N=15)	Control (No treatment) (N=15)
average age	42.33	41.13	42.4
average CD4 at treatment	214.67	220.07	516.4
log Viral Load at treatment	4.432	4.238	4.167
ethnicity			
Israeli Jew	(4)26.6%	(4)26.6%	(5) 33.3%
Israeli Arab	(2)13.3%	(6)40%	0
Ethiopian Jew	(4)26.6%	(1)6.6%	(7) 46.6%
Former USSR	(2)13.3%	(1)6.6%	(2)13.3%
Other	(3)20%	(3)20%	(1) 6.6%

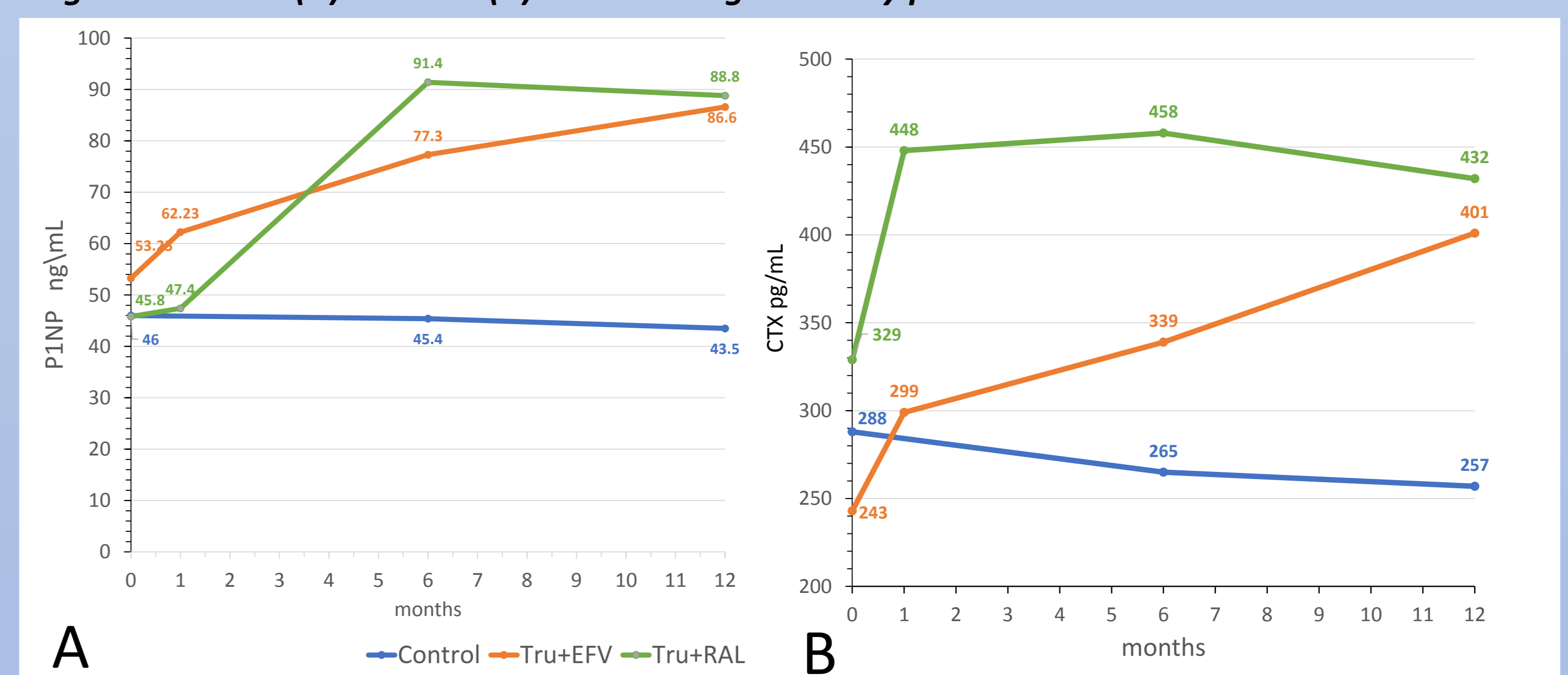
The median age was similar in 3 study groups, and the ethnicity was comparable (table 1). At treatment initiation CD4 levels were similar in the two treatment groups, but much higher in the control group, while the log viral load levels were alike in all three groups (Figure 1). The antiretroviral treatment resulted in a increase in CD4 levels as expected, and rapid decline in Viral load in the two treatment groups, while the control group patients had stable CD4 and viral loads (Figure 1 A and B respectively). There was no difference in CD4 and viral loads comparing the two treatment groups.

Figure 1 – CD4 (A) and viral loads (B) during the study period.



Both P1NP (A) and CTX (B) levels increased in the first months of treatment and then plateaued, while in the control group stable levels of both markers were found throughout the study period (figure 2). P1NP levels significantly increased in both treatment arms in comparison to control group (p=0.01 RAL vs. CONTROL, p=0.014 EFV vs. CONTROL after 12 months), and there was a trend for CTX increment in both treatment groups but this was not statistically significant (p=0.08 RAL vs. CONTROL, p=0.2 EFV vs. CONTROL)

Figure 2 – P1NP (A) and CTX (B) levels during the study period.



### Conclusions

Our study shows that both P1NP and CTX levels are markedly increased in early stages after treatment initiation which represent a significant early ART induced Osteoporosis. This can suggest that direct treatments that slow bone absorption such as Bisphosphonates should be considered in early stages even before clinical or radiological signs of Osteoporosis are seen.

We did not identify a significant difference between the two treatment groups, this might be attributed to small size sample and to dominant effect of Truvada in both regimens. Other backbones such as Kivexa or TAF should be evaluated.

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