Higher Efavirenz Mid-dose Plasma Concentration Is Associated With Less Weight Gain Among Virologically Suppressed People Living With HIV

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Background

- Pharmacogenetic studies have shown that slow and intermediate metabolizers of efavirenz (EFV) gained less weight compared to extensive metabolizers.
- This study investigated the effect of EFV mid-dose plasma concentration (C12) on long-term weight change among virologically suppressed people living with HIV (PLWH).

Methods

- Retrospective analysis of participants of a prospective EFV pharmacokinetic study **(Figure 1)**

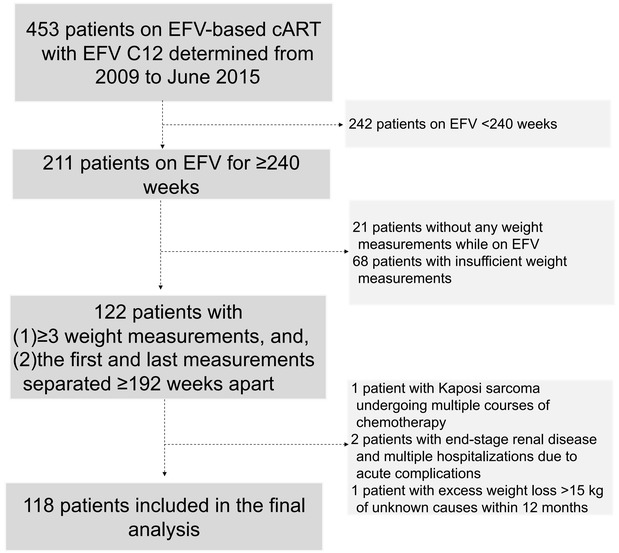

Figure 1. Participant selection process. *(Abbreviations: C12, mid-dose concentration; cART, combination antiretroviral therapy; EFV, efavirenz)*

Conclusion: Our findings supported that **increased EFV exposure was associated with less weight gain** among virologically suppressed people living with HIV.

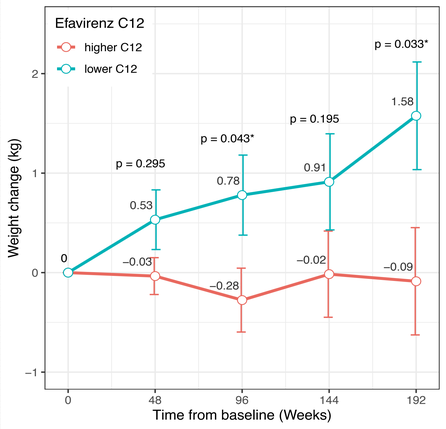

Figure 2. Weight changes over 192 weeks from baseline of the study among virologically suppressed people living with HIV who had higher and those who had lower efavirenz (EFV) mid-dose concentrations (C12).

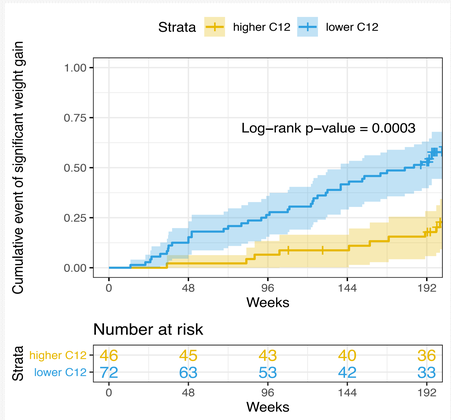

Figure 3. Cumulative events of significant weight gain (≥ 5% weight gain from baseline) among virologically suppressed people living with HIV who had higher and those who had lower efavirenz mid-dose concentration (C12) in Kaplan-Meier analysis.

- The weight changes and time to ≥ 5% of weight gain over 192 weeks were compared between PLWH with higher and those with lower EFV C12 (using mean population C12 as the cutoff).
- EFV C12 and CYP2B6 516G>T polymorphism were examined in generalized estimating equations (GEE) and in a Cox proportional hazards model for associations with weight gain, after adjustments for age, gender, companion antiretrovirals, CD4 lymphocyte count and plasma HIV RNA.

Results

- One-hundred and eighteen PLWH were included. They were predominantly male (93.6%) . At baseline, the median age was 35.4 years (IQR, 30.1-41.4) and mean CD4 lymphocyte count was 540 cells/μL (IQR, 421-671).
- PLWH with higher EFV C12 had less mean weight gain compared to those with higher C12 after 192 weeks (-0.09 Kg and +1.58 kg, respectively, p = 0.033). **(Figure 2)**
- PLWH with higher C12 were less likely to gain ≥ 5% weight in Kaplan-Meier analysis (p = 0.0003). **(Figure 3)**
- In both GEE and Cox proportional hazards models, a higher EFV C12 was associated with less weight gain, while CYP2B6 516G>T was not, after adjustments made for confounding factors. **(Table 1)**

	βcoefficient	95% confidence interval	p-value
Duration of observation, per 48-week increment	0.402	0.141 to 0.663	0.003
Weight at baseline, per 10-kg increment	-0.482	-0.919 to -0.045	0.031
Duration on cART at baseline, per 48-week increment	-0.184	-0.308 to -0.061	0.003
EFV C12 lower than the mean C12 of the cohort*	1.803	0.793 to 2.813	<0.001
CYP2B6 516G>T genotype, GT vs GG	-0.861	-2.033 to 0.313	0.151
Nadir CD4 lymphocyte count, per 100-cell/μL increment	-0.306	-0.583 to -0.028	0.031

Table 1. Factors associated with weight change in generalized estimating equations *(Abbreviations: C12, mid-dose concentration; cART, combination antiretroviral therapy; EFV, efavirenz)*

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