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

Wei-Chieh Huang, Sung-Hsi Huang, Chien-Ching Hung

IDWeek
Chasing the Sun
24 hours of COVID-19 followed by IDWeek

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)**
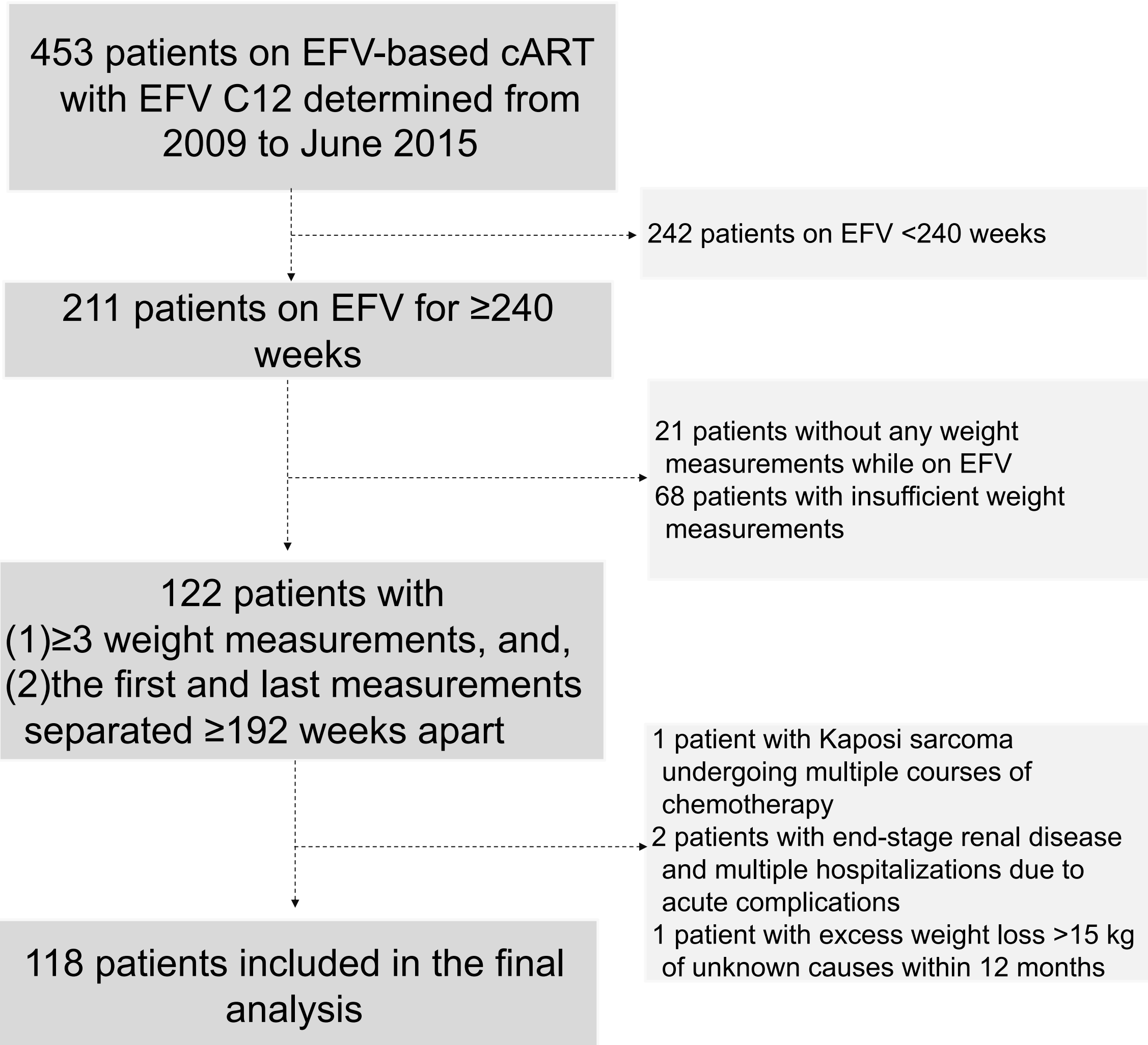
453 patients on EFV-based cART with EFV C12 determined from 2009 to June 2015

→ 242 patients on EFV <240 weeks

211 patients on EFV for ≥240 weeks

→ 21 patients without any weight measurements while on EFV
68 patients with insufficient weight measurements

122 patients with
(1)≥3 weight measurements, and,
(2)the first and last measurements separated ≥192 weeks apart

→ 1 patient with Kaposi sarcoma undergoing multiple courses of chemotherapy
2 patients with end-stage renal disease and multiple hospitalizations due to acute complications
1 patient with excess weight loss >15 kg of unknown causes within 12 months

118 patients included in the final analysis

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.*
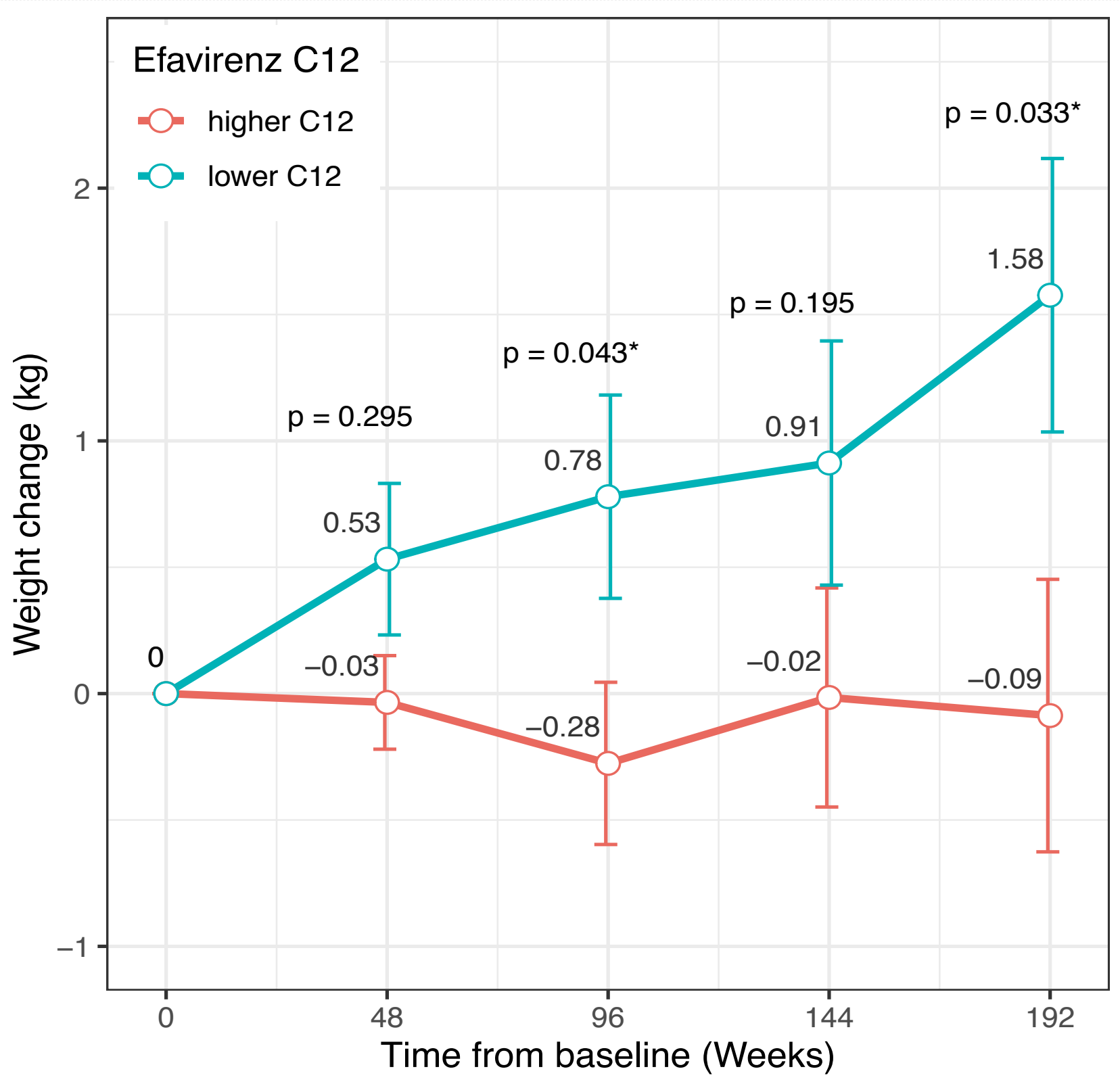

Figure 2. Weight changes over 192 weeks from baseline of the study among virologically suppressed people living with HIV who had higher and those who had lower efavirenz (EFV) mid-dose concentrations (C12).
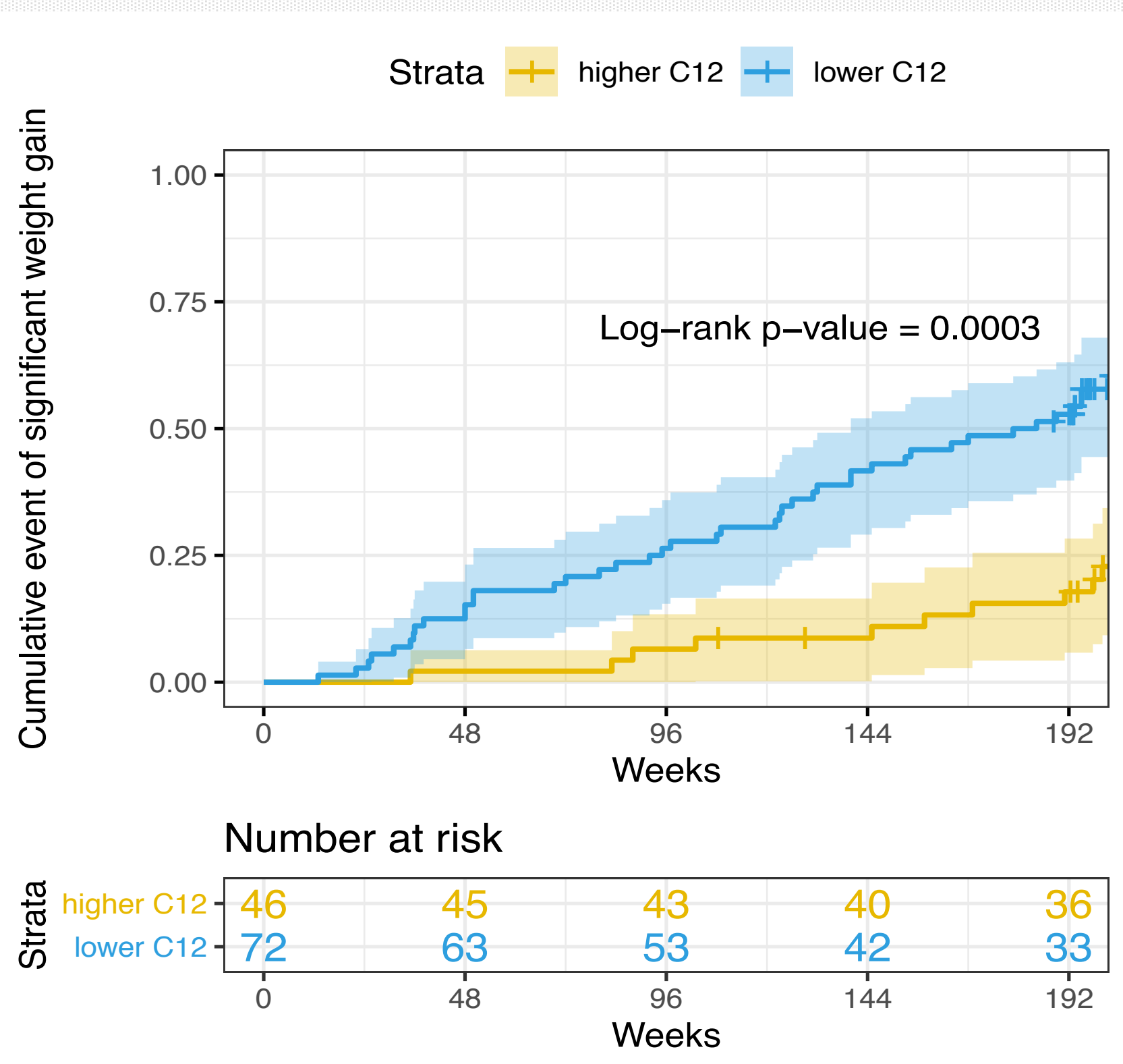

Figure 3. Cumulative events of significant weight gain (≥ 5% weight gain from baseline) among virologically suppressed people living with HIV who had higher and those who had lower efavirenz mid-dose concentration (C12) in Kaplan-Meier analysis.

- 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)*
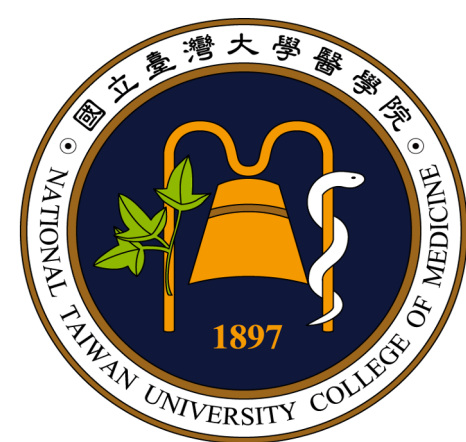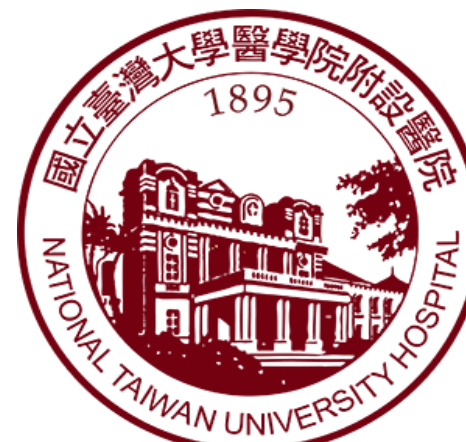
Chien-Ching Hung hcc0401@ntu.edu.tw
7, Chung-Shan South Rd., Taipei, Taiwan.