

Predictors for CD4 Cell Count Increase for Treatment Naïve Patients with Sustained Viral Load Suppression within 1 Year after Starting cART: The Swiss HIV Cohort Study (SHCS)

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Background: CD4 cell recovery in patients with continuous suppression of plasma HIV-1 viral load (VL) is highly variable. This study aimed to identify predictive factors for long-term CD4 increase in naïve patients starting cART.

Methods: All treatment-naïve patients in the SHCS starting cART with at least 2 subsequent VL and CD4 measurements were identified and those with two suppressed VL (<50 copies/ml) at least 3 months apart and within 12 months after starting cART were included. We studied CD4 cell count dynamics for

these patients until viral rebound (VL>400 copies/ml) or up to five years subdivided into three periods: year 1, years 2-3 and years 4-5 of suppression. Multiple median regression with adjustment for multiple CD4 measurements within patient with a cluster bootstrap was used to study the dependence of the CD4 slopes on time-updated clinical covariates and drug classes.

Results: Of 2860 patients starting cART, 1816 (63%) reached VL suppression. Median CD4 count increases in suppressed patients were 87, 52 and 19 cells/µl and year in the three periods, i.e. 1, 2-3 and 4-5 years after entry

into viral load suppression (Figure 1).

In the multiple median regression model (Table 1), median CD4 increase over all three periods was significantly higher for patients with female gender (p<0.001), lower age (p<0.001), higher VL at start of cART (p=0.002), CD4 cell count <650 cells/µl at start of the period (p=0.010) and low CD4 increase in the previous period (or increase from start of cART for the first period; p<0.001). Patients without hepatitis B (p=0.031) or with a CD4 above 200 cells/µl (p=0.017) also had a significantly higher CD4 increase but this was not confirmed in all sensitivity analyses.

Patients on tenofovir showed a significantly lower increase than patients on stavudine (p<0.001); the median CD4 change per year was between -39 and -44 cells/µl lower during the three periods. There was also a trend towards lower CD4 changes for patients on NNRTI-based cART (compared to boosted PI, p=0.067) and patients on lamivudine/zidovudine (compared to stavudine, p=0.065). Patients with a co-infection with chronic hepatitis C and patients without AIDS had a significantly lower CD4 increase in some periods but not overall. Other covariates did not significantly influence CD4 change.

Conclusions: In drug naïve patients with sustained VL suppression female gender, lower age, high VL at start of cART and CD4 cells<650/µl was associated with higher CD4 cell increase. CD4 increase was lower in regimens with tenofovir. Clinical relevance of these findings must be confirmed in large collaborative cohort projects but could influence guidelines in older patients and those starting cART at low CD4 cell levels.

Figure 1: Median and IQR of CD4 increases (cells/µl and year) during years 1, 2-3, and 4-5 of viral load suppression by CD4 cell count and selected cART regimens at the start of the time period.

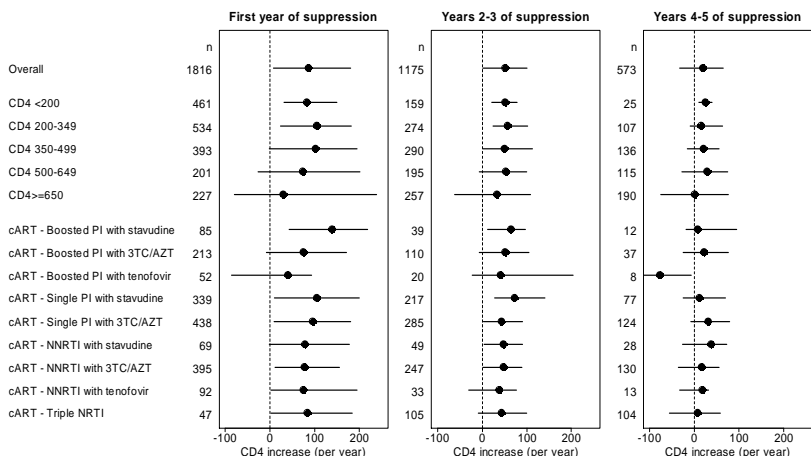


Table 1: Adjusted model for median CD4 increase during years 1, 2-3, and 4-5 of viral load suppression

| | CD4 increase in year 1 under suppression (n=1816 patients, 7007 CD4 cell counts) | | CD4 increase per year in year 2-3 under suppression (n=1175 patients, 6493 CD4 cell counts) | | CD4 increase per year in years 4-5 under suppression (n=573 patients, 3001 CD4 cell counts) | | Overall p-value |
|--|--|-------------|---|------------|---|------------|-----------------|
| | Estimate | 95% CI | Estimate | 95% CI | Estimate | 95% CI | |
| Intercept \$ | +126 | +99 to +152 | +75 | +52 to +94 | +46 | +13 to +84 | <0.001 |
| Female gender | +28 | +13 to +50 | +16 | +5 to +30 | +15 | -2 to +35 | <0.001 |
| Age (per 10 years) | -16 | -24 to -9 | -4 | -8 to +2 | -4 | -10 to +3 | <0.001 |
| Prior AIDS | +21 | +2 to +35 | +5 | -7 to +17 | -11 | -31 to +9 | 0.810 |
| Time from positive HIV test (years) † | 0 | -2 to +1 | -1 | -3 to 0 | -1 | -2 to +1 | 0.176 |
| Hepatitis B (Ag-HBs positive) | -25 | -56 to -4 | +6 | -16 to +24 | -31 | -77 to -9 | 0.031 |
| Hepatitis C positive | -20 | -37 to -1 | +8 | -4 to +27 | -21 | -47 to -2 | 0.156 |
| Time from first cART to suppression | +5 | +2 to +10 | -2 | -5 to 0 | -1 | -4 to +3 | 1.000 |
| Viral load at first cART (per log ₁₀ /ml) | +15 | +8 to +21 | +3 | -2 to +8 | +4 | -2 to +8 | 0.002 |
| CD4 at start of period (cells/µl): | | | | | | | |
| <200 | -29 | -48 to -9 | -10 | -26 to +5 | -12 | -48 to +12 | 0.017 |
| 200-350 | 0 | -- | 0 | -- | 0 | -- | -- |
| 350-500 | +34 | +11 to +59 | -1 | -17 to +12 | -30 | -53 to -14 | 0.206 |
| 500-649 | -3 | -43 to +38 | +4 | -16 to +20 | -3 | -29 to +19 | 1.000 |
| ≥650 | -15 | -67 to +32 | -10 | -32 to +15 | -37 | -71 to -12 | 0.010 |
| CD4 change per year during previous period (per 100 cells/µl increase) ‡ | -50 | -61 to -37 | -16 | -22 to -9 | -40 | -55 to -22 | <0.001 |
| cART regimen: | | | | | | | |
| Boosted PI | 0 | -- | 0 | -- | 0 | -- | -- |
| Single PI | -12 | -34 to +4 | 0 | -15 to +17 | -11 | -38 to +15 | 0.296 |
| NNRTI | -6 | -23 to +16 | -11 | -25 to +8 | -22 | -49 to +6 | 0.067 |
| Triple NRTI | -37 | -93 to +24 | -16 | -34 to +7 | -12 | -45 to +22 | 0.097 |
| Nucleoside pair: | | | | | | | |
| Any Stavudine | 0 | -- | 0 | -- | 0 | -- | -- |
| Zidovudine/lamivudine | -9 | -26 to +8 | -18 | -30 to -5 | -3 | -20 to +18 | 0.065 |
| Any Tenofovir | -39 | -78 to -16 | -42 | -67 to -16 | -44 | -185 to -7 | <0.001 |
| Other | +19 | +5 to +61 | -36 | -55 to -10 | +5 | -20 to +43 | 0.531 |
| On cotrimoxazole at entry into period | -22 | -39 to -5 | -9 | -22 to +5 | -10 | -40 to +25 | 0.145 |

\$ Intercept corresponds to a male, 40-year old patient, who took 4 months to enter suppression, a viral load of 5 log₁₀ copies/ml at start of cART and an increase of 100 cells/µl per year in the previous period.
† Imputed with the date of registration into the SHCS in case date of first positive HIV test was missing.
‡ This refers to the change from start of cART to first VL suppression for the first period.