INTRODUCTION

The goal of combination antiretroviral therapy (cART) is to reduce HIV viral replication to below the limit of detection. As viral replication falls, the CD4 count increases. The initial increase is rapid and usually lasts 3–6 months, followed by a phase of slower CD4 count increases, lasting 3–5 years. It is currently unclear whether CD4 counts will continue to increase to the levels seen in HIV-negative populations.

OBJECTIVES

Describe the relationship with CD4 count increases of:
- duration of treatment
- CD4 count at starting cART
- current CD4 count in antiretroviral naive patients starting cART who currently have viral load (VL) < 50 copies/ml.

METHODS

Patients

1577 antiretroviral naive patients from EuroSIDA, a pan-European observational study who satisfied the following inclusion criteria

Inclusion criteria
- 2 consecutive VL < 50 copies/ml
- on cART at both VL measurements
- no change in antiretrovirals (start or stop) between the VL
- CD4 count measured in the 6 months prior to starting cART
- distinct CD4 measured within at most 4 weeks of each VL measurement

Statistical methods

Change in CD4 occurring between each pair of consecutive VLs (5 copies/ml) was calculated and standardized for the time between viral load measurements to give the rate of change in CD4 (units of cells/mm³ per year). Each patient could contribute data from > 1 pair.

Generalised linear models, using a normal distribution and an identity link function, adjusted for repeated measures, were used to describe rate of CD4 change stratified by time since starting cART, CD4 at starting cART and current CD4.

Baseline (for descriptive purposes) was arbitrarily defined as the 1st VL ≤50 copies/ml after starting cART.

RESULTS

Baseline characteristics of the patients at baseline are described in Table 1 and 2.

Table 3 shows the mean, crude rate of change in CD4 per year stratified by current CD4, i.e., the CD4 immediately prior to the VL used with the viral load pair.

The correlation between the pair of CD4 used in analyses was 0.876, with 12.4% estimated from > 1 pair.

A multivariate model adjusted for nucleoside pair, cART regimen, age, change in CD4 count from baseline and time since starting cART, showed no evidence of any group of patients in which CD4 was not increasing (Figure 1). After adjustment, there was a slightly lower, but still significantly increasing, rate of change in CD4 among patients with a current CD4 count of > 700/mm³ (mean 28.3/mm³; 95% CI 7.2 – 49.8/mm³). The current median CD4 in these patients was 855/mm³ (IQR 766–979/mm³).

A multivariate model adjusted for nucleoside pair, cART regimen, age, change in CD4 and time since starting cART (start or stop) between the VL, showed no evidence of any group of patients in which CD4 was not increasing (Figure 2). The greatest rates of increase in CD4 were seen in the first year after starting cART, approximately 100/mm³, regardless of the absolute CD4 at cART initiation. Lower increases in CD4 (approximately 50/mm³ per year) continued to be observed up to 5 years after starting cART in patients whose current CD4 was below 500/mm³. The only group without significant increases in annual CD4 was in patients who had taken cART for more than 5 years with a current CD4 >1500/mm³. The current median CD4 in this patient group was 701/mm³ (IQR 601–863/mm³).

CONCLUSIONS

- Due to the inclusion criteria, all patients had VL ≤50 copies/ml and were taking cART with no interruptions between VL ≤50 copies/ml.
- Little evidence of plateau effect in CD4 rise except at near-normal CD4 levels, particularly if VL is maintained at ≤50 copies/ml for a sufficiently long period of time.
- The majority of patients continued to experience significant rises in CD4 count, even after 5 years of cART.
- Normalization of CD4 counts in HIV-infected patients for all infected individuals may be achievable if viral suppression with cART can be maintained for a sufficiently long period of time.

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