

Predictors for Changes in CD4 Cell Count 7 Years after Starting HAART

Luuk Gras¹, Ard van Sighem¹, Christophe Fraser², Jamie Griffin², Frank Miedema³, Joep Lange⁴, Frank de Wolf^{1,2}

¹ HIV Monitoring Foundation, Amsterdam, The Netherlands; ² Imperial College, London, UK; ³ University Medical Centre, Utrecht, The Netherlands, ⁴ Academic Medical Centre of the University of Amsterdam, Amsterdam, The Netherlands



1. Background

It is less well known whether, after 5-7 years of therapy, CD4 cell count in HIV infected patients continue to increase. We evaluated changes in CD4 cell count in a cohort of previously therapy-naive patients with 7 years of follow-up after starting HAART.

2. Methods

From the Dutch ATHENA national observational cohort 840 patients were selected who started HAART between 1 January 1997 and 30 June 1998 and had CD4 measurements available at the time of starting HAART and 336 weeks thereafter.

CD4 measurements closest to 48, 96, 144, 192, 240, 288 and 336 weeks (1-7 years) were selected and mean CD4 cell count and increases from pre-HAART levels were calculated and summarized. Predictors for changes in CD4 cell count after starting HAART were determined in 2 cohorts of patients:

A: Changes in CD4 cell count in patients with 7 years of follow-up

Linear regression models were used to associate gender, transmission risk group, region of origin, age at starting HAART, pre-HAART CD4 and CD8 cell count and HIV-RNA levels, CDC-C events prior to starting HAART, cumulative number of days using HAART with differences in CD4 count between start of HAART and after 7 years.

B: Annual changes in CD4 cell count in continuously treated patients

In a second analysis, repeated measurement models were used in a subset of patients who had used HAART for at least 44 weeks every 48 weeks after starting HAART. Annual changes in CD4 cell count were modelled according to time period, the amount of time with HIV-RNA<500 copies/ml, pre-HAART CD4 cell count and the variables listed in the first analysis.

3. Results

A: Changes in CD4 cell count in patients with 7 years of follow-up

A majority of the 840 patients were male, infected through homosexual contact and of Dutch origin (see Table 1). 80% of patients with pre-HAART CD4 cell count <350 cells/mm³ compared with 63% patients with ≥350 cells/mm³ (p<0.0001) used HAART containing regimens for more than 308 weeks in the first 336 weeks after HAART initiation.

Table 1. Characteristics of 840 patients who started HAART between 1 January 1997 and 30 June 1998.

	N	%	Pre-HAART	median	IQR
Male gender	708	84	CD4 cell count	260	100-400
Risk group			cells/mm ³		
MSM	525	62	CD8 cell count	950	600-1370
IDU	33	4	cells/mm ³		
Heterosexual	217	26	HIV-RNA	4.9	4.3-5.2
Other	66	8	log ₁₀ copies/ml		
Dutch origin	583	69	Age at starting HAART	37	32-45
CDC-C event pre-HAART	186	22			
CD4 count pre-HAART					
cells/mm ³					
0-50	148	18			
50-200	183	22			
200-350	224	27			
350-500	181	22			
≥500	104	12			

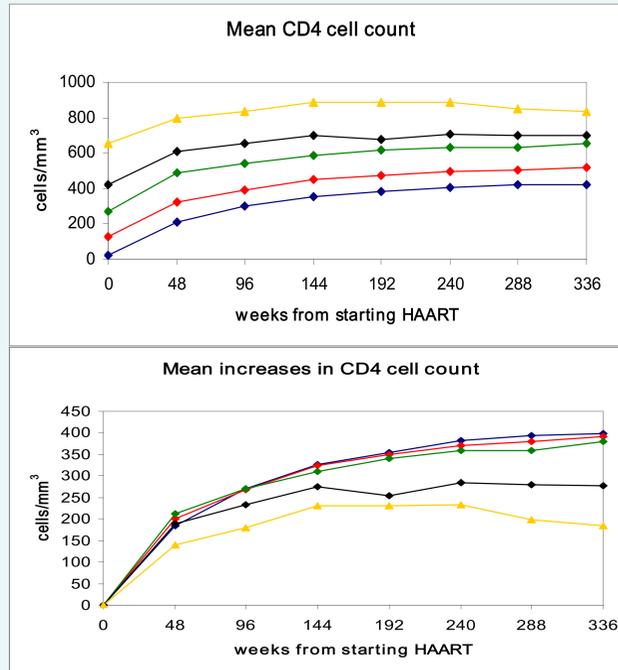


Figure 1. Mean CD4 cell count (top) and mean increases in CD4 cell count (bottom) in all patients with 7 years of follow-up according to pre-HAART levels:

<50
50-200
200-350
350-500
≥500

Mean increase in CD4 cell count 7 years after HAART initiation was 398, 392, 380, 278 and 184 cells/mm³ in those with pre-HAART CD4 count <50, 50-200, 200-350, 350-500 and ≥500 cells/mm³ respectively. Cumulative time not on HAART containing regimens and the other variables listed in Table 2 were the only variables which remained significant in multivariate analyses.

Table 2. Variables associated with changes in CD4 cell count between start of HAART and 7 years thereafter

Multivariate analyses	Increase in CD4 cell count (95% CI)	P
Overall increase in CD4 count*	268 (196, 341)	<0.0001
Risk group		
IDU	-132 (-226, -40)	0.005
Non-IDU	0	
CD4 count at starting HAART (cells/mm ³)		
0-50	101 (31, 171)	0.005
50-200	96 (29, 163)	0.005
200-350	115 (52, 178)	0.0003
350-500	48 (-16, 112)	0.14
≥500	0	
HIV-RNA at starting HAART (copies/ml)		
<10,000	0	
10,000-100,000	52 (-6, 109)	0.08
≥100,000	70 (11, 130)	0.02
Cumulative time without HAART	Per month increase -7 (-98, -6)	<0.0001

* Average increase in CD4 cell count 336 weeks after starting HAART for a patient not infected through intravenous drug use and with a baseline CD4 cell count >500 cells/mm³, HIV-RNA levels <10,000 copies/ml and who used HAART continuously.

3. Results - continued

B Annual changes in CD4 cell count in continuously treated patients

Among the 529 patients who used HAART continuously there were 345 patients (65%) with HIV-RNA <500 copies/ml at all measurements between 1-7 years.

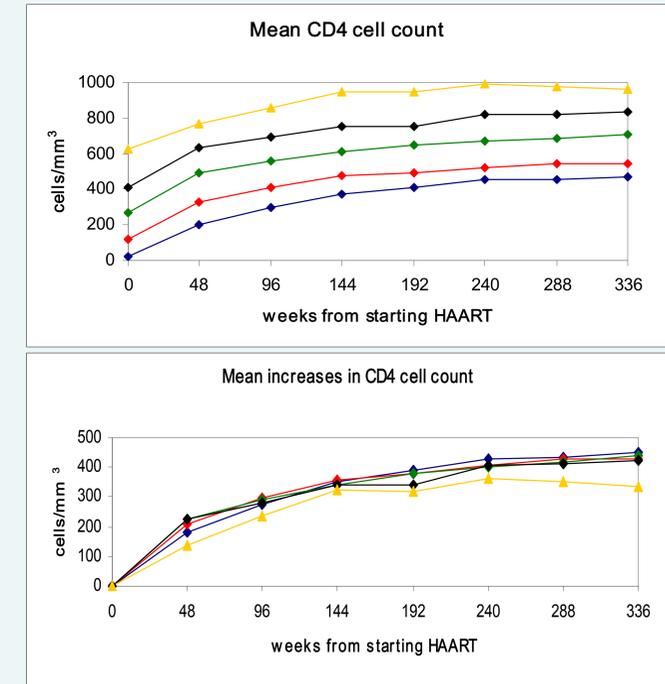


Figure 2. Mean CD4 cell count (top) and mean increases in CD4 cell count (bottom) in continuously treated patients by pre-HAART levels. Legend see Figure 1.

At 7 years mean increases in CD4 cell count from pre-HAART levels were 449, 429, 440, 423 and 336 cells/mm³ in those with pre-HAART CD4 cell count <50, 50-200, 200-350, 350-500 and ≥500 cells/mm³ respectively, see Figure 2.

Annual increases in CD4 cell count significantly declined with longer follow-up, linear test for trend, p<0.0001. Variables associated with smaller annual increases in CD4 cell count were older age (decrease of 6 CD4 cells/mm³/year (95% CI 1, 10; p=0.02) per 10 years older when starting HAART) and a longer time with HIV-RNA levels >500 copies/ml (decrease of 3 CD4 cells/mm³/year (95% CI 1, 5; p=0.007) per month longer. Estimated mean annual changes between 1-7 years are shown in Table 3.

Table 3. Estimated mean annual changes in CD4 cell count between 1-7 years after starting HAART in 529 continuously treated patients

Years after starting HAART	Pre-HAART CD4 cell count	Estimated mean annual change in CD4 cell count (95% CI)*	
		<500	≥500
1-3		72 (66, 94)	88 (62, 114)
3-5		32 (23, 40)	36 (11, 61)
5-7		16 (8, 25)	-9 (-34, 16)

* Average yearly increase in CD4 cell count for a patient, aged 37 years when starting HAART, HIV-RNA<500 copies/ml at all measurements.

Conclusions

A longer cumulative time on HAART and HIV-RNA suppression <500 copies/ml are associated with greater increases in CD4 cell count. The mean annual increases in CD4 cell count decline significantly with longer follow-up. In patients with pre-HAART CD4 cell count <500 cells/mm³ and HIV-RNA <500 copies/ml, mean CD4 cell count continue to increase between 5-7 years, albeit slowly.