

A CD4 threshold below 350 cells/mm³ for initiation of HAART is associated with a higher risk of AIDS



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Background

The optimal time to start HAART is still subject to debate. In 2000, the CD4 cell count range below which HAART should be started, according to guidelines in the Netherlands, was lowered from 350-500 to 200-350 cells/mm³. We analysed changes in CD4 cell counts and progression to AIDS and/or death after HIV diagnosis, comparing patients diagnosed before and after 2000.

Methods

- 4142 patients were selected from the ATENA national observational cohort who
 - had an HIV-1 diagnosis between 1998 and 2005.
 - were 16 years of age or older at diagnosis and were not infected through intravenous drug use.
 - did not have a concurrent AIDS diagnosis.
 - were either untreated during follow-up or started HAART whilst being antiretroviral therapy naïve.
- CD4 counts at diagnosis were categorised in < 50, 50-200, 200-350, 350-500, and ≥ 500 cells/mm³.
- A mixed effects model with random intercept and slope and an autoregressive covariance structure for measurements within the same patient was used to analyse longitudinal data on CD4 counts after diagnosis in 1422 (34.3%) patients with at least 4 years of follow-up, stratified according to CD4 counts at diagnosis and according to diagnosis in or before 2000 or thereafter.
- Progression to the earliest of AIDS or death was studied in 3111 (75.1%) patients with ≥ 200 cells/mm³ at diagnosis using Cox' proportional hazard model adjusting for age, CDC status, gender, and region of origin.
- "Intention-to-treat" analyses were performed, assuming that HAART was started according to the guidelines.

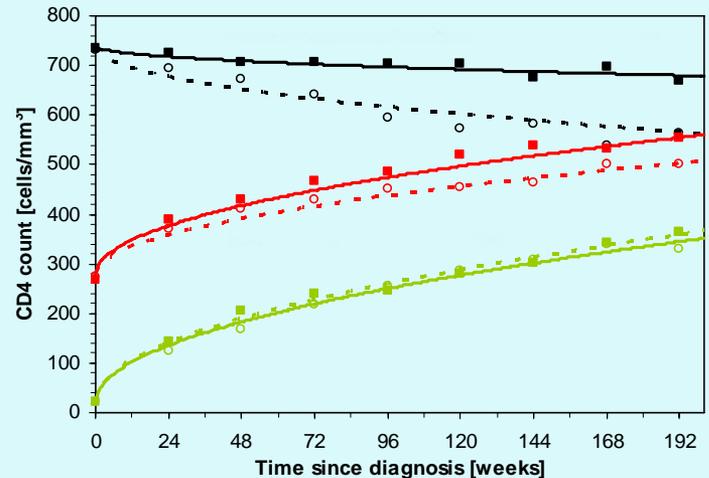
Study population

N = 4142	N / median	% / IQR
gender, male	3066	74.0%
transmission risk		
homosexual contact	2186	52.7%
heterosexual contact	1693	40.8%
other/unknown	263	6.3%
region of origin		
the Netherlands	2237	54.0%
sub-Saharan Africa	945	22.8%
CDC-B at diagnosis	426	7.8%
CD4 category at diagnosis		
< 50	263	6.3%
50-200	768	18.5%
200-350	953	23.0%
350-500	885	21.3%
≥ 500	1273	30.7%
HIV RNA at diagnosis (log ₁₀ copies/ml)	4.7	4.0-5.1
age at diagnosis (years)	35.9	29.7-42.8
ever initiated HAART	2719	65.6%
time from diagnosis to start of HAART (years)	0.2	0.1-0.6
progression to death	81	1.9%
progression to AIDS	255	6.1%
follow-up (years)	2.9	1.3-4.7
total person-years follow-up	13219	

- There was no difference in the distribution of CD4 counts in patients diagnosed in or before 2000 or thereafter in the 1422 patients with at least 4 years of follow-up.

Changes in CD4 counts over time

The plot shows data and predictions of the mixed effects model for patients diagnosed in or before 2000 (data: squares; prediction: solid lines) or thereafter (data: circles; prediction: dashed lines) with CD4 < 50, 200-350, or ≥ 500.



Compared to patients diagnosed in or before 2000, CD4 counts in patients diagnosed after 2000 decreased faster or increased slower for patients with CD4 counts at diagnosis ≥ 200 cells/mm³.

CD4 category at diagnosis	difference in CD4 slope ≤ 2000 vs. > 2000		
	mean	95% CI	P value
< 50	-1.0	-7.5 – 5.5	0.8
50-200	-2.1	-5.9 – 1.7	0.3
200-350	3.7	0.1 – 7.3	0.04
350-500	7.0	3.4 – 10.7	0.0001
≥ 500	8.2	5.0 – 11.5	<0.0001

Progression to AIDS and/or death

- Of the 3111 patients with ≥ 200 cells/mm³ at diagnosis, 45 died, 135 progressed to AIDS, and 165 progressed to AIDS/death.
- Hazard ratios (HR) associated with progression:

	HR	95% CI	P value	
log ₁₀ RNA at diagnosis per unit increase	1.5	1.2 – 1.8	0.0001	
CD4 at diagnosis	200-350	1.5	0.9 – 2.5	0.09
	350-500	1.1	0.6 – 1.8	0.8
	≥ 500	1 (ref)		
diagnosis ≤ 2000 vs. > 2000 per CD4 category	200-350	0.5	0.3 – 1.0	0.04
	350-500	1.0	0.5 – 1.9	1.0
	≥ 500	1.5	0.9 – 2.6	0.1

- log₁₀ RNA was the most important predictor of progression.
- Patients with CD4 counts 200-350 tended to have a lower risk of AIDS/death when diagnosed in or before 2000 than thereafter.

Conclusions & discussion

- CD4 counts after diagnosis are higher in patients diagnosed in or before 2000 compared to those diagnosed thereafter.
- Patients with CD4 counts 200-350 have a slightly higher risk of disease progression when diagnosed after 2000.
- As current HAART regimens are less toxic and easier to adhere to than before 2000, the CD4 threshold for starting HAART should be reconsidered.