

Lower mortality and earlier start of cART in patients tested repeatedly for HIV than in those with a positive first test

Luuk Gras¹, Ard van Sighem¹, Daniela Bezemer¹, Colette Smit¹, Ferdinand Wit², Frank de Wolf^{1,3} on behalf of the ATHENA national observational cohort study

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



HIV Monitoring Foundation
Meibergdreef 9
1105 AZ Amsterdam
the Netherlands
Phone: +31-20-5664172
E-mail: l.a.gras@amc.uva.nl

Background

- The life expectancy of HIV-infected patients is still lower than that of the general population.
- The main reason for this appears to be late diagnosis in infected individuals.
- Timely diagnosis of HIV-1 infection and a subsequent timely start of cART depends largely on sufficient HIV diagnostic testing
- However it is unknown whether patients who were more frequently tested have lower mortality rates and a more timely start of cART compared to patients less frequently tested for HIV.

Objective

- We compared mortality rates and CD4 cell counts at start of combination antiretroviral therapy (cART) in patients with different frequencies of diagnostic testing for HIV.

Methods

Patients

- Patients registered as being HIV-1 infected through sexual contact
- In follow-up anytime from 2004 through 2008.
- ≥16 years of age at HIV diagnosis
- Patients included in the PRIMO study were excluded

Grouped into 3 groups based on frequency of testing for HIV:

- patients seropositive the first time they were tested for HIV (thus without prior negative HIV antibody test)
- patients testing positive 1 to 2 years after having tested negative
- Patients with a maximum 1-year interval between tests

Outcome

- Incidence of death between 2004-2008.
- CD4 cell count at the start of cART (% patients <200 CD4 cells/mm³ at start cART).
- Incidence of loss to follow- prior to cART.

Statistical analysis

- Logistic regression for analysis of percentage of patients with less than 200 CD4 cells/mm³ and of those with an AIDS diagnosis at cART initiation Poisson regression was used for analysis of loss to follow-up and death.
- Adjusted for gender, region of origin, HIV-1 transmission risk group, and age (in January 2004 and year of cART initiation).

	Patients with positive first test	Patients with negative test 1-2 yr before testing positive	Patients with negative test <1 yr before testing positive
Total, N	4067	561	866
Male gender, N (%)	2931 (72.1)	510 (90.1)	817 (94.3)
Region of origin, N (%)			
the Netherlands	1995 (49.0)	392 (69.9)	648 (74.8)
W-Europe/N-America	226 (5.6)	47 (8.4)	63 (7.3)
South America/Caribbean	564 (13.9)	53 (9.4)	81 (9.3)
Sub-Saharan Africa	940 (23.1)	29 (5.2)	32 (3.7)
Other	342 (8.4)	40 (7.1)	42 (4.9)
MSM transmission risk group (N, %)	2083 (51.2)	474 (84.5)	769 (88.8)
Age in years on 1 Jan 2004, median (IQR)	36.0 (28.9-43.2)	34.8 (27.9-41.8)	34.7 (28.5-41.4)
Year of diagnosis, N (%)			
<2000	371 (9.1)	29 (5.2)	30 (3.4)
2001-2004	799 (19.6)	90 (16.0)	133 (15.4)
2005-2008	2897 (71.2)	442 (78.8)	703 (81.2)
Patients with CD4 cell count at diagnosis, N (%)	3334 (82.0)	510 (90.9)	891 (91.3)
CD4 cell count (cells/mm³) at diagnosis, median (IQR)	350 (150-550)	470 (360-660)	550 (380-710)
AIDS at HIV diagnosis, N (%)	652 (16.0)	17 (3.0)	13 (1.5)
Years between last negative and first positive HIV antibody test, median (IQR)	-	1.4 (1.2-1.7)	0.5 (0.3-0.7)

Table 1. Demographic and clinical characteristics.

Results

- In total, 5494 patients selected, subdivided in:
 - 4067 patients initially testing HIV positive
 - 561 tested positive between 1 and 2 years after testing negative
 - 866 tested positive within 1 year after being tested negative

Table 1

- Patients with a negative test date were more often male, born in the Netherlands, and more often MSM compared to patients initially testing positive.
- The median CD4 cell count at HIV diagnosis was lowest for patients with a positive first test.
- AIDS at HIV diagnosis was more often diagnosed in patients with a positive first test compared with those with a prior negative test.

Table 2

- The incidence and adjusted risk of death was highest among patients initially testing positive.
- In total, 631 patients were lost to follow-up 2004–2008 (incidence, 3.91/100 PY). The adjusted relative risk of those lost to follow-up was not significantly different between patients with a prior negative test and those initially testing positive (overall *P* value=0.15).
- Higher median CD4 cell counts at cART initiation in patients with a prior negative test than in those initially testing positive.
- The percentage of patients with a CD4 cell count <200 cells/mm³ at cART initiation was highest in patients with a positive first test but also considerable among patients with a negative test.
- Reasons for starting late were not recorded but: 70% already had low CD4 cell counts (<300 cells/mm³) at HIV diagnosis (71%, patients initially testing positive; 59%, patients with a negative test 1-2 years before testing positive; and 35%, patients receiving tests within 1 year).
- Among the remaining 442 patients with ≥300 cells/mm³ at HIV diagnosis and <200 cells/mm³ at cART initiation, 36% of the patients with a positive first test did not have a follow-up visit for at least 9 months in the 6 months before cART initiation. This percentage was 17% in patients with a negative test 1-2 years before testing positive and 18% in those receiving tests within one year.

	HIV positive patients at their first test, n=4067	Patients with negative test 1-2 yr before testing positive, n=561	Patients with negative test <1 yr before testing positive, n=866
PY follow-up between 2004 and 2008	12384	1551	2220
Number of patients died	165	9	12
Incidence/100 PY (95% CI)	1.33 (1.13-1.55)	0.58 (0.27-1.10)	0.54 (0.28-0.94)
Adjusted relative risk (95% CI; p-value)	1.00	0.50 (0.25-0.98)	0.49 (0.27-0.89)
Number of patients lost to follow-up	534	34	63
Incidence /100 PY (95% CI)	4.31 (3.95-4.69)	2.19 (1.52-3.06)	2.84 (2.18-3.63)
Adjusted relative risk (95% CI)	1.00	0.70 (0.49-1.00)	0.96 (0.73-1.27)
Number of cART treated patients (%)	2772 (68)	281 (50)	374 (43)
Median (IQR) number of CD4 cells/mm³ at the start of cART	190 (80-270)	250 (190-320)	260 (200-320)
Number of patients <200 cells/mm ³ (%)	1333 (48)	74 (26)	86 (23)
Adjusted odds ratio (95% CI)	1.00	0.43 (0.32-0.57)	0.37 (0.28-0.48)
Number (%) of AIDS diagnoses at the start of cART (cells/mm³)	667 (24)	24 (9)	31 (8)
Adjusted odds ratio (95% CI)	1.00	0.28 (0.17-0.48)	0.32 (0.20-0.51)

Table 2. Incidence of death and lost to follow-up in all 5494 patients in follow-up between 2004 through 2008 and CD4 cell count and AIDS diagnoses at the start of cART among 3448 patients starting cART in 2004 through 2008.

Conclusion

Frequent testing for HIV shortens the time between infection and diagnosis and improves the likelihood of timely treatment, with prevention of clinical progression to AIDS and death. However, annual testing for HIV did not prevent a late start of cART in a substantial proportion of patients.