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Western Blot in treated people with HIV-1 chronic infection: frequency of negative HIV-1 Pol genes

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BACKGROUND & AIM

Western Blot (WB) test has a key role in HIV-1 diagnosis; there is a lack of literature data on its role in chronic infection. For this reason, we evaluate the performance of WB in predicting immune-responses against HIV-1 Gag, Env and Pol genes in adult people with HIV-1 chronic infection, with long exposure to antiretroviral therapy (ART).

MATERIALS AND METHODS

We conducted a retrospective analysis on all adult people with HIV-1 chronic infection, followed at the Infectious Diseases Clinic of the San Raffaele Hospital, Milan, Italy, with a WB test performed after at least 12 months of ART (if multiple WB tests per patient were available, the most recent was considered).
Patients' characteristics at WB determination were described by median (Q1, Q3) or frequency (%) and compared by Mann-Whitney test or chi-square test. A multivariate logistic regression was performed to assess factors associated with a negative HIV-1 Pol and included: age, gender, HCV co-infection, years of ART, change in CD4+ between ART start and WB test (slope), years of HIV-RNA<50 copies/mL and months to ART start.

TABLE 1 – Patients' characteristics in the overall sample and according to HIV-1 Pol result

Characteristics	OVERALL (n=530)	NEGATIVE HIV-1 Pol (n=88)	POSITIVE HIV-1 Pol (n=442)	p-value
Age (years)	51 (47-56)	54 (49 - 58)	51 (46 - 55)	0.001
Male gender	380 (72%)	70 (80%)	310 (70%)	0.092
Years of HIV	19.3 (14.1-24.6)	19.8 (15.3 – 22.9)	19.3 (13.7 – 24.8)	0.749
Years of ART	16.3 (10.4-19.1)	17.2 (11.3 – 20.1)	16.2 (10.2 – 19.1)	0.191
Months between HIV diagnosis and ART start	18.7 (2.5-67.2)	6.4 (1.4-38.7)	24.0 (2.6-72.6)	0.013
Pre-ART CD4+ (cells/µL)	317 (177-471) (available in n=305)	283 (177 - 420) (available in n=54)	327 (171 - 478) (available in n=251)	0.487
Pre-ART CD4+/CD8+ ratio	0.33 (0.18-0.52) (available in n=274)	0.30 (0.20-0.40) (available in n=44)	0.34 (0.18-0.55) (available in n=230)	0.314
HIV-RNA <50 copies/mL at WB test	464 (92%)	79 (90%)	385 (87%)	<.0001
Years with HIV-RNA <50 copies/mL	4.6 (1.2 - 10.6)	7.08 (2.2 - 11.5)	4.25 (1.1 - 10.3)	0.046
CD4+ at WB test (cells/µL)	632/µL (443-878) (available in n=496)	698 (561 - 952) (available in n=82)	620 (410 - 868) (available in n=414)	0.009
CD4+/CD8+ ratio at WB test (available in n=425)	0.81 (0.54 - 1.16)	0.98 (0.7 - 1.38) (available in n=74)	0.79 (0.48 - 1.11) (available in n=351)	0.001

Results are described as median (Q1, Q3) or frequency (%).

RESULTS

Overall, 530 patients were included in this analysis: patients' characteristics at WB determination are presented in Table 1.
A negative HIV-1 Pol was found in 88 (16.6%) patients; these patients were slightly older (p=0.001), had a longer duration of HIV-RNA<50 copies/ml (p=0.046), a shorter time to ART start (p=0.013) and a better immunological profile at WB test (CD4+: p=0.009; CD4+/CD8+ratio: p=0.001) than those with a positive HIV-1 Pol (Table 1, Figure 1).
Changes in CD4+ and CD4+/CD8+ ratio between ART start and WB test tended to show a greater increase in subjects with a negative vs positive HIV-1 Pol (Figure 2); pre-ART CD4+ and CD4+/CD8+ ratio were similar between patients with a negative vs positive HIV-1 Pol gene (pre-ART CD4+:p=0.487; pre-ART CD4+CD8+ ratio: p=0.314).

FIGURE 1 – Patients' characteristics according to HIV-1 Pol result

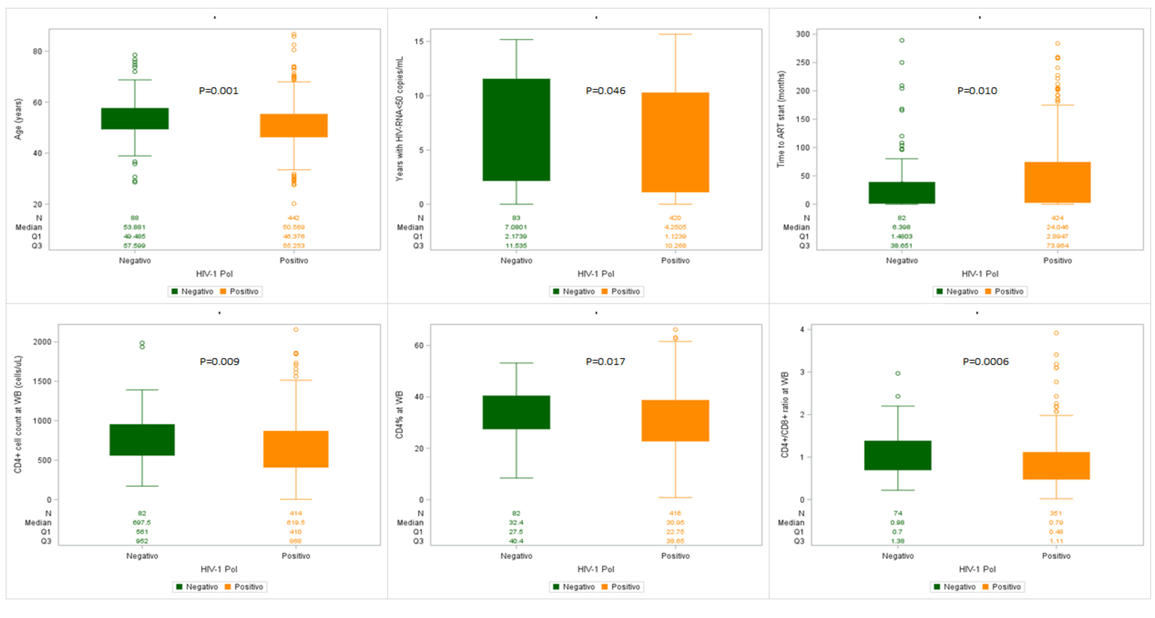
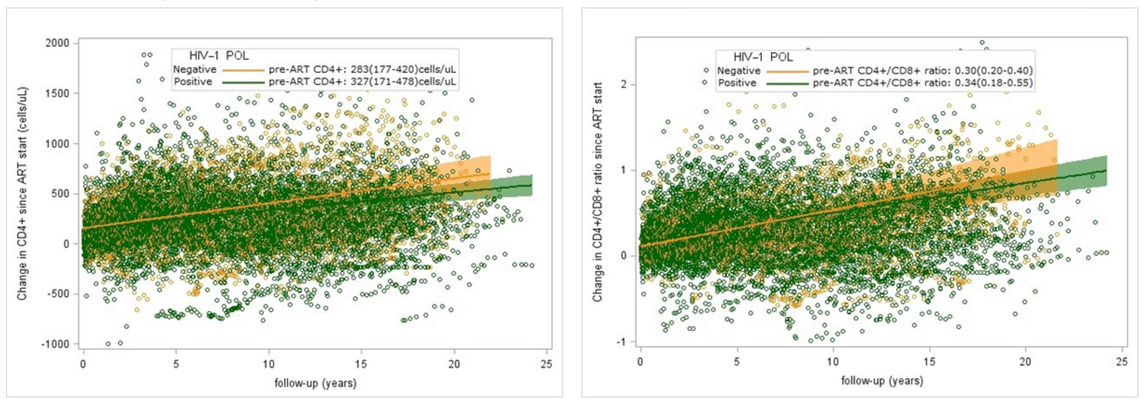


FIGURE 2 - Change in CD4+ cell count since ART start in subjects with a negative or positive HIV-1 Pol



HIV-1 POL	Univariate mixed linear model with random intercept and slope (n subjects=305)		
	Crude mean (95%CI) change in CD4+ since ART start, cells/year	P-value	P-value
Negative (n=54)	24.8 (16.3, 33.3)	<.0001	0.209
Positive (n=251)	17.8 (13.3, 22.3)	<.0001	

HIV-1 POL	Univariate mixed linear model with random intercept and slope (n subjects=273)		
	Crude mean (95%CI) change in CD4+/CD8+ ratio since ART start, units/year	P-value	P-value
Negative (n=44)	0.041 (0.026, 0.057)	<.0001	0.217
Positive (n=229)	0.035 (0.028, 0.043)	<.0001	

TABLE 2 - Multivariate logistic regression: factors associated with the risk of having a negative HIV-1 Pol

Characteristics		Adjusted odds ratio	95% Confidence Interval		p-value
Age	Per 3-years older	1.091	0.964	1.235	0.169
Gender	F vs M	0.724	0.318	1.651	0.443
Months between HIV diagnosis and ART start	Per 6-months longer	0.945	0.904	0.988	0.012
ART duration	Per 3-years longer	1.118	0.871	1.436	0.382
Years with HIV-RNA<50 copies/mL	Per 3-years longer	1.200	0.943	1.525	0.137
Change in CD4+ between ART start and WB test	Per 10-cells/µL/year higher	1.111	1.011	1.236	0.049
HCV	No vs Yes	0.462	0.209	1.023	0.866
	Unknown vs Yes	0.263	0.027	2.604	0.404

By multivariate logistic regression, a negative HIV-1 Pol gene was associated with an early ART start [adjusted odds ratio(AOR) per 6-months longer=0.95 (95%CI)=0.90-0.99), p=0.012] and a greater CD4+ recovery since ART start [AOR per 10-cells/µL/year higher=1.11 (95%CI=1.01-1.24), p=0.049] (Table 2).

CONCLUSIONS

A negative HIV-1 Pol was found in around 17% of HIV-1 infected subjects with a long exposure to ART. This finding is associated with an early ART start and a better immunological profile. The relationship between ART efficacy, recognition of the Pol gene by the immune system and the production of specific antibodies need to be investigated.

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