African ethnicity can influence immunological responses to highly-active antiretroviral therapy (HAART) and immunological success at 48 months: a retrospective pilot cohort study.

eP831

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Introduction and purpose

- African people still bear the heaviest burden of Human Immunodeficiency Virus (HIV) pandemic [1].
- People of African origin (PAO) have an absolute CD4 count similar to Caucasians but significant immunological discrepancies have been evidenced in PAO in comparison with Caucasians [2-5].
- During the natural course of HIV infection, absolute CD4 count decreases more slowly in PAO than in Caucasians but one investigation reported evidence of a lesser CD4 increase in PAO comparatively to Caucasian patients during the first three months of Highly Active Antiretroviral Therapy (HAART) [6-7].
- In the present study, we conducted a retrospective epidemiological investigation to assess whether African ethnicity was independently associated with a poorer CD4 reconstitution with HAART, taking into account all previously described factors affecting CD4 reconstitution [8,9].

Methods

- *Inclusion criteria:* All HIV-1 adult patients previously treated by HAART on 31/12/2011 in Reims University hospital centre (France), who gave informed consent for the digitization of their medical records using Nadis® software were included.
- *Data collection:* Socio-demographic and clinical data, blood CD4 lymphocyte counts (absolute number) and HIV-1 viral loads at baseline and during follow up at 6, 9, 12, 18, 24, 36 and 48 months after the beginning of HAART were extracted from Nadis® software for each of the study patients. This database has been declared to the "Commission Nationale Informatique et Liberté" (number 1585477).
- *Exclusion criteria:* Patients with an HIV-1 viral load >20 copies/ml (Taqman, Roche®) 6 months after the beginning of HAART and patients with one HIV-1 viral load >200 copies/ml, or more than one HIV-1 viral load between 20 and 200 copies/ml during follow up were excluded. Patients lost to follow-up, with duration of follow-up inferior to 9 months or patients with a blood CD4 lymphocyte counts above 500 cells/mm3 at the beginning of the first line of HAART were also excluded.

Acknowledgements : ViiV healthcare® and Fediadis Medica®.

- *Primary outcome*: Immunological success (IS) defined as the presence of peripheral blood CD4 lymphocyte counts above 500 cells/mm3 [10] in more than 50% of the values collected during follow up at 6, 9, 12, 18, 24, 36 and 48 months after the beginning of HAART.
- The following variables: age, CDC Classification category B or C and HIV-1 viral load at baseline were those obtained before first line of HAART in case of patient with multiples lines. Baseline CD4 lymphocyte count corresponds to the lowest absolute value before HAART. The last line of HAART was considered for immunological and virological data collection at 6, 9, 12, 18, 24, 36 and 48 months except when a previous line lasted more than 4 years without any significant HIV-1 viral load variations (see exclusion criteria described above). HIV-1 subtype was defined as non-B in presence of mutation at position 35, 36, 61, 69 and 89 during routine HIV-1 pol gene sequencing, according to ANRS Algorithm [11].
- *Statistical analysis:* Quantitative variables were compared using the Mann Whitney U-test and qualitative variables were compared using Fisher's exact test or Pearson's Chi-square test, as appropriate. A *p* value<0.05 was considered as significant. All variables with a *p* value <0.20 were entered into a multiple logistic regression model. Statistical analyses were performed using Stat view 5.0 (SAS institute).

Results

- Among the 575 HIV-1 patients followed-up, 280 patients met inclusion criteria and no exclusion criteria. Excluded patients were Caucasian and PAO in 238 (80.6%) and 57 (19.3%) cases respectively. Study cohort patients consisted of Caucasian and PAO in 220 (78.6%) and 60 (21.4%) cases respectively (Table 1).
- CD4 count values collected at 6, 9, 12, 18 and 24 months after the beginning of HAART were not statistically different between PAO and Caucasian (not shown). Interestingly at 36 and 48 months, CD4 counts were different between African (n=38 and 31) and Caucasian patients (n=167 and 148): 469 [93-677] versus 528 [45-1383] at 36 months (p=0.03), and 449 [65-975] versus 569 [131-1698] cells/mm3 at 48 months (p=0.02).
- Blood CD4 reconstitution dynamics is depicted in figure 1 for the 150 Caucasian and the 27 PAO with CD4 count available at baseline and 48 months after the beginning of HAART.
- Immunological success (IS) was present in 142 of the 220 Caucasian patients (64.5%) versus 29 of the 60 patients of African origin (48.3%) (p=0.02).

Table 1: Characteristics of Caucasians and PAO. *Fischer's exact test

	PAO n=60 (100%)	Caucasian n=220 (100%)	Missing Data	p
Mean Age (years)	40.1	50.3	0	**<0.0001**
Male sex (n=)	15 (25.0%)	174 (79.1%)	0	**<0.0001**
Sexual transmission (n=)	54 (90.0%)	192 (87.2%)	15	0.14*
Chronic B or C viral hepatitis (n=)	10 (16.6%)	32 (14.5%)	0	0.68
Median number of years since HIV-1 seropositivity (years) [min-max]	7 [2-20]	14 [2-28]	0	**<0.0001**
Age >50 years at the beginning of HAART (n=)	3 (5.0%)	61 (27.7%)	0	**<0.0002**
Patients with HIV-1 viral load > 5 log^{10} (copies/ml) at the beginning of HAART (n=)	12 (20.0%)	53 (24.1%)	9	0.73
Median baseline CD4 (cells/mm3) [min-max]	219 [3-415]	204 [1-479]	9	0.72
CDC Classification category B or C (n=)	18 (30.0%)	103 (46.9%)	0	**0.02**
HIV-1 subtype non B (n=)	32 (53.3%)	6 (2.7%)	89	**<0.0001**

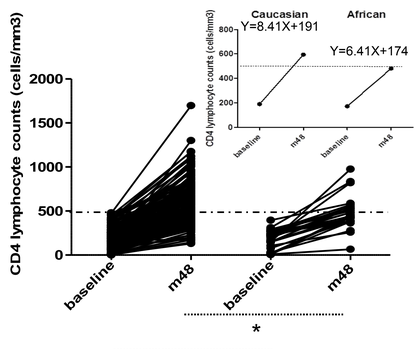

Figure 1: CD4 counts evolution at baseline and 48 months (m48) after the beginning of HAART) in HIV-1 positive Caucasian and PAO.

* Median CD4 count values at 48 months were 574 [131-1698] versus 449 [65-975] cells/mm3 in Caucasian and PAO respectively (p=0.02).

** Median CD4 count values at baseline were 188 [1-479] and 195 [4-396] cells/mm3 in Caucasian patients and in PAO respectively (p=0.63).

Upper-right corner: Mean CD4 counts evolution at baseline and 48 months after the beginning of HAART in Caucasian patients and PAO (p=0.09).

- The variables significantly associated with the absence of immunological success were depicted in table 2.

Table 2 : Variables significantly associated with the absence of immunological success. MD: Missing data, P*: p univariate analysis, OR: Odds ratio, 95% CI: 95% Confidence Interval, P: p multivariate analysis. Hosmer and Lemeshow goodness of fit gives p=0.163**

					Multivariate analysis		
	No IS n=109 (100%)	IS n=171 (100%)	MD	P*	OR	95% CI	P**
African origin (n=)	**31 (28.4%)**	**29 (16.9%)**	**0**	**0.02**	**2.22**	**[1.097-4.504]**	**0.02**
Male sex (n=)	77 (70.6%)	112 (65.5%)	0	0.37			
Sexual transmission (n=)	96 (88.1%)	150 (87.7%)	15	0.27			
Chronic B or C viral hepatitis (n=)	15 (13.8%)	27 (15.8%)	0	0.64			
Median number of years since HIV-1 seropositivity (years) [min-max]	**10 [2-26]**	**12 [2-28]**	**0**	**0.04**	**0.96**	**[0.922-1.007]**	**0.09**
Age >50 years at the beginning of HAART (n=)	29 (26.6%)	35 (20.5%)	0	0.23			
Patients with HIV-1 viral load > 5 log^{10} (copies/ml) at the beginning of HAART (n=)	29 (26.6%)	36 (21.0%)	9	0.33			
Median baseline CD4 (cells/mm3) [min-max]	**144 [1-338]**	**248 [1-479]**	**9**	**<0.0001**	**0.99**	**[0.988-0.994]**	**<0.0001**
CDC Classification category B or C (n=)	**54 (49.5%)**	**67 (39.2%)**	**0**	**0.09**	**0.78**	**[0.408-1.485]**	**0.44**
HIV-1 subtype non B (n=)	20 (18.3%)	18 (10.5%)	89	0.21			

Conclusions and references

•Our findings suggested that African ethnicity influences significantly rates of CD4 cell count recovery at 48 months after the initiation of HAART and therefore immunological success.

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