Poster Number 576

Immunologic response in treatment-naïve HIV-2-infected patients: the IeDEA West Africa cohort

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and the International epidemiological Database to Evaluate AIDS (IeDEA) West Africa Collaboration

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Background

Owing to its low prevalence and its geographical restriction to West Africa, response to antiretroviral therapy (ART) in HIV-2 infection is still poorly understood. Limited data are available on the response to the different first-line regimens used in HIV-2 patients.

The World Health Organization (WHO) recommends since 2013 treating patients living with HIV-2 in limited-resources countries with an ART regimen containing three nucleoside reverse transcriptase inhibitors (NRTIs) or a ritonavir-boosted protease inhibitor (PI) plus two NRTIs. However, this recommendation is based on weak evidence according to WHO grading criteria (Ekouevi, BMC InfectDis 2014).

Objective

We aimed at investigating the immunologic response of the two different recommended first-line ART regimens among HIV-2-infected patients in the West Africa region.

Methods

Description of the cohort

A network of adult and pediatric HIV clinics has been organized since 2006 in West Africa as part of the global IeDEA Collaboration (figure 1). Within this collaboration, the IeDEA West Africa HIV-2 cohort was established in order to better understand the epidemiology, care patterns and treatment of HIV-2 infection. This cohort includes HIV-2 and dually HIV-1 and HIV-2-infected patients.

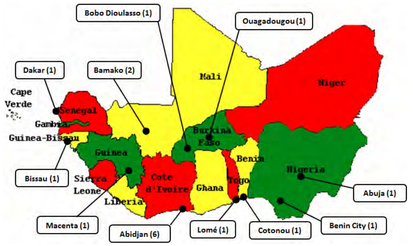

Figure 1. The International epidemiologic Databases to Evaluate AIDS (IeDEA) West Africa Collaboration: geographical repartition of the adults cohorts in 2014

Inclusion criteria
- HIV-2-infected patients confirmed by rapid HIV tests
- Patients aged >17 years at ART initiation
- treated with 3 NRTIs or a PI-based regimen
- Documented CD4 count at ART initiation
- Patients with unknown gender were excluded

Statistical analysis
- CD4 count trajectories over the first 24 months of ART were modeled using linear mixed models (LMM)
- Baseline being defined as the date of ART initiation
- We modelled the CD4 count changes over time using fractional polynomials of one and two degrees
- Random effects on the different fractional polynomial terms accounted for the correlation of repeated measurements within each subject
- CD4 count changes were adjusted for baseline CD4 count, initial ART regimen and gender
- Sensitivity analyses:
  - ➢ To address possible informative dropout: analysis restricted to patients remaining in care
  - ➢ To take into account original treatment group modification: right-censure at the date of the treatment modification
  - ➢ Analysis restricted to patients exclusively treated with recommended ART combinations

Results

Table 1. Baseline characteristics of the HIV-2-infected patients on antiretroviral therapy (n=422)

	Initial ART regimen			
	PI*-based	***3 NRTIs*****	***PI vs NRTI***	***Total***
	N=389	***N=33***	***p-value[¥]***	***N=422***
Female (%)	55.5	42.4	0.148	54.5
Age (in years) median (IQR[†])	45.3 (38.2;51.8)	46.1 (40.7;51.9)	0.498	45.3 (38.3;51.8)
Baseline clinical stage (%)			0.167	
WHO I/II or CDC A	19.5	12.1		19.0
WHO III or CDC B	49.1	39.4		48.3
WHO IV or AIDS	17.0	21.2		17.3
missing	14.4	27.3		15.4
Baseline hemoglobin (g/dl) median (IQR)	11.2 (9.8-12.4)	11.5 (10.2-12.3)	0.378	11.2 (9.8-12.4)
Baseline CD4 count (cells/µl) median (IQR)	164 (76-250)	192 (114-308)	0.072	166 (79-251)
Baseline CD4 count (%)			0.307	
0-49	15.9	3.0		14.9
50-99	16.7	15.2		16.6)
100-199	28.3	33.3		28.7)
200-349	27.2	30.3		27.5
>349	11.8	18.2		12.3
Year of ART initiation (%)			<0.001	
<2004	5.9	27.3		7.6
2004-2005	18.3	9.1		17.5
2006-2007	24.4	-		22.5
2008-2009	27.5)	33.3		28.0
2010-2012	23.9	30.3		24.4
Follow-up duration (months) median (IQR)	22.8 (5.1-46.4)	12.9 (0-38.9)	0.337	22.5 (4.3-45.6)
Deceased (%)[‡]	4.1	3.0	1.000[£]	4.0
Lost to follow-up (%)[‡]	33.2	33.3	0.984	33.2

[†] Inter-quartile range; * Protease inhibitor; ** Nucleoside reverse-transcriptase inhibitor;
[‡] during the first 24 months after ART initiation; [¥] Chi square test for qualitative variables and Kruskal-Wallis test for quantitative variables; [£] Fisher's exact test

Table 2. Mean CD4 count changes at M6, M12 and M24 compared to the reference group (female treated by protease inhibitor) and estimated with multivariable linear mixed model (n=422; 1,341 observations)

Variables	Mean CD4 change difference (cells/µl) at M6 (95% CI*)	Mean CD4 change difference (cells/µl) at M12 (95% CI)	Mean CD4 change difference (cells/µl) at M24 (95% CI)	p-value
Baseline CD4 count (cells/µl)				0.0469
<50	Reference	Reference	Reference	
50-99	-19 (-70; +32)	-43 (-100; +13)	-94 (-177; -12)	
100-199	-12 (-57; +33)	-30 (-81; +21)	-66 (-139; +7)	
200-349	-28 (-74; +18)	-50 (-102; +1)	-93 (-167; -19)	
≥350	-61 (-115; -6)	-101 (-163; -39)	-173 (-264; -81)	
Gender				0.0158
Female	Reference	Reference	Reference	
Male	-22 (-49; +5)	-37 (-68; -6)	-65 (-109; -21)	
First ART[†] regimen				0.0608
PI**-based	Reference	Reference	Reference	
NRTI[‡]-based	-53 (-105; -1)	-43 (-102; +17)	+4 (-81; +89)	

* 95% confidence interval; [†] antiretroviral treatment; ** protease inhibitor; [‡] nucleoside reverse-transcriptase inhibitors

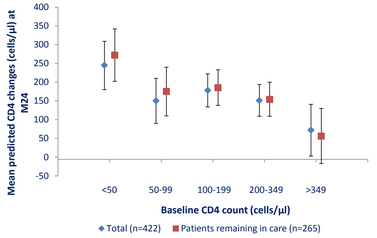

Figure 2. Adjusted mean CD4 count change at M24 with 95% confidence interval, by baseline CD4 count and for the reference group (female treated by protease inhibitor) estimated for patients remaining in care (n=265) and for all patients (n=422)

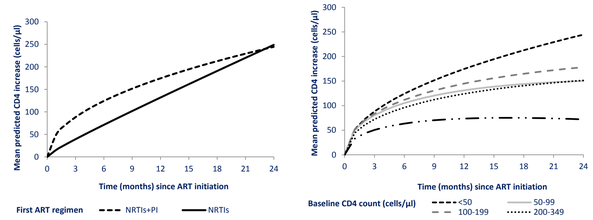

Figure 3a-3b. Mean predicted and adjusted CD4 count change after antiretroviral treatment initiation according to antiretroviral treatment (3a-left panel) and by baseline CD4 count (3b-right panel)

Immunologic response to ART

A higher CD4 count change was associated with (Table 2):
- Low baseline CD4 count (<100 cells/µL)
- Gender (female)

Compared to patients treated with NRTIs, patients treated with PI had a higher CD4 count recovery at month 6, **but no difference found at month 12 and month 24**.

No association between CD4 response and: age, baseline hemoglobinemia, initial clinical stage.

Similar results found with patients remaining in care (Figure 2).

Conclusion

- ➢ We found CD4 count response to be higher for patients treated with PI-based regimens than three NRTIs regimens 6 months after ART initiation, differences in CD4 response was diminished at month 12; CD4 count response at month-24 did not differ by treatment group
- ➢ There is a need to compare directly the efficacy of three NRTI combinations with PI-based first-line ART within a randomized clinical trial design. A clinical trial, named First-Line Treatment for HIV-2 (FIT-2), (NCT02150993); funded by the "Agence Nationale de Recherches sur le Sida et les hépatites virales" (ANRS) will start in mid June 2015 in five countries in West Africa and will try to answer the question "what to start" in HIV-2 infected patients, that is a critical issue as the choice of second-line ART regimens is still limited for HIV-2 infected patients in West Africa

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