ANRS 12168 - DynaM-O study, comparing the immuno-virological and clinical responses to HAART between HIV-1 group O and group M-infected patients : results at 96 weeks

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BACKGROUND

The divergent HIV-1 group O strains (HIV-1/O) are endemic in Cameroon and naturally resistant to NNRTI, largely used as first-line therapy in this country. Alternative therapeutic strategies are thus needed.

OBJECTIVES

DynaM-O is a prospective open-label study.

The main objective is to compare the immuno-virological response to HAART, including two NRTI and one PI in HIV-1/O and HIV-1 group M (HIV-1/M) infected-naïve patients.

Secondary objectives are to compare the kinetic of viral load responses, the CD4 restoration and the clinical events.

PATIENTS AND METHODS

PATIENTS

All consecutive HIV-1/O naïve patients with treatment initiation criteria were recruited from 2 hospitals Yaoundé and the Center Pasteur of Yaoundé (CPC), and included and followed up between June 2010 and July 2013. HIV-1/O patients were matched with HIV-1/M with a ratio of 1:2 on the basis of sex, age 18-40 and > 40 years, CD4 before initiation >350/mm^3 - [350-100]/mm^3 - <100/mm^3, Hb level <8g/l or >8g/l, and HBV status.

HAART Treatment : HIV-1/M and HIV-1/O initiated the same treatment: AZT+3TC+LPV/r, or TDF+3TC+LPV/r for patients with anemia or HBV co-infection.

METHODS

- Primary end point: percentage of patients with an undetectable viral load (VL < 60 cp/mL) at W48.

- Statistical analysis

Primary endpoint analysis: Comparison of proportion of patients with undetectable VL according to the HIV-1 group at W96 with analyses on Intention to Treat Analysis/ITT (Death and Missing=Failure) and Per Protocol/PP. Secondary endpoint analysis : Proportion of patients with a gain of more than 50% of CD4 at W12 and W48 according to the HIV-1 group

RESULTS

47 Cameroonian patients HIV-1/O and 94 HIV-1/M were included; results were available for 128 patients (13 died or were lost-to follow-up; Fig.1).

At baseline, VL was significantly lower (p< 0.0001) in HIV-1/O with a median at 4.3 log cp/mL vs 5.1 log cp/mL in HIV-1/M.

Median CD4 counts were well balanced between the two groups (227 vs 215, in HIV-1/O and HIV-1/M respectively, p=0.68)

At W96, 94.7 % [88.8 – 100] of HIV-1/O samples were < 60 cp/mL vs 84.1 % [77.5% - 90.8%] of HIV-1/M in per protocol analysis (p=0.14); and no difference was observed at the threshold of 200 cp/mL (97% in both groups; Fig.2).

Between treatment initiation and W96, CD4 cells count increase is significantly higher (p=0,04) in the HIV-1/M group than in the HIV-1/O group (+2.0 CD4 per month for the HIV-1/M, compare to HIV-1/O; Fig. 3).
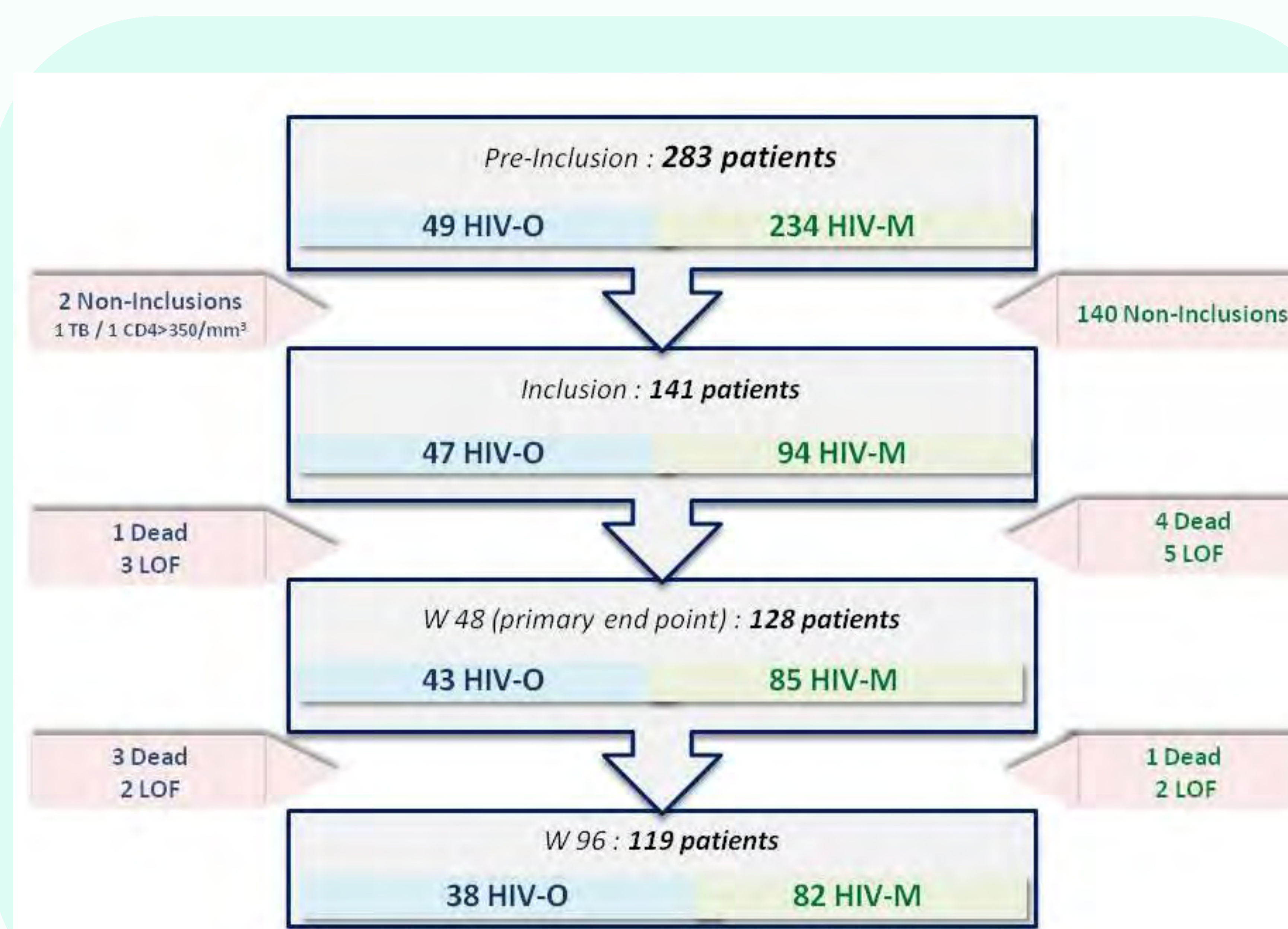

Fig.1 Flow Chart

	Percent of patients with undetectable VL at W96 [95% CI]	P-value adjusted*
Per Protocol		
HIV-1/O (n=38)	94.7% [88.8 – 100%]	0,14
HIV-1/M (n=81)	84.1% [77.5 – 90.8%]	
Intention To Treat		
HIV-1/O (n=47)	76.6% [64.4% – 88.7%]	0,79
HIV-1/M (n=94)	73.4% [64.4% – 82.3%]	

Fig.2 Comparison of patients with undetectable VL depending on the type of analysis and according to the HIV-1 group at W96

*Adjusted on sex, age class (18-40 years or >40 years), CD4 level(<100/ mm^3 , 100-350/mm^3 or >350/mm^3) and Hblevel (≤8 g/l or >8 g/l)
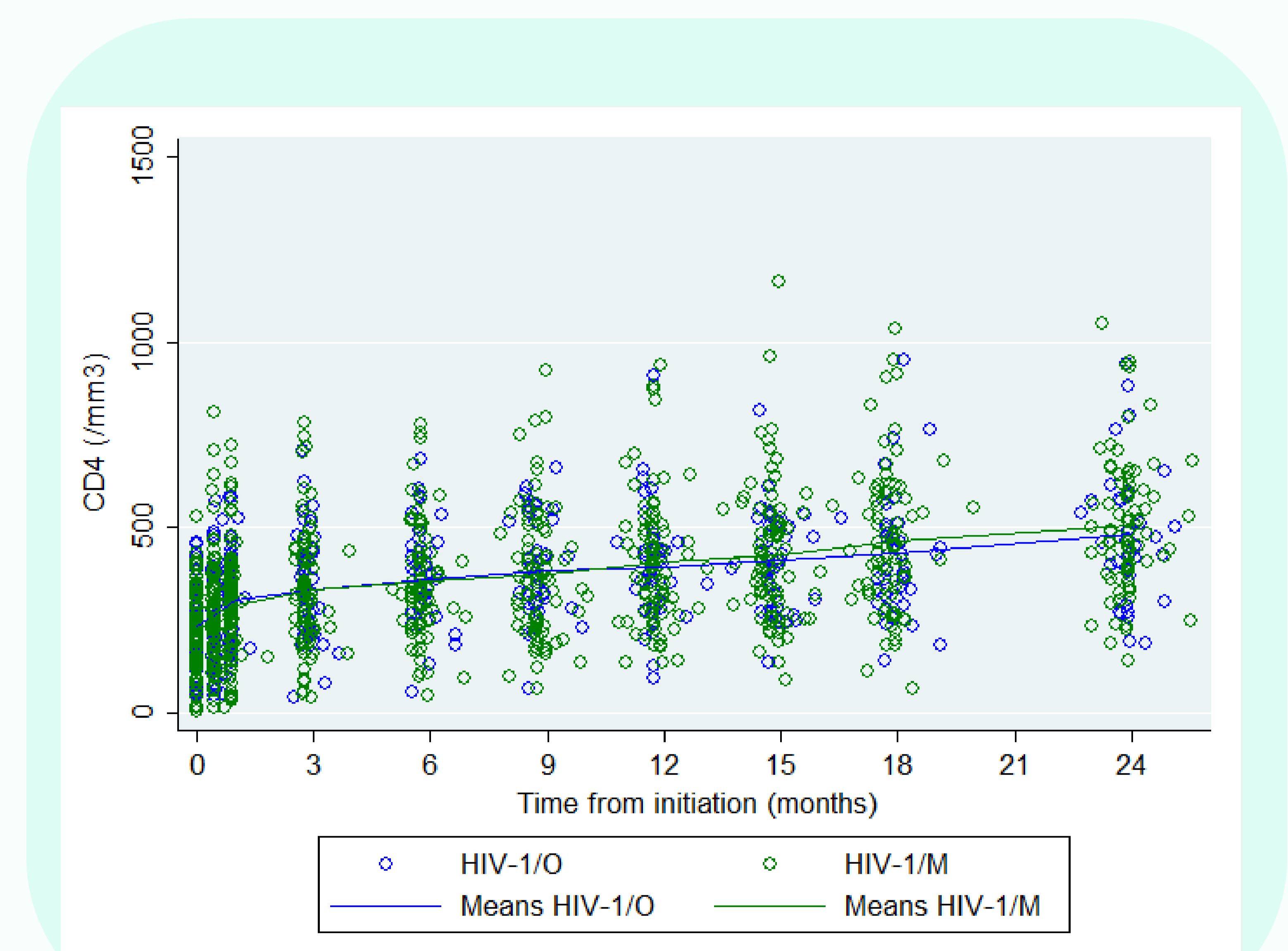

Fig.3 CD4 evolution from inclusion to W96

CONCLUSION

DynaM-O is the unique study analyzing the HAART responses in HIV-1/O infected patients compared to HIV-1/M patients. Data at W96 showed good efficacy of the regimens in both groups, but with a higher rate of achievement of the virological response in HIV-1/O infected patients. In contrast, the CD4 restoration was lower in HIV-1/O than that observed for HIV-1/M patients. These data indicate that group O infected patients should be successfully treated by treatment excluding NNRTI. Moreover, studying the mechanisms underlying these differences in response to HAART between these highly divergent HIV-1 strains are of importance in our understanding of the HIV natural history.

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