

Effect of a CCR5 antagonist in immune activation in highly suppressed HIV-1 infected patients

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Background

Low level viremia (0-50 copies/mL) can be detected with more sensitive methods in HIV-1-infected patients with suppressive antiretroviral therapy (ART) for prolonged periods of time. This low viral replication could modulate the immune activation of these patients. Reduced cell activation after intensification could reflect decreased residual viral replication in the reservoirs.

In this study we have evaluated the effect of a CCR5 antagonist (Maraviroc, MVC) over the cellular activation on CD4 and CD8 cells in HIV-1-infected patients with suppressive antiretroviral treatment in the context of an intensification clinical trial. We have evaluated these variables after 12 and 24 weeks of MVC intensification.

Material and Methods

Nine patients who had been under suppressive treatment with viral load <50 copies/mL and CD4 cell count above 350 cells/mm³ during at least two years and demonstrated CCR5 tropism were included. We analyzed the immune activation at baseline and after 12 and 24 weeks with MVC. The proportion of activated CD4 cells (CD3+CD4+CD38+HLA-DR+) and activated CD8 cells (CD3+CD8+CD38+HLA-DR+) was measured. Absolute CD4 cells and naïve CD4 cells (CD45RA+CD62L+) were also measured.

Results

The characteristics of the patients are shown in table 1. The patients had received ART for a median of 72 months. Absolute CD4 cell count was not statistically different at baseline compared to that after 12 or 24 weeks of intensification (Fig. 1). The level of naïve CD4 cells was similar during the follow up, with no statistic significance (Fig. 1).

Table 1: Baseline characteristics of the patients.

Patient	Gender	Age	CD4 count (cells/mm ³)	CD8 count (cells/mm ³)	HIV Viral Load (copies/mL)	ART	Duration of ART (months)
1	M	49	1169	683	<50	ddl+3TC+NVP	124
2	M	47	486	673	<50	FTC+TDF+ATV/r	75
3	M	46	796	650	<50	3TC+ABC+ATV	78
4	F	46	787	1109	<50	FTC+TDF+LPV/r	57
5	M	45	534	784	<50	AZT+3TC+ABC	142
6	M	58	728	639	<50	AZT+3TC+ABC	144
7	M	32	694	1608	<50	FTC+TDF+ATV/r	50
8	M	30	1241	1414	<50	FTC+TDF+LPV/r	42
9	M	30	589	1064	<50	FTC+TDF+EFV	38
Median [IQR]		46 [31-48]	711 [547-793]	784 [673-1109]	<50		75 [38-144]

Acknowledgements

We would like to thank C. Page, A. Moreno, M.J. Pérez-Eliás and all the patients who participated in this study. We also want to thank our sponsors RIS, ISCIII and FEDER.

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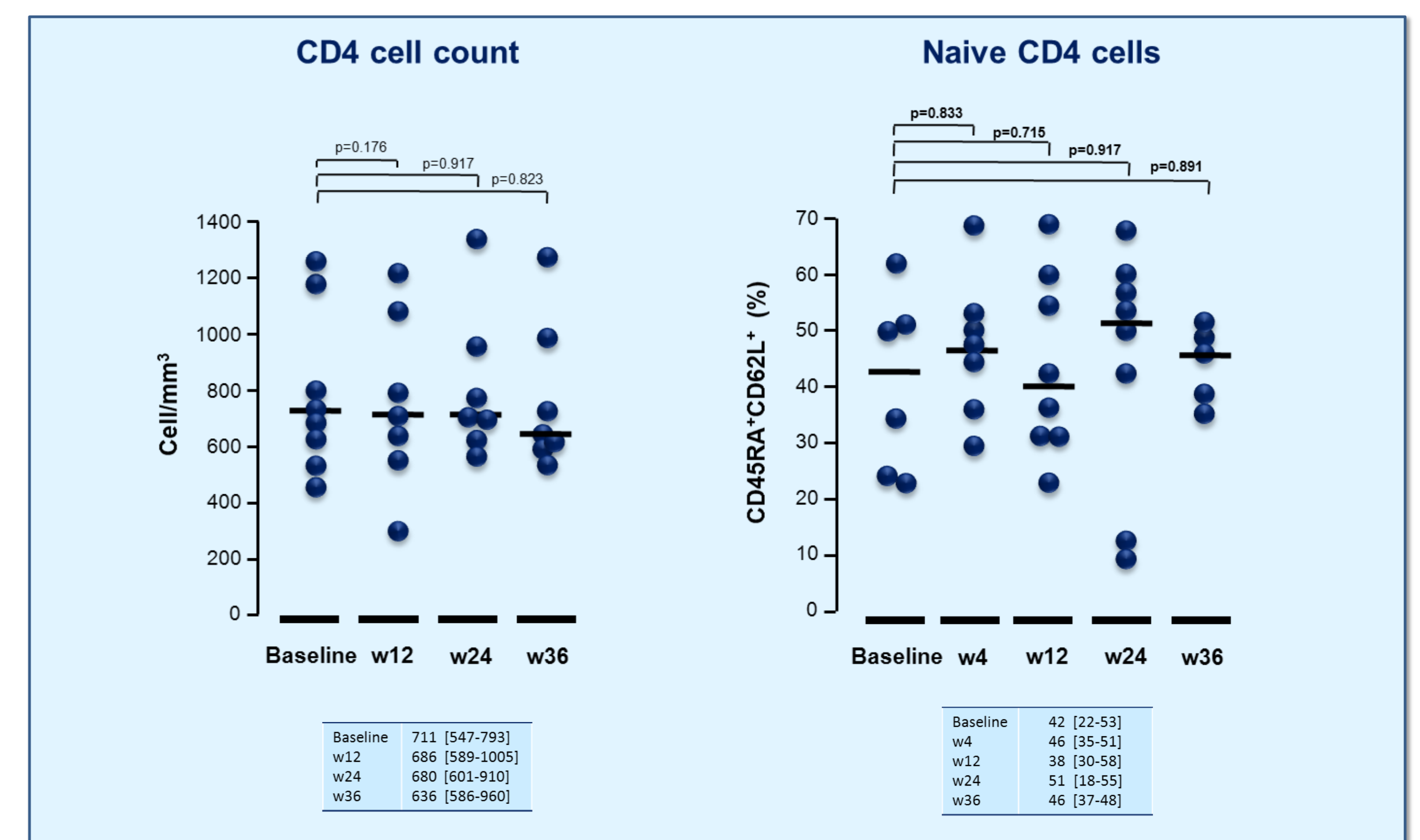


Figure 1: Level of absolute CD4 cell count and proportion of naïve CD4 cells of the studied patients during the intensification treatment with MVC.

A significant decrease in the proportion of activated CD4 cells was observed after 12 weeks of intensification (median 3.2% at baseline vs. 0.8% after intensification, $p=0.03$) (Fig. 2). After 24 weeks of intensification a trend to increase the level of activated CD4 cells was observed, although the level at week 36 is statistically lower compared to baseline. On the other hand, a lower level in activated CD8 cells was observed at week 12 after intensification (median 5.4% at baseline vs 2.3% and 3.3% after 12 or 24 weeks of intensification, $p=0.07$ and $p=0.19$, respectively), while no difference was observed at weeks 24 and 36 (Fig. 2).

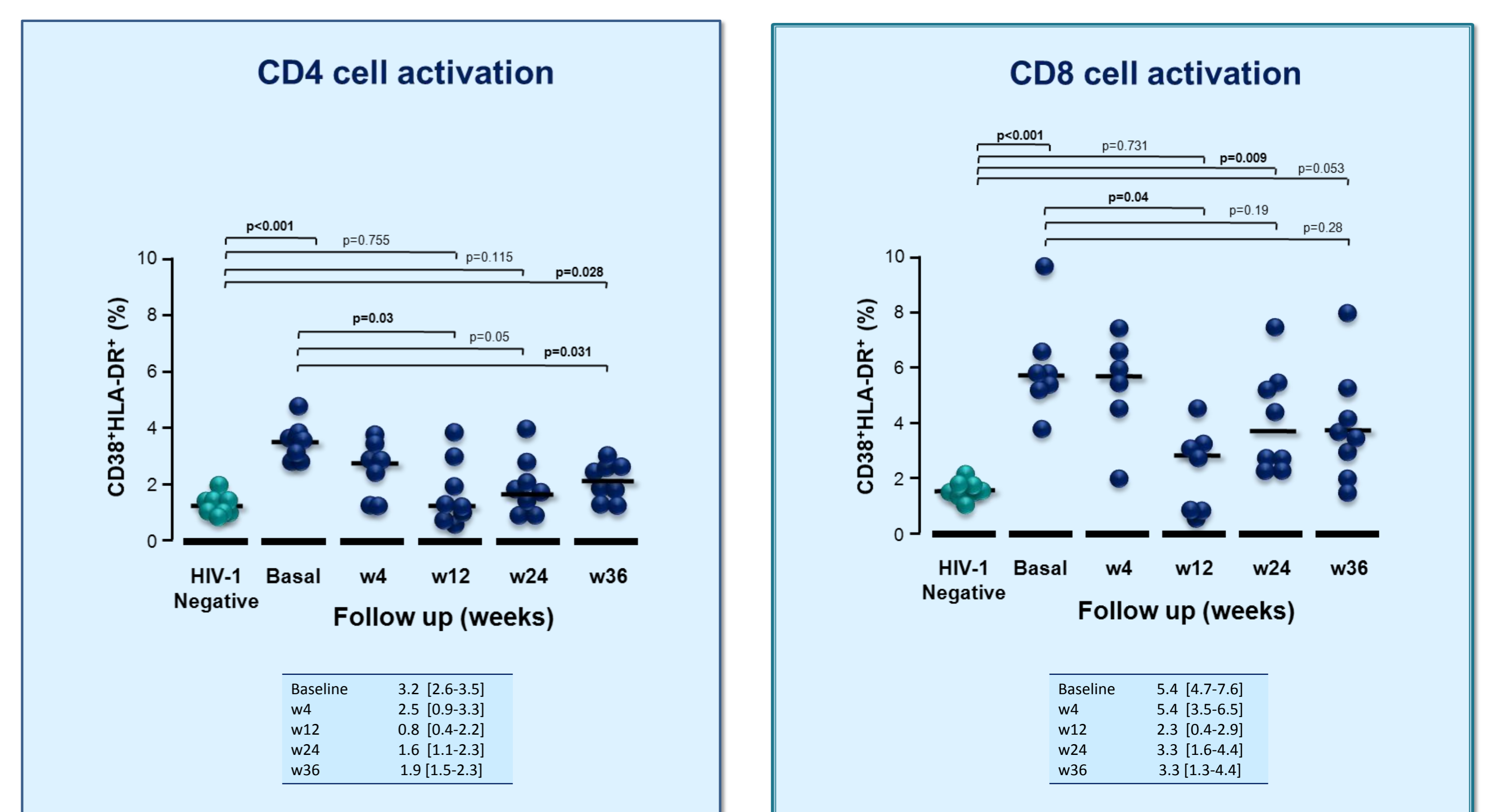


Figure 2: Immune activation after 36 weeks of intensification with MVC

Conclusions

Treatment intensification with MVC in chronically HIV-1-infected patients with undetectable VL for a prolonged period of time reduces the proportion of CD4 cell activation after 36 weeks. On the other hand, neither CD4 count nor naïve CD4 count were different after intensification. There is only a transient reduction in the activated CD8 cells at week 12. This reduction in the immune activation could reflect a reduction in the residual viral load or a modulation of the immune activation driven by MVC that can involve other mechanisms that should be further studied.