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Is CAB/RPV-LA able to modulate residual immune activation in people living with HIV? A pilot single-arm longitudinal study

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Introduction

Cabotegravir/rilpivirine (CAB/RPV) long-acting (LA) has revolutionized the concept of ART, and immunological impact data are needed to understand whether this strategy with dual INI/NNRTI dual therapy can be less or more active in controlling residual immune activation in chronic aviremic PLWH.

Study Design

On blood samples from PLWH on long-acting injectable HIV antiretroviral a longitudinal immunophenotyping analysis of peripheral blood cells was performed.

Methods

On the blood samples obtained from PLWH before CAB/RPV-LA (T0), after 4 weeks (T1) and 28 weeks (T2), by flow cytometry, the percentages of CD4 and CD8, their subsets (CD27, CD45RO), their activation (CD38+HLA-DR+) and immunosenescent (CD28-CD57+) phenotypes were investigated.

Moreover, monocyte, macrophage and dendritic cells (HLA-DR, CD14, CD16, CD11c, CD123) were investigated too.

Finally, plasma monocyte/macrophage activation markers (sCD14, sCD163) were evaluated.

Results

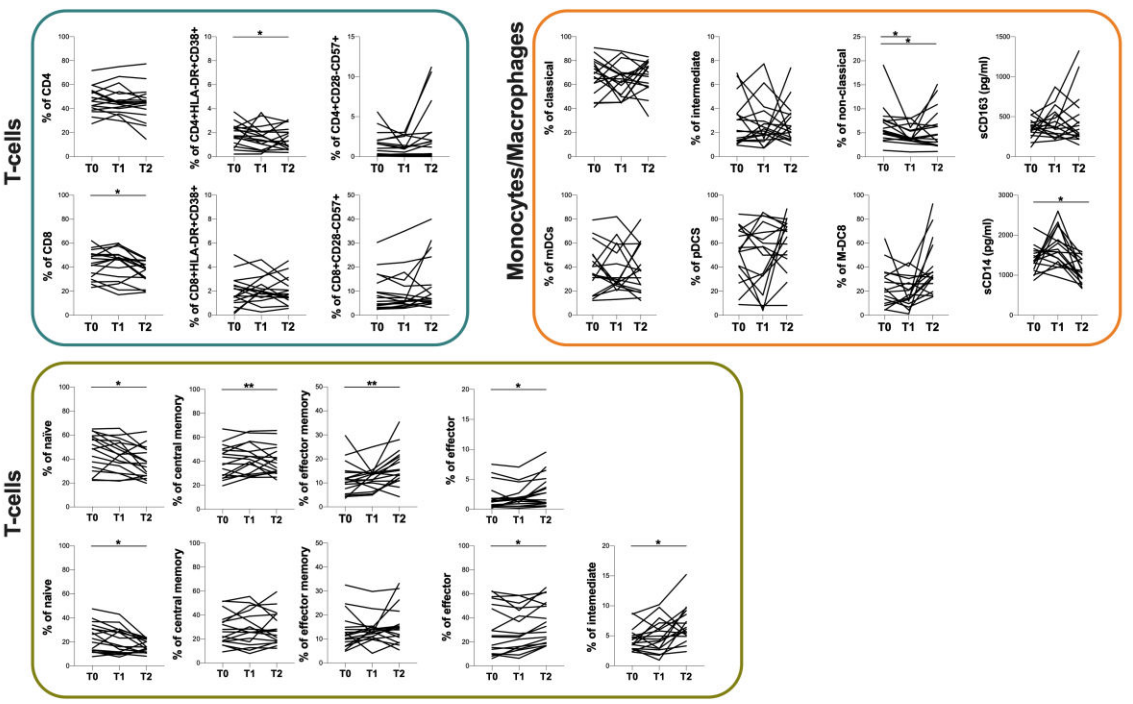
Seventeen aviremic PLWH switching to injectable CAB/RPV-LA were enrolled. At both T1 and T2, no virological failures were observed.

At T2, a significant reduction in the percentages of total CD8 compared to T0 were observed (38.7 [30.9-43.9] and 43.3 [31.0-51.0], respectively; p=0.0202) as well as significant reductions in the percentages of non-classical monocyte (4.6 [2.4-7.9] and 5.5 [4.3-7.7], respectively; p=0.0327) and in the plasma levels of sCD14 (1100 [857-1405] and 1355 [1135-1577], respectively; p=0.0202) were observed (Figure).

At T2 compared to T0, a significant decrease in the percentages of naïve CD4 (36 [26-48] and 49 [32-59], respectively; p=0.0202) and CD8 (16 [11-22] and 23 [12-33], respectively; p=0.0121) as well as a significant increase in the percentages of effector CD4 (2.7 [1.1-4.9] and 1.4 [0.6-2.5], respectively; p=0.0327) and CD8 were observed (32.9 [19.0-51.9] and 25.1 [12.0-53.9], respectively; p=0.0202) (Figure).

A significant increase in the percentages of effector memory CD4 was observed (15.2 [11.5-21.3] and 11.3 [6.5-14.7], respectively; p=0.0022) as well as in the percentages of intermediate CD8 (6.1 [5.0-8-9 and 3.8 [2.8-5.3], respectively; p=0.0202) (Figure).

At T2 compared to T0, no significant differences in the percentages of HLA-DR+CD38+ T-lymphocyte were observed neither in the percentages of CD28-CD57+ T-lymphocyte. No differences in the percentages of central memory T-lymphocyte were observed neither in the percentages of effector memory CD8. Similarly, no differences in the percentages of classical monocytes, intermediate monocytes, M-DC8, pDCs, mDCs and in the plasma levels of sCD163 were observed (Figure).



Conclusion

Although our study presents several limitations especially due to the small sample size and absence of a control group, our preliminary results show that CAB/RPV-LA reduces some features of residual immune activation and modulate the effector compartment of T-lymphocyte. We can only speculate that the HIV reservoir was knocked down by a more stable ART with good tissue penetration, but a more careful analysis of viral load should be done in the study.