# Effect of Tenofovir on T-cell Maturational Subsets in Long Term Aviraemic HIV Adults

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## BACKGROUND

We have reported that HIV adults receiving antiretroviral therapy who maintain virological suppression for 10 years experience blood telomere length gains (1). However, telomere length increases were lower in participants treated with tenofovir than in those treated with tenofovir-sparing regimens. It remains unknown if this difference is due to an interference with the immune reconstitution process that shifts T-lymphocyte subpopulations towards less mature T-cell lymphocytes with longer telomere length.

## METHODS

This is a longitudinal study of 108 HIV-infected adults enrolled in a previously described prospective cohort at La Paz University Hospital (Madrid, Spain) HIV unit (1).

Participants enrolled in this cohort had maintained plasma viral loads <50 HIV RNA copies/mL, under antiretroviral treatment, for at least 7 years prior to entering the study. Of these 108 participants, 41 had continuously received tenofovir for at least 6 years (tenofovir difumarate n=15 and tenofovir alafenamide n=26) and 67 had never received a drug regimen that included tenofovir (abacavir n=49 and N(t)RTI-sparing regimens n=18)

We tested by flow cytometry at year 4 and at year 6 of follow-up CD4 and CD8 T-cell maturational subsets from fresh PBMCs: Recent Thymic Emigrants (RTE) ($CD31^+CD45RA^+CD27^+$), naïve ($CD45RA^+CD27^+$), central memory ($CD45RA^-CD27^+$), effector memory ($CD45RA^-CD27^-$), TEMRA ($CD45RA^+CD27^-$), senescent ($CD28^{--}CD57^+$) and exhausted ($PD1^+$) (**Figure 1**).

## RESULTS

At baseline, male: 77.1%, median age (y): 52.8 (IQR 49.1-57.1) Caucasian: 92.7%, years since HIV diagnosis: 21.1 (IQR 16.4-25.5), time with virological suppression (y) 11.4 (IQR 10.7-11.8), CD4 T-cell nadir (cells/μL): 183 (IQR 105-273). and CD4 and CD8 counts (cells/μL): 774 (IQR 585-970) and 630 (IQR 448-823), respectively.

**Tenofovir treatment** was associated with **lower recovery** from **exhaustion** in **CD4** and **CD8 T-cells**

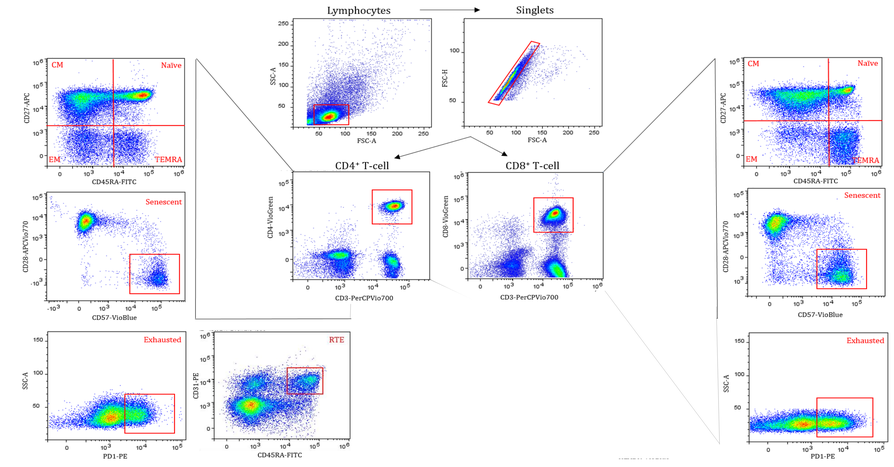



**Figure 1.** Gating strategies of flow cytometry

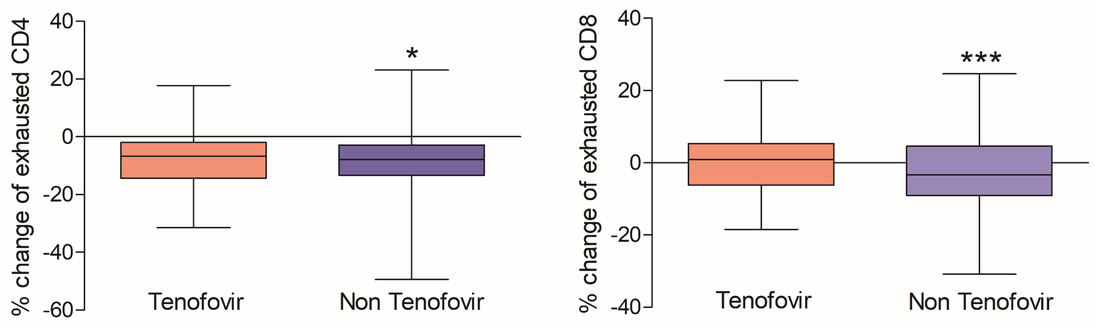



**Figure 2.** Box-and-whisker plot (min to max) of percentage of change of exhausted CD4 and CD8 T-cells after two years of follow-up. Significance levels: *p<0.05, ***p<0.001

Adjusting for sex, race, CD4 T-cell nadir, CMV serology, time of follow up and additionally by age, years since HIV diagnosis and percentage of the appropriate T-cell subset at baseline; participants treated with tenofovir had significantly lower decrease of exhausted CD4 T-cells (%) between year 4 and 6 of follow-up: -6.8 (IQR -13.4-2.1) than participants not receiving tenofovir: -7.9 (IQR -13.3--3), P = 0.04. Moreover, the percentage of exhausted CD8 T-cells remained similar in participants treated with tenofovir: 0.9 (IQR -5.2-5.0) and decreased in participants never exposed to tenofovir: -3.4 (IQR -8.8-4.6), P < 0.001 (**Figure 2**).

No differences were observed in the other T-cell maturational subsets between groups.

## CONCLUSIONS

In long-term aviraemic HIV adults, tenofovir treatment was associated with a lower longitudinal decrease in the percentage of exhaustion in CD4 T-cells and an blockage of the recovery in the percentage of exhausted CD8 T-cells.

Further studies are needed to elucidate the relevance and the mechanisms underlying this biological phenomenon.

## ADDITIONAL KEY INFORMATION

References: (1): Montejano R *et al*. J Infect Dis. 2018; 218(10):1531-1540.

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