Doubling dolutegravir dosage reduces HIV persistence markers in ART-treated adults

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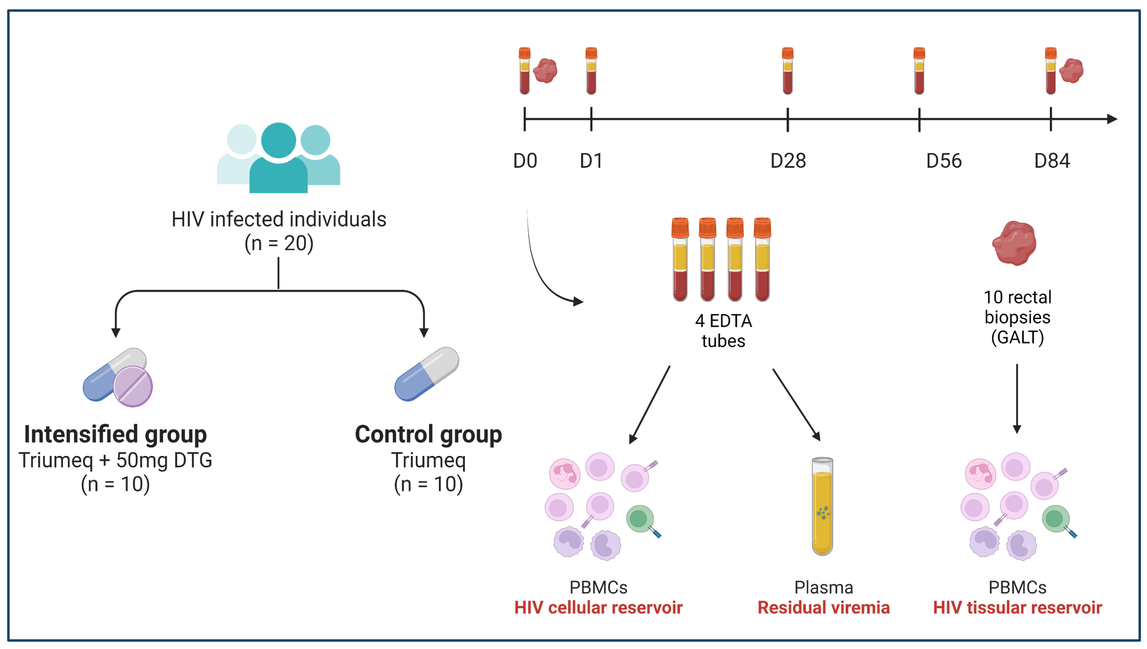
INTRODUCTION

Whether ongoing viral replication occurs in people living with HIV (PLWH) despite antiretroviral therapy (ART) and leads to low-level residual viremia is still debated. Here we report on a study, in which we intensified the ART regimen by **doubling dolutegravir (DTG) dosage**. We investigated the impact of this strategy **on HIV blood and tissue latent reservoirs**, **residual viremia**, **immune activation**, and **inflammation**.

MATERIALS AND METHODS



On these samples we performed:

- Total HIV DNA and CA US HIV RNA quantification
- Intact Proviral DNA Assay (IPDA)
- Ultrasensitive plasma viral load
- Flow cytometry (HLA-DR, CD38, PD-1, TIGIT, LAG-3)
- Inflammatory plasma biomarkers quantification
- DTG concentration measurement

RESULTS

1 Impact of treatment intensification on HIV latent reservoir and residual viremia

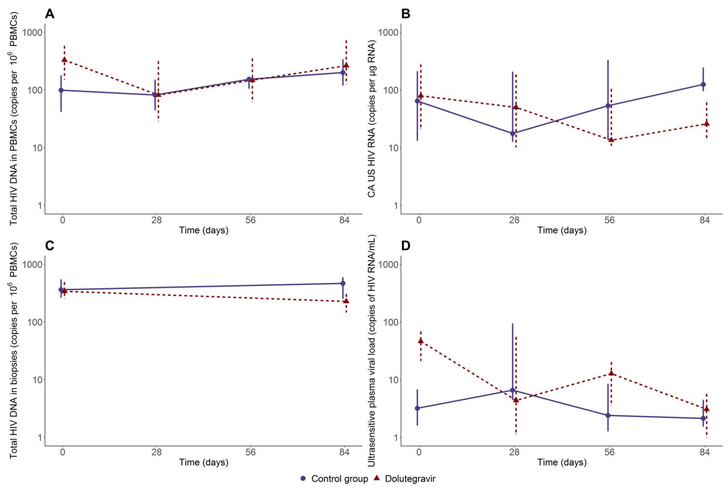


Figure 1: Cell-associated virological markers during ART intensification
Median (IQR) concentrations of total HIV DNA in PBMCs (A), cell-associated unspliced HIV RNA (B), total HIV DNA in rectal biopsies (C) and ultrasensitive plasma viral load (D).

→ No significant differences in total HIV DNA in PBMCs and in rectal biopsies between day 0 and day 84 in both groups.
→ Significant decrease in US HIV RNA in PBMCs (**p=0.020**) and in ultrasensitive plasma viral load (**p=0.016**) between day 0 and day 84 in the intensified group.

2 Impact of treatment intensification on immune activation and inflammation

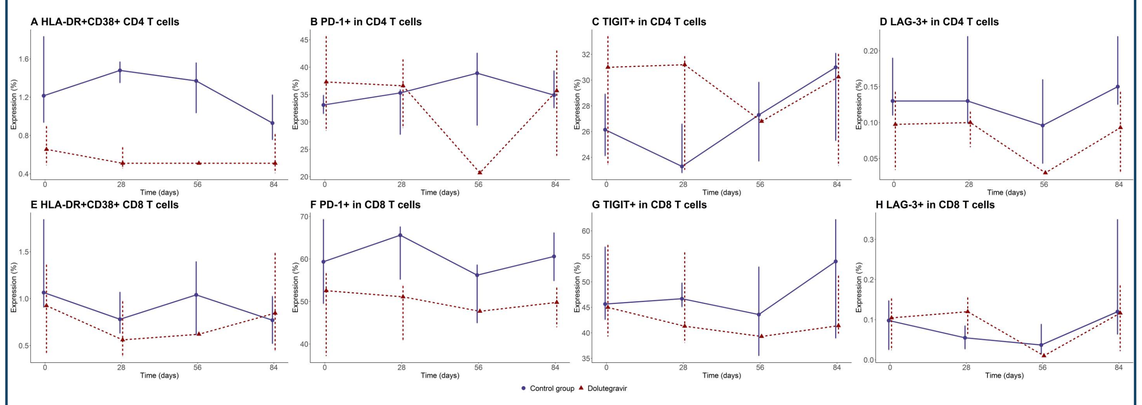


Figure 2: T-cell activation and exhaustion during ART intensification.
Percentage of CD4+ T cells expressing HLA-DR and CD38 (A), PD-1 (B), TIGIT (C), LAG-3 (D) measured by flow cytometry. Percentage of CD8+ T cells expressing HLA-DR and CD38 (E), PD-1 (F), TIGIT (G), LAG-3 (H) measured by flow cytometry.

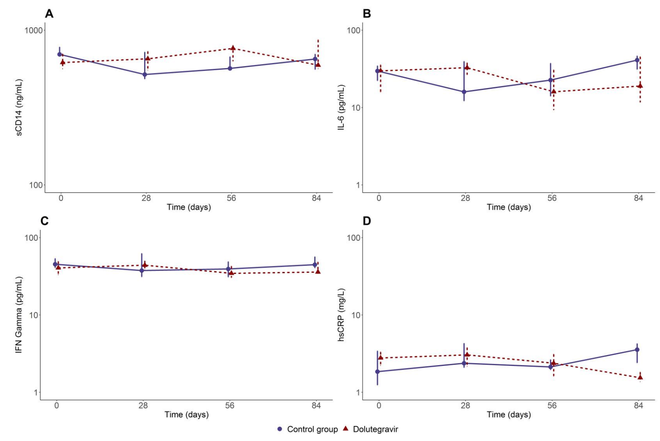


Figure 3: Biomarkers of inflammation during ART intensification.
Median (IQR) concentrations of sCD14 (A), IL-6 (B), IFN-γ (C) and hsCRP (D). sCD14=soluble CD14, IL-6=interleukin-6, IFN-γ=interferon-gamma, hsCRP=high sensitivity C-reactive protein.

→ No significant difference were observed between both groups in terms of immune activation and inflammation.

3 Correlations between the evolution of HIV persistence markers, immune activation and inflammation

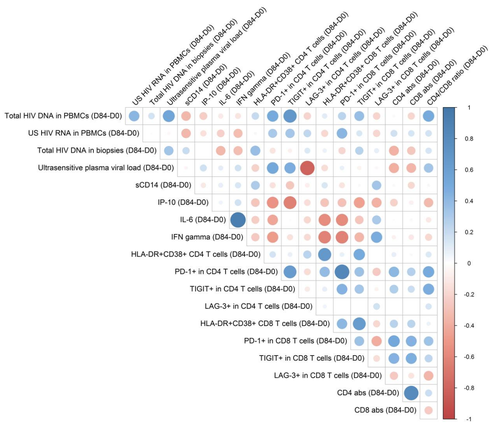


Figure 4: Spearman correlation between the evolution of HIV persistence markers, immune activation and inflammation during ART intensification.
Circle size reflects the magnitude of the correlation coefficient. Color represents the level of Spearman's correlations (blue means positive correlation and red means negative correlation).

CONCLUSION

We observed a decrease in US HIV RNA and ultrasensitive plasma viral load following DTG intensification, **suggesting ongoing viral replication in some participants**. However, it had no measurable impact on immune activation or inflammation. If confirmed in larger clinical trials, these results could have an **impact on the clinical management of PLWH**.

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