Impact of DTG+3TC as First-Line ART on HIV-1 Reservoir and Inflammatory Markers in Peripheral Blood

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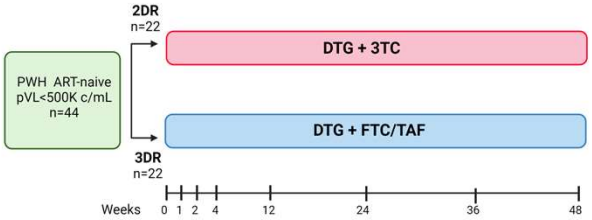
BACKGROUND

The objective of the DUALITY study was to compare the dynamic effect of DTG+3TC versus DTG+ emtricitabine/tenofovir alafenamide (FTC/TAF) in HIV-1 persistence, as well as in immune activation, exhaustion, and inflammatory biomarkers in people with HIV (PWH) starting first-line ART.

METHODS

- 48-week, single-centre, randomized, open-label clinical trial in ART-naïve PWH. Main exclusion criteria: plasma viral load (pVL) >500K copies/mL, positive HBsAg, eGFR <50 ml/min.
- Total and intact proviral (IPDA) HIV-1 DNA copies were measured in CD4+ T cells by ddPCR, HIV-1 ca-RNA was quantified by using RT-ddPCR. The frequency of infected CD4+ T cells able to produce p24 upon stimulation were measured by the viral protein spot (VIPSPOT) assay.
- Residual viremia (LLQ 0.5 c/ml) was measured by Abbott Real-Time HIV-1 assay (Abbott Molecular Inc.) after ultracentrifugation of 9 ml of plasma.
- Plasma levels of inflammatory markers were determined by ELISA.
- Activation (HLA-DR/CD38) and exhaustion (PD-1/TIGIT) markers were assessed in both CD4+ and CD8+ T cells by multiparametric flow cytometry.

Study design.



RESULTS

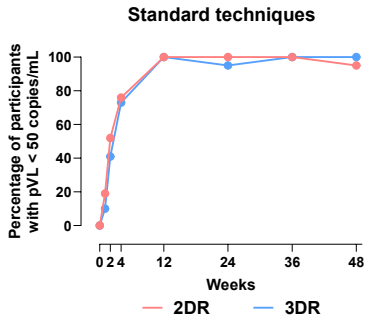
A total of 44 PWH were included in the study.

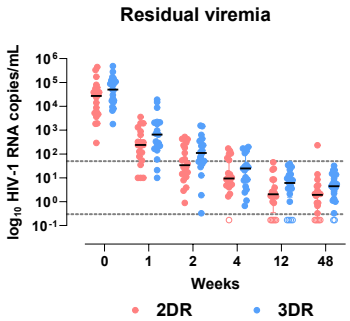
Baseline characteristics of study participants.

	2D group (n=22)	3D group (n=22)	Total (n=44)
Age, years	30.8 (27.7 - 35.2)	33.5 (27.5 - 35.3)	31.4 (27.3 - 35.4)
Male gender*	22 (100.0)	22 (100.0)	44 (100.0)
Ethnicity*			
Caucasian	14 (63.6)	12 (54.5)	26 (59.1)
Hispanic-latino	8 (36.4)	8 (36.4)	16 (36.4)
Other	0 (0.0)	2 (9.1)	2 (4.5)
Transmission group MSM*	19 (86.4)	20 (90.9)	39 (88.6)
pVL, copies/mL	34,907 (10,140 - 117,388)	22,536 (7,290 - 59,467)	30,519 (8,600 - 84,022)
pVL >5 log copies/mL*	7 (32)	3 (14)	10 (23)
CD4+ T cell count, cells/mm^3	497 (334 - 607)	443 (367 - 528)	455 (335 - 567)
CD4 <200 cells/mm^3*	0 (0.0)	2 (9.1)	2 (4.5)
CD4/CD8 ratio	0.5 (0.4 - 0.8)	0.5 (0.4 - 0.8)	0.5 (0.4 - 0.8)

Data are expressed as median and IQR unless when noticed. *n (%)

Dynamics of plasma viral load.

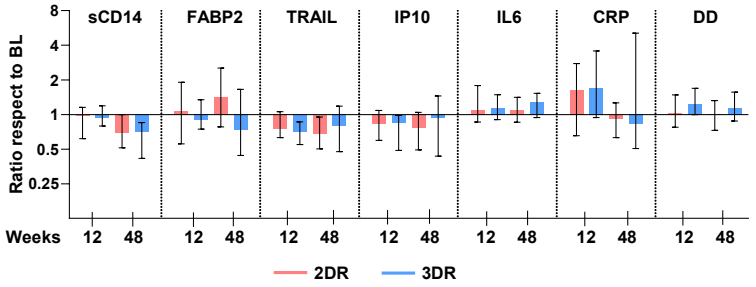




p>0.05 for all comparisons between groups

Changes in soluble inflammatory biomarkers.

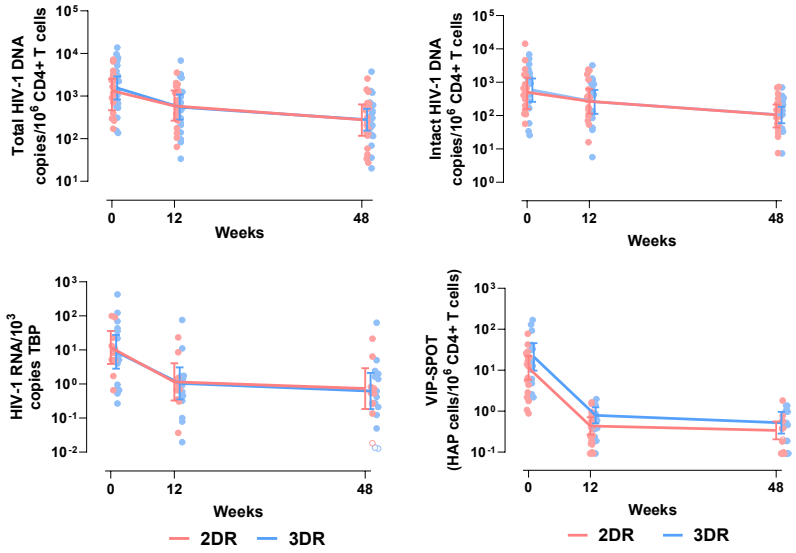
Median and IQR are presented.



p>0.05 for all comparisons between groups

Evolution of viral reservoir during the study.

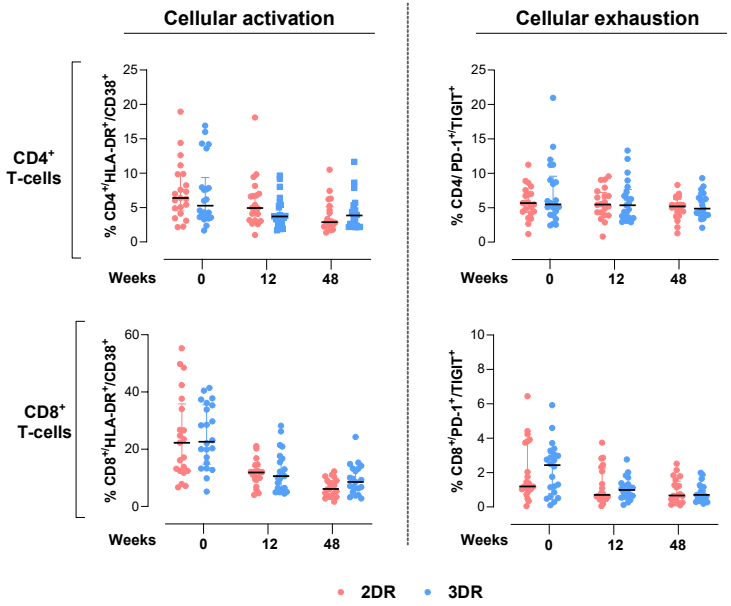
a) Total HIV-1 DNA, b) Intact HIV-1 DNA, c) ca-RNA, d) HIV-1 p24 producing cells (VIPSPOT).
Individual values are presented with their corresponding GM and 95%CI.



p>0.05 for all comparisons between groups

Evolution of immune activation and exhaustion markers.

Median and IQR are shown.



p>0.05 for all comparisons between groups

CONCLUSIONS: First-line 2DR with DTG+3TC resulted in a similar decay in HIV-1 persistence and in immune-associated markers compared to 3DR with DTG+FTC/TAF.

This study was funded by Viiv Healthcare and Lluita contra les Infeccions Foundation.