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STABLE TOTAL HIV-DNA AFTER 1 YEAR ON SWITCH TO TAF-BASED REGIMENS IN REAL WORLD DATA

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Introduction

TAF more efficiently delivers TFV to HIV-1 target cells resulting in lower plasma and kidney exposures. However, the impact of TDF-TAF switch on peripheral reservoir is poorly investigated.

Objective

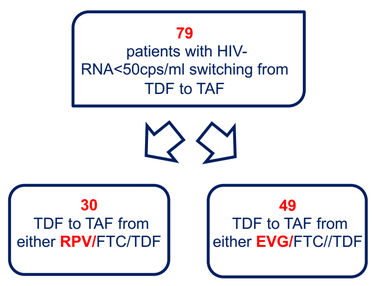
Here, we study the change of peripheral HIV-DNA over 1 year of therapy with TAF after a switch from either RPV/FTC/TDF or EVG/FTC/TDF in virologically suppressed patients.

Methods

This is a prospective study based on 79 patients with HIV-RNA <50 cps/ml switching from TDF to TAF from either RPV/FTC/TDF (n=30) or EVG/FTC/TDF (n=49) who remained with suppressed viral load for 12 months.

- Total HIV-DNA (LTR-5' ddPCR assay, normalized by cps/10^6CD4), CD4 (cell/mm^3), CD4/CD8, IL-6 and CRP (Luminex), CD38+HLA-DR+CD8+ (Flow Cytometry) were retrospectively tested on stored samples at baseline of switch (T0) and 12 months after (T12).
- Pearson correlation and multiple linear regression analyses were used to estimate biomarkers changes from T0 to T12 and the association with specific anchor drugs used.

Results



Patients' characteristics

Characteristics	Overall (N=79)	RPV (N=30)	EVG (N=49)	P-value*
Male, n (%)	62 (78.5)	25 (83.3)	37 (75.5)	0.574
Italians, n (%)	72 (91.1)	30 (100)	42 (85.7)	0.040
Age, years, median (IQR)	47 (40-55)	46 (38-54)	48 (41-56)	0.457
Year of first ARV, median (IGR)	2013 (2009-2015)	2013 (2010-2015)	2013 (2008-2015)	0.683
Exposure to TDF, years, median (IQR)	3.0 (2.0-6.0)	3.7 (2.0-5.7)	3.3 (2.4-5.8)	0.594
Risk factor, n (%):				
Homosexual	43 (54.4)	19 (63.3)	24 (49.0)	
Heterosexual	28 (35.4)	7 (23.3)	21 (42.9)	0.185
Other/unknown	8 (10.2)	4 (13.4)	4 (8.1)	
Coinfection, n (%):				
HBV (N=72)	1 (1.4)	1 (3.3)	0 (0.0)	0.380
HCV (N=75)	11 (14.7)	4 (13.3)	7 (14.3)	1.00

* Statistically significant differences were assessed by Mann-Whitney test and Fisher exact test, as appropriate.
EVG: elvitegravir; RPV: rilpivirine

By evaluating the viro-immunological parameters and inflammatory markers at T0 and T12, no significant differences were found between patients treated with RPV and patients treated with EVG.

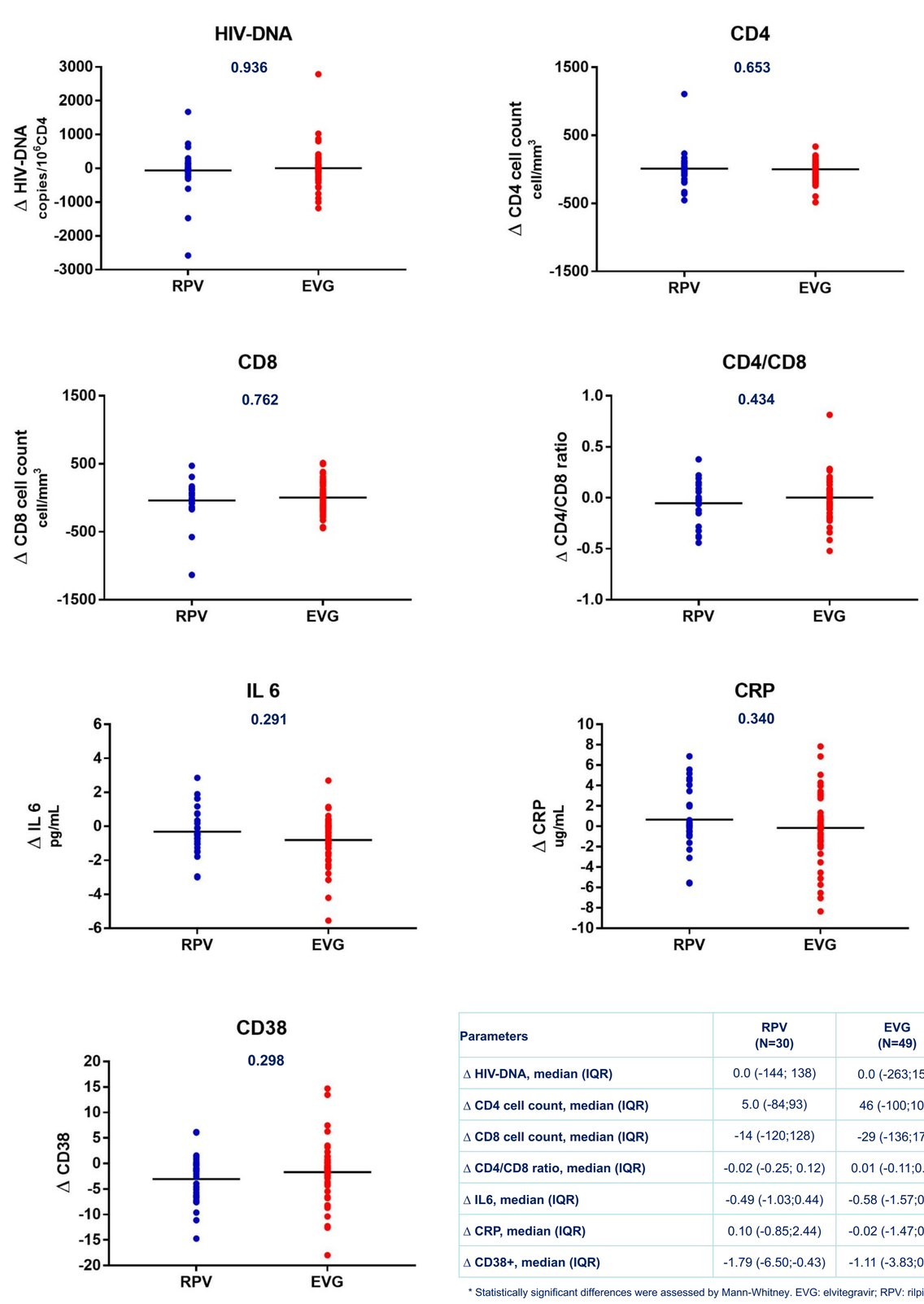
Characteristics	Overall (N=79)	RPV (N=30)	EVG (N=49)	P-value*
T0				
HIV-DNA, copies/10^4CD4, median (IQR)	275 (72-840)	220 (86-625)	320 (44-913)	0.584
CD4 cell count, cell/mm^3, median (IQR)	698 (517-896)	707 (541-873)	698 (475-900)	0.956
CD8 cell count, cell/mm^3, median (IQR)	860 (650-1170)	850 (626-1038)	874 (679-1296)	0.391
CD4/CD8 ratio, median (IQR)	0.79 (0.58-1.06)	0.78 (0.63-1.21)	0.81 (0.54-1.02)	0.558
IL6, pg/mL, median (IQR)	2.2 (1.5-3.3)	2.0 (1.5-2.9)	2.3 (1.4-3.8)	0.589
CRP, ug/mL, median (IQR)	1.6 (0.8-3.1)	1.3 (0.6-2.4)	1.9 (0.8-4.8)	0.156
CD38+, median (IQR)	7.7 (3.0-12.9)	8.3 (3.3-15.9)	6.9 (2.7-12.7)	0.299
Delta time T0-T12, months, median (IQR)	12.2 (11.4-13.4)	12.2 (11.0-13.2)	12.2 (11.5-13.5)	0.996
T12				
HIV-DNA, copies/10^4CD4, median (IQR)	289 (47-719)	262 (59-666)	306 (45-867.5)	0.871
CD4 cell count, cell/mm^3, median (IQR)	670 (534-892)	635 (537-884)	699 (508-952)	0.720
CD8 cell count, cell/mm^3, median (IQR), (n=62)	860 (622-1126)	724 (612-1062)	919 (720-1176)	0.243
CD4/CD8 ratio, median (IQR), (n=62)	0.88 (0.54-1.05)	0.93 (0.57-1.16)	0.81 (0.51-1.02)	0.348
IL6, pg/mL, median (IQR)	1.7 (1.1-2.5)	1.8 (1.1-2.6)	1.6 (1.1-2.4)	0.555
CRP, ug/mL, median (IQR)	1.6 (0.7-5.9)	1.4 (0.7-4.3)	1.6 (0.8-6.4)	0.497
CD38+, median (IQR)	4.3 (1.8-10.6)	3.6 (1.6-10.8)	4.3 (1.8-9.9)	0.781

* Statistically significant differences were assessed by Mann-Whitney test.
EVG: elvitegravir; RPV: rilpivirine

In the overall population:

- no changes in HIV-DNA was found over T0-T12 (mean difference [SD]: -20.1 [619] cps/10^6CD4, P=0.77);
- no changes in CD4 and CD4/CD8 were found over T0-T12 (+4.8 [197] and 0.0 [0.21], P=0.83 and 0.76);
- A significant reduction in IL6 and CD38+HLA-DR+CD8+ at T12 as compared to T0 was found in the overall population in unadjusted analysis and after controlling for HIV-DNA change over T0-T12 (-0.56 and -2.22, p<0.005, respectively).

Figure. Differences in viro-immunological and inflammatory markers between T12 and T0, according with treatment



Parameters	RPV (N=30)	EVG (N=49)
Δ HIV-DNA, median (IQR)	0.0 (-144; 138)	0.0 (-263;152)
Δ CD4 cell count, median (IQR)	5.0 (-84;93)	46 (-100;101)
Δ CD8 cell count, median (IQR)	-14 (-120;128)	-29 (-136;177)
Δ CD4/CD8 ratio, median (IQR)	-0.02 (-0.25; 0.12)	0.01 (-0.11;0.09)
Δ IL6, median (IQR)	-0.49 (-1.03;0.44)	-0.58 (-1.57;0.05)
Δ CRP, median (IQR)	0.10 (-0.85;2.44)	-0.02 (-1.47;0.91)
Δ CD38+, median (IQR)	-1.79 (-6.50;-0.43)	-1.11 (-3.83;0.33)

* Statistically significant differences were assessed by Mann-Whitney. EVG: elvitegravir; RPV: rilpivirine

Linear regression model confirms no differences in HIV-DNA, CD4, CD4/CD8, inflammatory markers and RPV- or EVG-FTC/TAF treatment (Table).

Table. Mean change in biomarkers concentration over T0-T12 by anchor drug. Unadjusted, adjusted estimates and p-values are from fitting a linear regression model with anchor group included as a covariate.

			Mean difference: RPV vs. EVG over T0-T12			
Biomarker	Difference T0-T12 Mean (SD)		Unadjusted		Adjusted[&]	
	RPV (n=30)	EVG (n=49)	Mean (95% CI)	p-value	Mean (95% CI)	p-value
HIV-DNA, cps/10^6CD4	-62.4 (678)	+5.9 (586)	-68 (-355;+219)	0.64	-94 (-380;+192)	0.52
CD4 count, cells/mm3	+12.2 (259)	+0.3 (150)	+11 (-80;+103)	0.80	+16 (-74;+107)	0.72
CD4/CD8 ratio	-0.03 (0.21)	0.0 (0.22)	-0.03 (-0.15;+0.08)	0.57	-0.03 (-0.15;+0.08)	0.57
IL-6	-0.3 (1.3)	-0.7 (1.4)	+0.40 (-0.22;+1.03)	0.21	+0.35 (-0.28;+0.98)	0.28
CD8+CD38+ HLA-DR+	-3.2 (4.7)	-1.7 (5.7)	-1.52 (-4.02;+0.97)	0.23	-1.39 (-3.90;+1.13)	0.28
HsCRP	+0.7 (3.0)	-0.1 (3.3)	+0.75 (-0.73;+2.23)	0.32	+0.69 (-0.82;+2.19)	0.91

[&]for other markers shown in Table as well as months from HIV diagnosis. Models for inflammation markers included CD4 and CD8 count.

Conclusion

Twelve months of TAF-containing regimens resulted in containment of HIV-DNA levels, despite a reduction in inflammatory markers. While suggesting that maintenance of peripheral reservoir appears to be independent of residual inflammation, these data also indicate a possible role of TAF in the containment of other sources of residual inflammation upon suppressive cART. Results were similar regardless of the third drug used.

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