Soluble CD14 levels decrease after switching from a dual regimen with 3TC+PI/r to 3TC+DTG in virologically-suppressed HIV-infected patients

P103

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BACKGROUND

Understanding the effects of different antiretroviral regimens on HIV-related residual systemic inflammation is a topic of interest because heightened inflammation and immune activation have been associated with morbidity and mortality in virologically-suppressed patients.

OBJECTIVE

The aim of our study was to evaluate the impact of switching treatment from a dual regimen with ritonavir-boosted protease inhibitors (PI/r) plus lamivudine (3TC) to dolutegravir (DTG) + 3TC on a marker of monocyte activation, soluble CD14 (sCD14), inflammation, interleukin-6 (IL-6) and C-reactive protein (CRP) coagulation, D-dimer, and enterocyte damage/microbial translocation, intestinal fatty acid–binding protein (I-FABP).

METHODS

Study design

- Retrospective case-crossover study
- Integrase-naïve patients
- Virological suppression (HIV-RNA <50 copies/mL)
- ≥48 weeks on a dual regimen with 3TC + PI/r
- Switch and mainteined for ≥48 weeks dual with 3TC +DTG

Plasma levels of markers of monocyte activation (soluble CD14, **sCD14**), inflammation (interleukin 6, **IL-6**); C-reactive protein, **CRP**; **D-dimer**) and enterocyte damage/microbial translocation (intestinal fatty acid-binding protein, **I-FABP**) were tested by standardized ELISA assays on stored samples at three time points: at switch (**BL)**, 48 weeks before (**-48W**) and 48 weeks after switch (**+48W**).
We performed a mixed model for repeated measures to evaluate the changes in biomarkers over time. Bonferroni adjustment was made when conducting multiple comparisons. Relationship between changes in biomarkers and other biological parameters was assessed using Spearman's correlation

RESULTS

Patients Characteristich at switch

Patients	n=67
Caucasian, n (%)	67 (100)
Male, n (%)	49 (73.1)
Age, median (IQR)	49.4 (41.2-54.9)
Body mass index (Kg/m²), media (IRQ)	23.5 (21.5-25.7)
Time since HIV diagnosis, median (IQR)	11.9 (6.4-18.8)
Time on cART, median (IQR)	10.9 (4.8-16.4)
Risk factor, n (%)	
Homo/bisexual	34 (50.7)
Heterosexual	27 (40.3)
IDU	6 (9.0)
Nadir CD4 count cell/mm³, median (IQR)	237 (64-306)
Zenith viral load (log_{10} copies/mL), median (IQR)	4.8 (4.4-5.4)
Past AIDS-defining events, n (%)	16 (23.9)
Hystory of cardiovascular disease[a], n (%)	8 (11.9)
History of cancer[b], n (%)	9 (13.4)

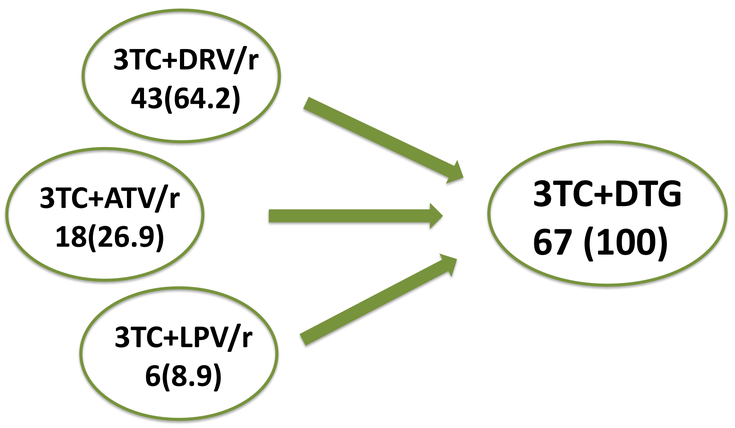
[a]cIncludes cardiomyopathy, ischaemic stroke and myocardial infarction.
[b]dIncludes AIDS- and non-AIDS-related malignancies.

Evolution of biological parameters over time

	-48W	BL	+48W	p[a]	p[b]
Viral load <50 copies/mL, n (%)	67 (100)	67 (100)	67 (100)	1	1
CD4 count (cell/µL), median (IQR)	694 (559-860)	700 (571-920)	730 (600-890)	0.744	0.698
CD4/CD8, median (IQR)	0.77 (0.61-1.00)	0.83 (0.70-1.00)	0.86 (0.68-1.06)	0.095	0.06
Co-morbidities, n (%)					
Diabetes	1(1.5)	1(1.5)	1(1.5)	1,000	1,000
Hypertension	9 (13.4)	11 (16.4)	13 (19.4)	0,160	0,155
HCV-coinfection	0 (0)	0 (0)	0 (0)	1,000	1,000
Lipid profile (mg/dL), median (IQR)					
Total cholesterol	208 (186-244)	208 (177-246)	183 (163-218)	1.000	**<0.001**
HDL*	45 (37-56)	46 (36-55)	44 (35-58)	0.951	1
LDL*	130 (103-161)	119 (98-157)	110 (92-145)	1.000	**0.037**
Triglycerides	145 (106-219)	137 (102-218)	107 (71-162)	1.000	**<0.001**
Log_{10} sCD14 pg/mL, median (IQR)	6.07 (5.93-6.16)	6.04 (5.92-6.12)	5.95 (5.84-6.07)	0.235	**<0.001**
Log_{10} IL-6 pg/L, median (IQR)	3.25 (3.03-3.39)	3.12 (2.88-3.38)	3.11(2.91-3.44)	0.419	1.000
Log_{10} CPR pg/mL, median (IQR)	7.14 (6.96-7.42)	7.10 (6.79-7.33)	7.03 (6.73-7.23)	0.517	0.082
Log_{10} D-dimer pg/mL, median (IQR)	5.57 (5.15-5.70)	5.43 (5.18-5.71)	5.33 (5.12-5.64)	1.000	0.441
Log_{10} I-FABP pg/mL, median (IQR)	3.14 (2.96-3.34)	3.20 (3.04-3.32)	3.13 (2.99-3.23)	1.000	0.238

[a] Between -48W and BL
[b] Between BL and +48W
*Data are available for 73% (n=49) of patients
In bold statistically significant p values

Percentage of patients on previous PI/r regimen



Reasons of switch

Dyslipidemia	37 (55.2)
Toxicity-GI tract	9 (13.4)
Drug interaction	3 (4.5)
Proactive switch	18 (26.9)

No correlation was observed between the decrease in sCD14 and the change in lipid profile parameters

		ρ	p
Δ sCD14	Δ Cholesterol	+0.223	0.074
Δ sCD14	Δ Tryglicerides	-0.010	0.938
Δ sCD14	Δ LDL	+0.086	0.583

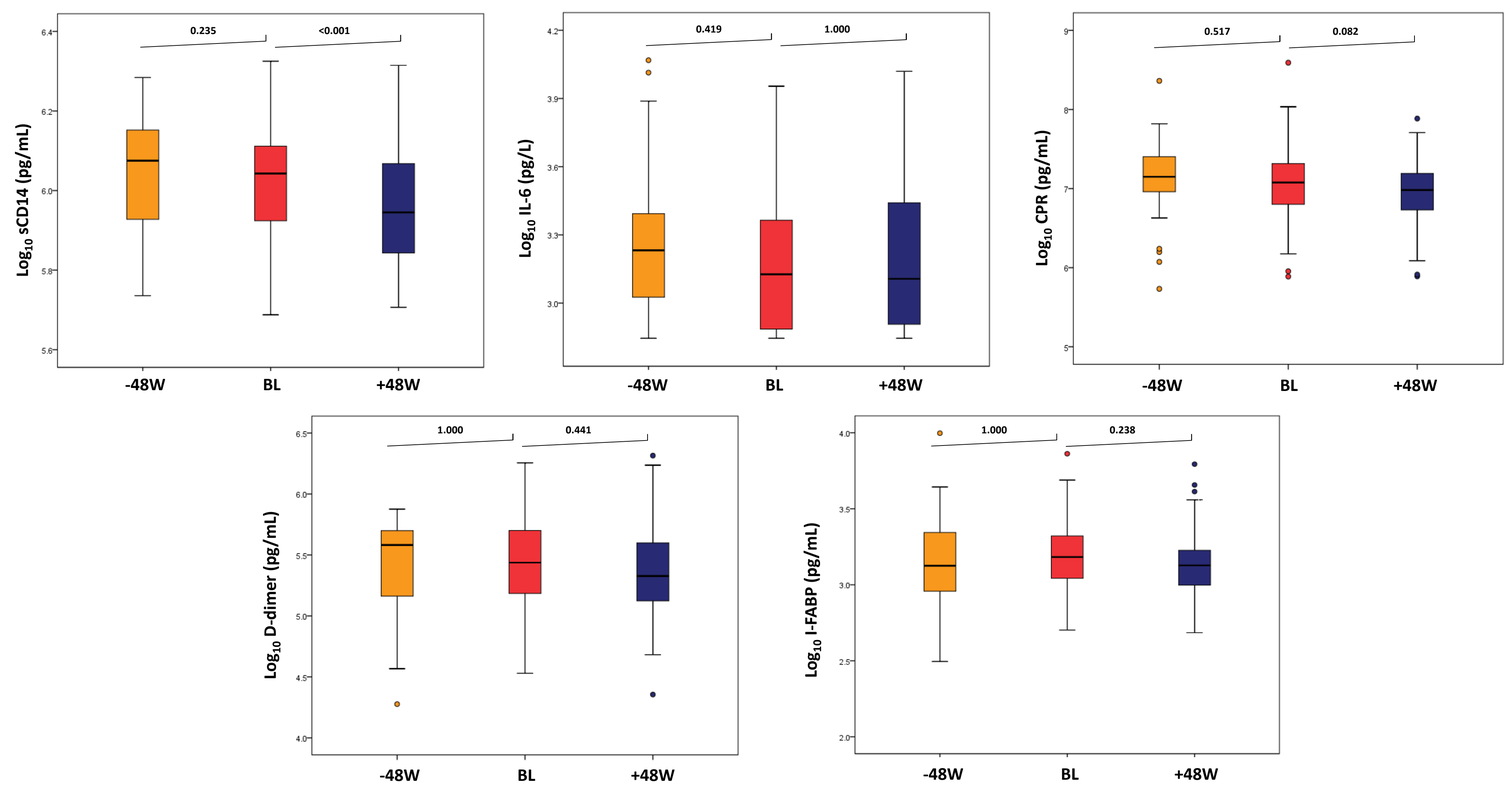


Figure.**Median levels of biomarkers at switch to DTG+3tC (BL), 48 weeks before (-48W) and 48 weeks after switch (+48W).**
In the box plots, boundaries indicate the 25th the 75th percentile, black lines within the box mark the median and whiskers above and below the box indicate the 10th and 90th percentiles. A general linear model (GLM) for repeated measures with Bonferroni adjustment was used for multiple comparisons. *p*-values for these comparisons are shown.

CONCLUSION

In virologically-suppressed HIV-infected patients on a 3TC+PI/r dual therapy, switching to 3TC+DTG was associated with a significant decline in sCD14. These data suggest reduced monocyte activation following substitution of boosted PI with DTG, which could have important implications for morbidity and mortality