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T-cell homeostasis and microbial translocation in PLWH switching from triple to dual INSTI-based combination antiretroviral therapy (cART)

Valeria Bono[1], Camilla Tincati[1], Matteo Augello[1], Roberta Rovito[1], Sabrina Marozin[1], Andrea Santoro[1], Giulia Marchetti[1]

[1] *Clinic of Infectious Diseases, Department of Health Sciences, ASST Santi Paolo e Carlo, University of Milan, Milan*

Introduction

Dual cART regimens containing a second-generation INSTI are used in both first-line and switch strategies. While effective in viro-immunological control, their impact on immune dysregulation and microbial translocation remains unclear.

Materials and Methods

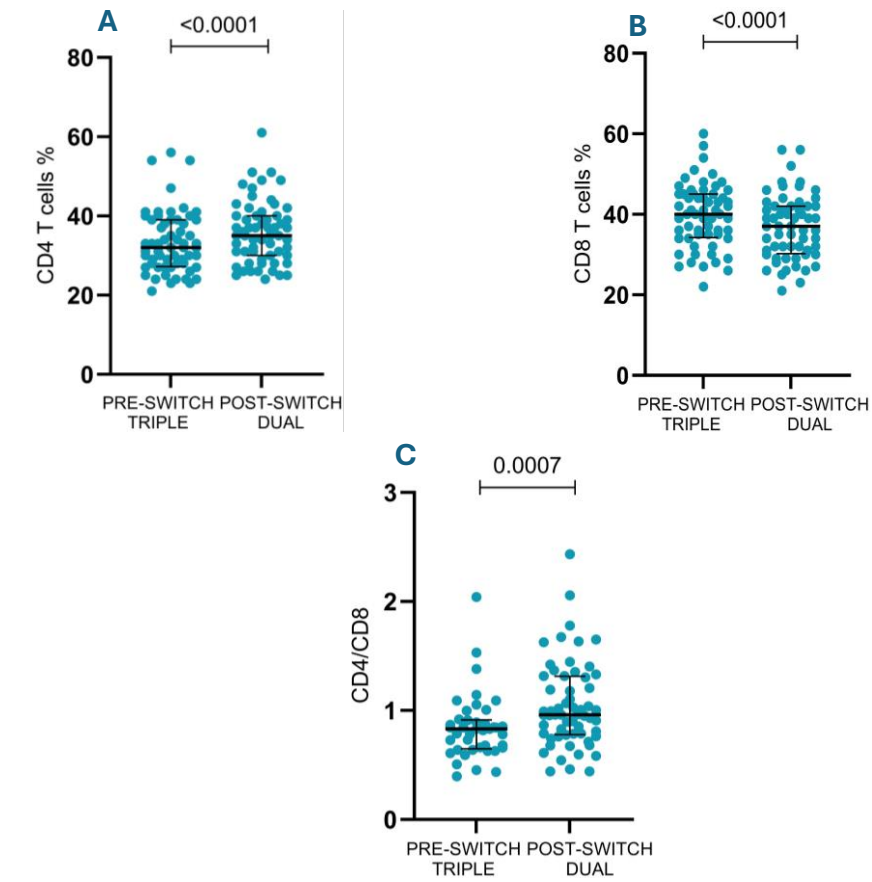
Retrospective study on virally-suppressed PLWH on three drug (3DR) cART who switched to an INSTI-based 2DR regimen. Subjects with available samples at switch and 12 months post-switch were studied (**Table 1**). We measured T-cell maturation (CD127/CD45RA) and activation (CD38/CD45R0) by flow cytometry, gut barrier dysfunction (E-cadherin, I-FABP) and microbial translocation (sCD14, LBP) by ELISA. Wilcoxon test was used for statistics.

Table 1. Demographic and clinical features of the study population (n=60) on suppressive 3 DR (pre-switch).

Age, years, median (IQR)	48 (42-58)
Sex, n (%)	
Male	50 (83.33%)
Female	10 (16.66%)
Ethnicity, n (%)	
Caucasian	55 (91.66%)
Asian	2 (3.33%)
Hispanic	3 (5%)
Risk factors for HIV infection, n (%)	
MSM	40 (66.66%)
Heterosexual	17 (28.33%)
IDU	3 (5%)
Time since HIV diagnosis (years), median (IQR)	14 (10-18)
Time since HIV diagnosis to cART start (months), median (IQR)	0 (0-4)
Time on cART (years), median (IQR)	13 (10-18)
Time from switch (months), median (IQR)	11 (8-14.7)
CD4 cell count nadir (cells/mm3), median (IQR)	275 (182.5-407.5)
Time with viral load <50cps/mL (years), median (IQR)	9 (7-9)
Past AIDS-defining events (CDC C), n (%)	9 (15%)
Number of cART lines prior to switch, n (%)	
0-3	47 (78.33%)
4-8	11 (18.33%)
3DR cART prior to switch, n (%)	
INSTI-based	41 (68.33%)
NNRTI-based	14 (23.33%)
PI-based	4 (6.66)
INSTI + PI-based	1 (1.66%)
2DR cART regimen post switch, n (%)	
3TC/DTG	53 (88.33%)
DTG/RPV	7 (11.66%)

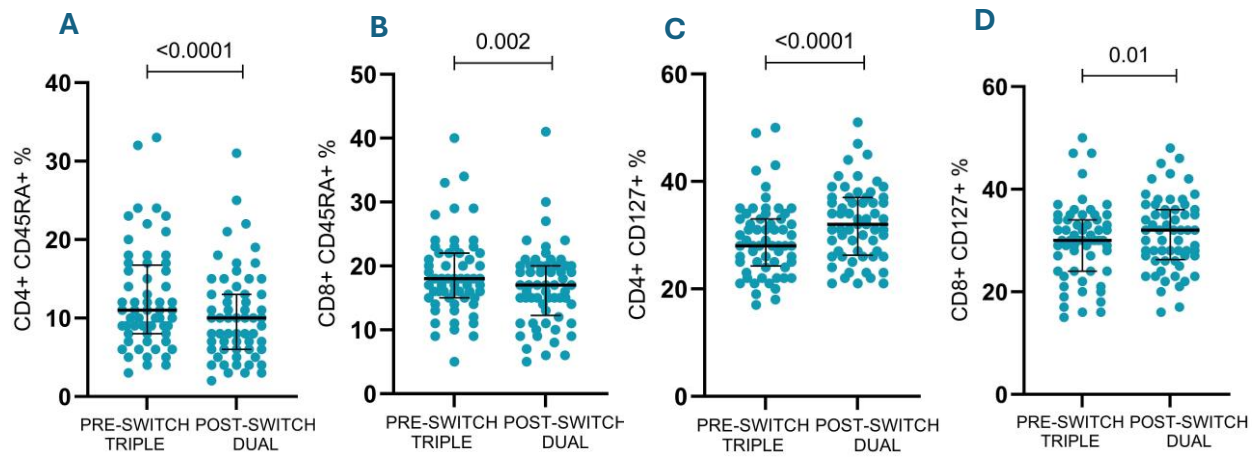
Results

Figure 1. CD4 and CD8 T-cell counts pre- and post-switching to 2DR.



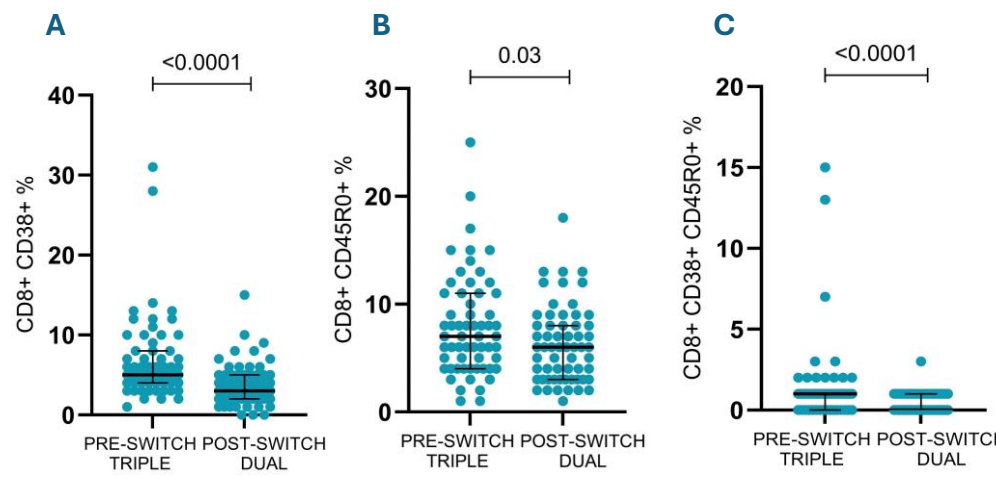
Switching to 2DR led to significant CD4 increases (32% [27-39] vs 35% [30-40]), reduction in CD8 lymphocytes (40% [34-45] vs 37% [30-42]) and rise in CD4/CD8 ratio (0.83 [0.65- 0.91] vs 0.96 [0.76-1.3]).

Figure 2. CD4 and CD8 T-cell maturation pre- and post-switching to 2DR.



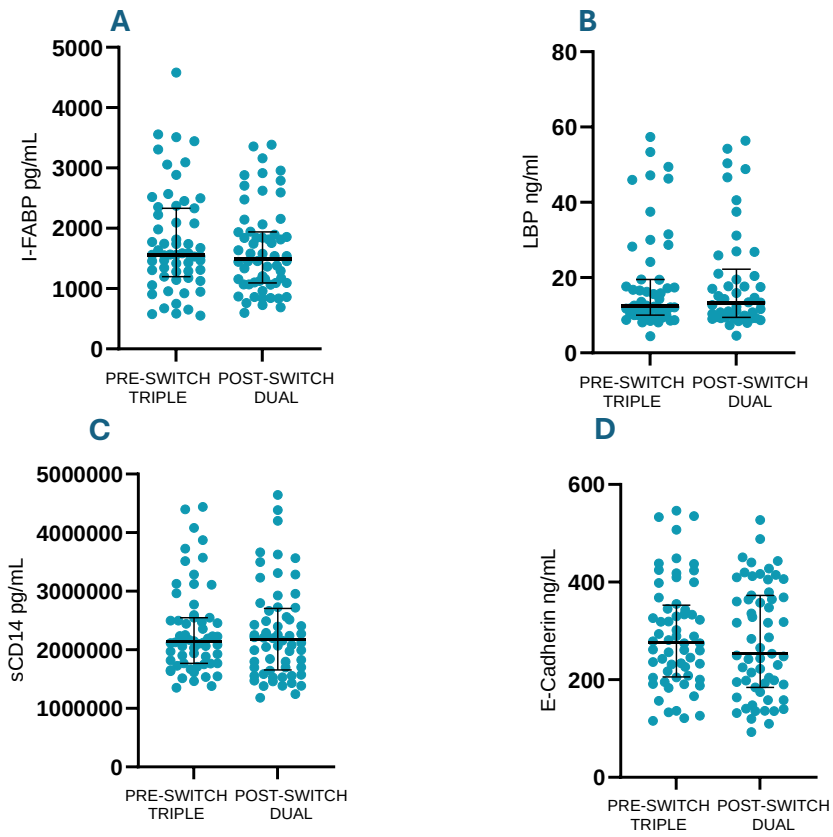
Moreover, switch to 2DR resulted in a decrease of naïve T cells (CD4/CD45RA: 11% [8-17] vs 10% [6-13]; CD8/CD45RA: 18% [15-22] vs 17% [12-20], and significant expansion of central memory phenotypes (CD4/CD127: 28% [24-33] vs 32% [26-37]; CD8/CD127: 30% [24-34] vs 32% [26-36]).

Figure 3. CD8 T-cell activation pre- and post-switching to 2DR.



A marked reduction in activation phenotypes was observed (CD8/CD38: 5% [4-8] vs 3% [2-5]; CD8/CD45RO: 7% [4-11] vs 6 [3-8]; CD8/CD38/CD45RO: 1% [0-1] vs 0% [0-1].

Figure 4. Gut barrier dysfunction and microbial translocation markers pre- and post-switching to 2DR.



No changes in markers of intestinal damage and microbial translocation were detected prior to and after the switch.

Conclusions

Switching from 3DR to 2DR appears to improve T-cell homeostasis through the increase of central memory cells and reduction of T-cell activation, suggesting a possible effect also on peripheral T-cell function. In contrast, the stable gut barrier/function and microbial translocation markers, suggest little/no effect of dual cART on gastrointestinal permeability. Whether the reported changes in T-cell homeostasis are specific to 2DR cART and persist over time remains to be investigated.

Contacts: valeria.bono@unimi.it, camilla.tincati@unimi.it