T-cell Homeostasis Parameters Following Switch to Injectable Cabotegravir plus Rilpivirine in Virally-Suppressed People Living with HIV (PLWH)

Camilla Tincati*[1,2], Leonardo Francesco Rezzonico[1], Andrea Santoro[1], Emanuela Ferrante[1], Teresa Bini[2], Lidia Gazzola[2] and Giulia Marchetti [1,2]

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

P103
*camilla.tincati@unimi.it

Background

Long-acting injectable (LAI) cART containing cabotegravir (CAB) plus rilpivirine (RPV) is an antiretroviral regimen showing solid results in terms of virological suppression; in contrast, its effect on T-lymphocyte homeostasis and activation is less established. We assessed peripheral T-cell homeostasis parameters in virally-suppressed, PLWH switching to injectable CAB+RPV.

Materials and Methods

Retrospective single-center study. Individuals who switched to CAB+RPV and followed for one year were included. Lymphocyte subpopulations were evaluated at four different time points (0, 3, 6, and 12 months). The following surface expression markers were assessed on whole blood by flow cytometry: CD4+/CD8+CD127+ (central memory), CD4+/CD8+CD45RA+ (naïve), CD8+CD45R0+ (memory), CD8+CD38+ (activated), CD8+CD38+CD45R0+ (activated memory). Data were analyzed by fitting a mixed model (GraphPad Prism Software).

Results

57 subjects were included in the analysis; 36 switching from 2-DR and 21 from 3-DR (Table 1). No virological failures were observed.

Table 1. Clinical and HIV-related parameters

	N=57
Gender, male, n (%)	51 (90)
Age at switch, years, median [IQR]	47 (40-53)
Previous AIDS, n (%)	7 (12)
Previous ART regimens, median [IQR]	3 (2 -4)
CD4+ at nadir, cells/mmc, median [IQR]	300 (235-505)
CD4+ at switch, cells/mmc, median [IQR]	745 (586-943)
CD4/CD8 ratio at switch, median [IQR]	0.95 (0.72 -1.21)
Regimen before switch, n (%)	
DTG/RPV	19 (33)
DTG/3TC	17 (30)
TAF/FTC/RPV	12 (21)
BIC/TAF/FTC	7 (12)

Overall, the CD4/CD8 ratio and T-cell homeostasis parameters remained stable, except for a trend to decreases in CD8+CD127+ (central memory) cells (Table 2).

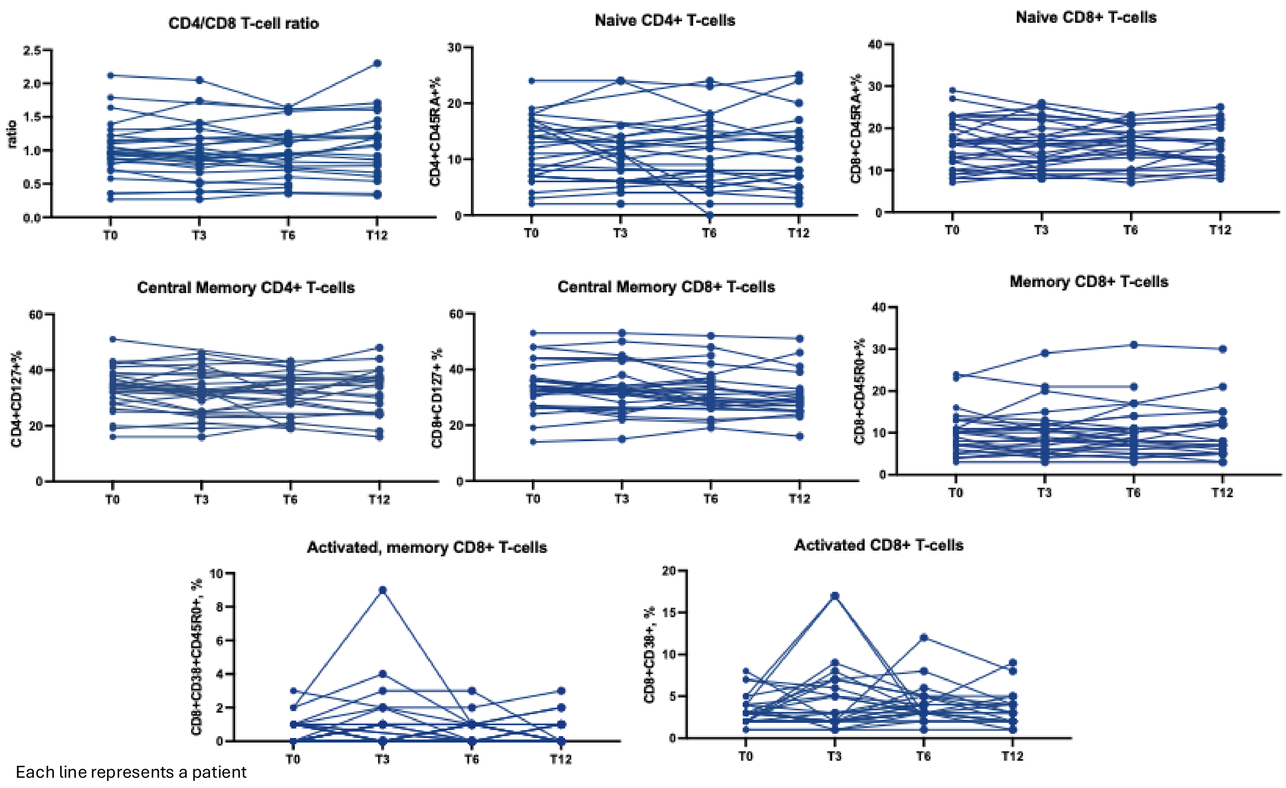
Table 2. T-cell homeostasis parameters in the study population

Parameter	T0	T3	T6	T12	P-value
CD4/CD8 T-cell ratio					
CD4/CD8	0.95 (0.71-1.17)	0.89 (0.73)	0.92 (0.73-1.19)	0.97 (0.76-1.34)	0.26
Central Memory T-cells					
CD4+CD127+					
%	34 (28-38)	33 (25-38)	33 (28-38)	33 (27-37)	0.05
N (cell/ul)	707 (510-872)	614 (535-820)	648 (527-824)	663 (516-808)	0.06
CD8+CD127+					
%	33 (28-38)	33 (27-38)	34 (28-38)	32 (28-38)	0.10
N (cell/ul)	763 (522-975)	662 (500-845)	691 (501-865)	591 (461-870)	**0.04**
Naïve T-cells					
CD4+CD45RA+					
%	9 (6-14)	9 (6-13)	9 (5-14)	9 (5-14)	0.80
N (cell/ul)	165 (121-321)	158 (126-270)	178 (109-306)	179 (105-276)	0.55
CD8+CD45RA+					
%	16 (12-20)	16 (10-19)	16 (11-19)	15 (11-20)	0.43
N (cell/ul)	326 (239-486)	326 (207-411)	336 (223-441)	296 (189-469)	0.22
Memory T-cells					
CD8+CD45R0+					
%	9 (6-12)	8 (7-14)	9 (5-13)	9 (5-15)	0.10
N (cell/ul)	188 (126-291)	171 (123-250)	187 (125-266)	169 (115-281)	0.29
Activated T-cells					
CD8+CD38+					
%	3 (2-4)	2 (2-4)	3 (2-4)	3 (2-4)	0.57
N (cell/ul)	54 (38-92)	49 (31-83)	65 (43-93)	60 (37-88)	0.97
Actaivated Memory CD8+ T-cells					
CD8+CD38+CD45R0+					
%	0 (0-1)	1 (0-1)	1 (0-1)	0 (0-1)	0.11
N (cell/ul)	325 (239-486)	326 (207-411)	336 (223-441)	296 (190-469)	0.22

Data are presented as median, IQR

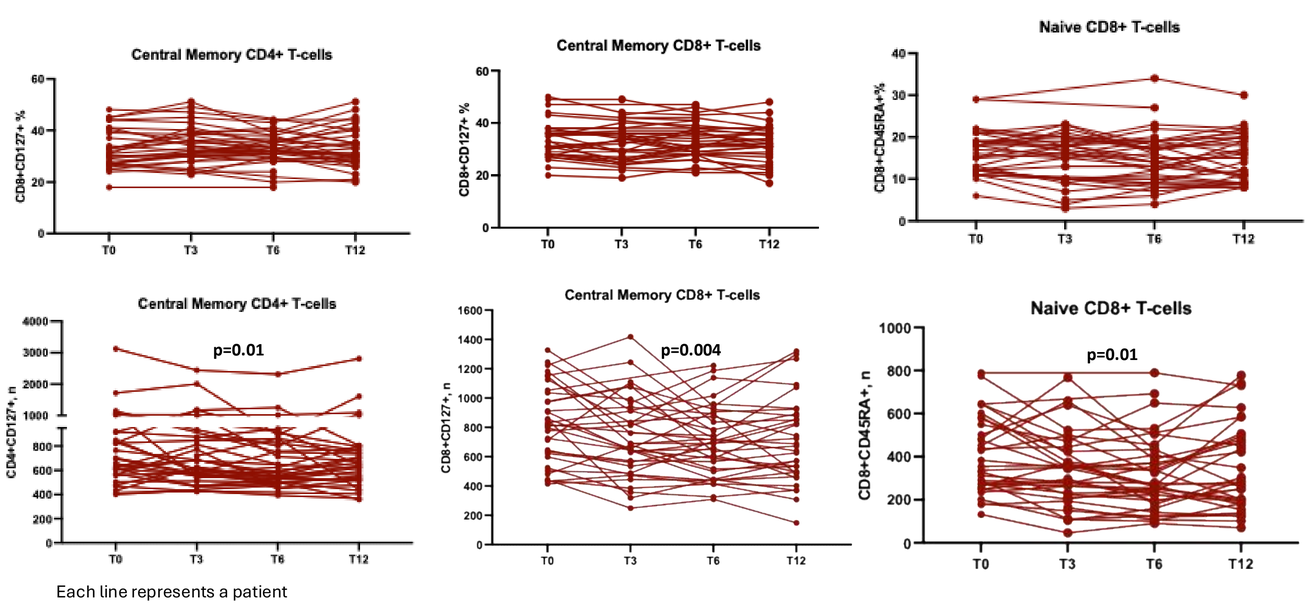
In line with these findings, subjects switching from 3-DR to CAB/RPV showed no major changes in T-cell parameters (Figure 1).

Figure 1. T-cell homeostasis parameters in individuals switching to LAI from 3-DR oral cART



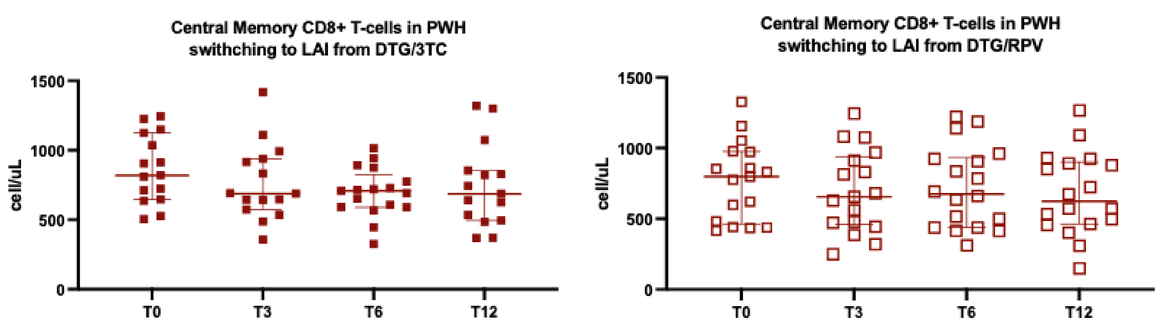
Conversely, in the 2-DR subgroup, we detected a decline in absolute CD127-expressing CD4+ (T0: 703/uL, IQR [567-966]; T3: 627/uL, IQR [553-874]; T6: 584/uL, IQR [503-852]; T12: 647/uL, IQR [524-786], p=0.01) and CD8+ cells (T0: 819/uL, IQR [609-1045]; T3: 679/uL, IQR [512-927]; T6: 700/uL, IQR [529-888); T12: 673/uL IQR [490-885], p=0.004) as well as naïve CD8+CD45RA+ cells (T0: 354/uL IQR [267-562]; T3: 345/uL, IQR [207-435]; T6: 273/uL, [203-426]; T12: 281/uL IQR [188-486], p=0.01) (Figure 2, bottom row).

Figure 2. T-cell homeostasis parameters in individuals switching to LAI from 2-DR oral cART (top: percentage values; bottom: absolute values)



Of note, individuals switching from dolutegravir (DTG)/lamivudine (3TC), yet not those from DTG/RPV, showed a tendency to significant decreases CD8+ central memory cells (T0: 819/uL, IQR [645-1125]; T12: 687/uL, IQR [496-854], p=0.05) (Figure 3).

Figure 3. Central memory CD8+ T-cells in PWH switching to LAI from DTG/3TC and DTC/RPV



Conclusions

Switching to injectable CAB/RPV did not have major effects on T-cell homeostasis. While central memory CD4+ and CD8+ T-cells as well as naïve CD8+ cells show a decreasing trend in individuals switching from oral 2-DR, the mechanism(s) by which long-acting injectables may influence T-cell homeostasis in the long-term needs careful investigation.