CD4/CD8 ratio slope after switching from triple- to double combinations or PI-monotherapy.

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Background

A low CD4/CD8 ratio has been associated to AIDS and non-AIDS associated events. Long-term side effects have led to NRTI's sparing regimens including double- or mono- PI therapy. Aim of the study was to evaluate if decreasing the number of drugs could result in change in CD4/CD8 ratio.

Methods

Icona cohort participants were included if:
- started cART,
- reached undetectable viral load (<=50 copies/mL)
- switched to double- or mono-PI therapy.

All the consecutive computable CD4/CD8 ratio of the period between one year before and one year after the switch during viral load suppression were considered. For each single patients the slope before and the slope after switch were estimated using linear regression. The change between slopes pre and post switch was calculated and tested if different from zero using t-Student test.
Multivariable linear regression (adjusted for gender, age at switch, date of 1st HIV positivity, HCV-Ab and CMV status, years of ART at switch, CD4 count at switch, mono or dual therapies at switch) was used to analyze factors associated with slope change.

Results

138 pts were included, patients' characteristics are showed below

Characteristics	N=138
Male gender, n(%)	110 (79.7%)
Age, yrs, median (IQR)	46 (39-50)
Mode of HIV transmission, n(%)	
heterosexual	47 (34.1%)
IVDU	13 (9.4%)
homosexual	73 (52.9%)
other/unknown	5 (3.6%)
Years from first HIV test and first visit, median (IQR)	4.0 (2-10)
Years of ARV therapy, median (IQR)	2.1 (1.3-5.9)
HCV Ab, n(%)	
positive	18 (13.0%)
negative	26 (18.8%)
unknown	94 (68.1%)
HBV Ag, n(%)	
positive	-
negative	24 (17.4%)
unknown	114 (82.6%)
CD4 cell/mmc at switch, median (IQR)	571 (418-726)
CD4/CD8 at switch, median (IQR)	0.74 (0.53-1.00)
Line of therapy	
1	88 (63.8%)
2	25 (18.1%)
>=3	25 (18.1%)
Regimen after switch	
lpv/r	18 (13.0%)
drv/r	44 (31.9%)
atv/r	11 (8.0%)
dual	65 (47.1%)

Table 1. General characteristics of patients

Table 2. median value of CD4, CD8 and CD4/CD8 ratio at 3 different time-point.

	At 1 year before switch	At switch	At 1 year after switch
CD4/CD8 ratio, median (IQR)	0.43 (0.29-0.64)	0.74 (0.53-1.00)	0.77 (0.53-1.12)
CD4, median (IQR)	427 (306-570)	572 (418-726)	662 (453-832)
CD8, median (IQR)	972 (686-1358)	785 (564-1162)	828 (587-1190)

The mean slope of ratio during last year before switch was 0.24 (SD 0.28), it became 0.06 (0.28) during the first year of mono/dual therapy. The mean slope change was 0.18 (SD 0.36). The slope change was significantly (p<0.001) different from zero.

Table 3. Factors associated with the slope change before and after switch

	Beta	95% CI		P
Male gender vs female	-0.26	-0.98	0.45	0.468
Age, per 10 yrs older	0.04	-0.25	0.33	0.787
Mode of HIV transmission				
heterosexual	ref			
IVDU	-0.45	-1.50	0.60	0.398
homosexual	-0.05	-0.69	0.58	0.868
other/unknown	-1.08	-2.65	0.49	0.175
Years of HIV infection, per 1 year more	-0.02	-0.07	0.02	0.305
Years of ARV therapy at switch, per 1 year more	-0.06	-0.12	0.01	0.103
HCV Ab				
positive	ref			
negative	0.01	-1.01	1.03	0.990
unknown	0.45	-0.29	1.19	0.234
HBV Ag				
positive	ref			
negative	-			
unknown	0.15	-0.60	0.91	0.685
CMV serology				
positive	ref			
negative	0.48	-1.26	2.21	0.588
unknown	0.30	-0.30	0.90	0.330
CD4 cell/mmc at switch, per 100 cells higher	0.06	-0.04	0.15	0.254
CD4/CD8 at switch pre cART	1.74	0.42	3.06	0.010
Line of therapy				
1	ref			
2	-0.62	-1.38	0.13	0.105
>=3	0.02	-0.75	0.78	0.962
Mono vs dual therapy after switch	-0.06	-0.63	0.52	0.850

Conclusions

Switching to dual or mono-PI therapies leads to a slower increase in CD4/CD8 ratio. It will be important to understand if this phenomenon could be related to an increase in low level viremia and inflammation, thus having an impact on future clinical events especially for patients switching in presence of a low CD4/CD8 ratio.

ICONA Foundation Study Group