



Oral Communication

Session/Topic: Immunological response under cART and co-infections

N. Title:

OC 17 CD4/CD8 ratio in patients who switch therapy: better triple therapy than dual/mono?

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Abstract:

Background: A low CD4/CD8 ratio has been associated to AIDS and non-AIDS events. Long-term side effects have led to non-conventional NRTI- sparing regimens as double- or mono- therapy, some of them also present in national and international guidelines. The aim of the study was to evaluate if in subjects who switched treatment, decreasing the number of drugs could result in changes in CD4 /CD8 ratio after 12 months.

Material and Methods: Patients from the Icona cohort were included if: started a cART regimen including 3 antiretrovirals from ART-naïve; reached a confirmed HIV-RNA \leq 50 copies/mL; switched to another triple regimen or to double- or mono- therapy; at 12 months they maintained virological suppression on the same regimen. End-points were: change in CD4/CD8 ratio and CD8 count at 12 months compared to baseline. Multivariable linear regressions were used to evaluate the association between endpoints and type of regimen.

Results: 905 patients were included, 104 switched to a mono/double regimen (51 mono, 53 double therapies), while 801 switched to a triple regimen. 76.1% were males, mean age: 43 years, 90.1% Italian, 17.2 % HCV positive, a median time of viral suppression of 20 months (range 10-37). Patients who switched to dual/mono therapy were more frequently MSM, HCV-Ab negative. At switch, there were no differences between groups concerning duration of viral suppression and CD4, while CD4/CD8 ratio was significantly lower in patients who switched to triple therapy (0.65 vs 0.77; $p < 0.013$). Six months after switch CD4/CD8 ratio increased in patients on triple regimen [0.06 (-0.01,0.14)], while it was stable in those on a mono/double therapy [-0.005 (-0.009,0.07) ($p < 0.001$)]. At 12 months, the trend continued: 0.10 (0.01,0.20) vs. 0.05 (-0.03,0.14) ($p = 0.007$) in triple and mono/dual, respectively. The difference was not due to the increase of CD4 (median cells/ μ L: 34 vs. 28 at 6 months, $p = 0.607$; 63 vs. 69 at 12 months, $p = 0.045$), but to CD8 cell count. Indeed, at 6 months the median value in the triple group was -26 cells/ μ L (-141,99) vs. +19 (-172,99) in the mono/double group ($p = 0.04$) and at 12 months was -20 cells/ μ L (-172,127) and +28 (-98,166) ($p = 0.018$), respectively. At multivariable linear regression analysis, patients on mono/dual therapy showed higher mean increase of CD8 compared to those on triple regimen (Table).

Conclusions: Patients who switch to a double/mono therapy, despite viral suppression, could not completely benefit of immune-reconstitution as those who remained on a triple regimen.

Table. Multivariable linear regression models with the dependent variables: (A) CD8 change at 12 months from baseline, (B) CD4/CD8 ratio change at 12 months from baseline

	(A) CD8 Cell Count				(B) CD4/CD8 ratio			
	beta	95% CI		p-value	beta	95% CI		p-value
Gender								
Male vs. female	63.73	7.81	119.65	0.026	-0.03	-0.07	0.01	0.103
Age								
per 10 years older	0.81	-1.32	2.94	0.455	-0.01	-0.02	0.01	0.224
Mode of HIV transmission								
Heterosexual	ref				ref			
IDU	-22.99	-113.35	67.37	0.618	-0.01	-0.08	0.05	0.658
MSM	-19.72	-72.66	33.22	0.465	-0.01	-0.04	0.03	0.735
Other/unknown	19.33	-71.93	110.58	0.678	0.00	-0.06	0.07	0.966
Nationality								
Migrants vs. natives	4.54	-65.87	74.94	0.899	-0.01	-0.06	0.04	0.801
Previous AIDS event	55.51	-8.12	119.15	0.087	-0.04	-0.08	0.01	0.124
Years of infection								
per 1 year more	4.14	-0.59	8.88	0.086	0.00	0.00	0.00	0.518
HCV positivity								
No	ref				ref			
Yes	-35.28	-115.08	44.52	0.386	0.02	-0.03	0.08	0.411
Unknown	-7.45	-123.76	108.86	0.900	0.04	-0.04	0.13	0.284
CD4 before cART, cell/mm³								
<200	ref				ref			
201-350	40.95	-19.67	101.57	0.185	-0.03	-0.07	0.01	0.167
351-500	15.66	-54.21	85.53	0.660	0.01	-0.04	0.06	0.677
>500	18.72	-60.48	97.92	0.643	0.04	-0.01	0.10	0.152
Missing	91.92	-57.46	241.30	0.227	-0.08	-0.18	0.03	0.147
HIV-RNA before cART, cps/ml								
<20,000	ref				ref			
20,000-100,000	-23.65	-75.69	28.39	0.373	0.01	-0.03	0.04	0.761
100,000-250,000	31.82	-30.83	94.47	0.319	0.01	-0.04	0.05	0.751
>250,000	-10.24	-78.08	57.60	0.767	0.01	-0.03	0.06	0.555
Missing	-20.20	-131.50	91.11	0.722	0.04	-0.04	0.12	0.323
CD4 at switch, cell/mm³								
<350	ref				ref			
350-500	-73.26	-137.74	-8.78	0.026	-0.01	-0.05	0.04	0.684
>500	-82.96	-148.75	-17.17	0.014	-0.03	-0.08	0.02	0.201
Months of viral suppression	-0.23	-1.14	0.67	0.614	0.00	0.00	0.00	0.003
CD8 at switch								
per 100 cells/mm ³ increase	-0.34	-0.39	-0.29	0.000	0.00	0.00	0.01	0.023
Regimen after switch								
Triple	ref				ref			
Mono/Dual	77.93	13.64	142.22	0.018	-0.04	-0.09	0.00	0.075