Changing Antiretrovirals whilst Viral Load ‹50 copies/ml and Relationship with CD4 Count Changes

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INTRODUCTION

The main goal of combination antiretroviral therapy (cART) is to suppress viral replication to as low a limit as possible, currently 50 copies/ml. Treatment discontinuations after starting cART are common and often due to toxicity rather than treatment failure. The frequency and reasons for switching antiretrovirals (ARVs) in patients who are on a fully suppressed cART regimen is not well described, nor is the effect of such a change on CD4 count.

AIM

- To describe the rate and reason for switching antiretrovirals in patients on cART with a viral load (VL) ‹ 50 copies/ml
- To investigate the change in CD4 count following such a switch

METHODS

- EuroSIDA patients included in this analysis were on cART, defined as a regimen containing exactly 2 nucleosides or nucleotides plus either a protease inhibitor (PI), boosted-PI, or non-nucleoside reverse transcriptase inhibitor (NNRTI)
- Patients were required to have a confirmed viral load ‹ 50 copies/ml after starting cART and whilst still on cART and a CD4 count measured within 28 days of both the initial and confirmatory viral load measurement
- Baseline was defined as the date of the confirmed viral load
- A treatment switch was defined as any change in ARVs whilst VL‹ 50 copies/ml
- Kaplan Meier methods estimated the probability of ARV change
- Cox proportional hazards models identified factors associated with ARV change
- Mixed models modelled the change in CD4 count after the first ARV change
- Patients were followed up until the earliest of the VL increasing above 50 copies/ml (for any reason), the last viral load measurement (if all ‹ 50 copies/ml), the second switch in cART or at stopping cART

RESULTS

- 7071 patients were included in the analysis, **table 1** gives the baseline characteristics.
- 1110 (15.7%) patients changed 1420 ARVs
- 100 (9%) of the patients switching ARVs added an ARV that they had taken previously
- 254 (22.9%) switched to a new class of ARVs at the date of the switch, 26 started a PI containing regimen and 228 a NNRTI containing regimen
- 12 months after baseline 9.8% (95% CI 9.0-10.6%) of patients were estimated to have switched at least 1 ARV (**figure 1)**
- The incidence of switching was 11.2 per 100 person-years of follow-up (95% CI 10.5-11.8)
- 531 (37%) switches were due to toxicity and 440 (31%) due to patient/physician choice (**table 2**)
- There were significant differences in the reasons for stopping nucleosides (p‹.0001), more patients stopped a stavudine containing nucleoside pair due to toxicites
- There were no differences in the reasons for stopping the third drug (single PI, boosted PI, or NNRTI) in the regimen (p=0.17)
- Those who switched ARVs had an additional annual increase in CD4 cell counts of 5.9/mm³ per year (95% CI 2.9-8.9mm3) compared to those who did not switch (**figure 2)**
- Patients who switched ›1 ARV had an additional annual increase in CD4 cell count of 6.6/mm³ per year (95% CI 0.5-12.6/mm³) compared to those who switch 1 ARV (**figure 2)**

CONCLUSION

- Approximately 10% of patients with virologic suppression switched treatment every year
- This was most commonly due to toxicities or patient or physician wish, which will likely be strongly correlated with toxicities
- Patients who changed ARVs had a small but significant boost in CD4 levels, and the increase was higher in those who started ›1 new ARV
- These results are potentially of most relevance to patients with low CD4 counts in whom cART had not induced optimal immunologic recovery

Table 1

Baseline Characteristics
Baseline is first viral load ‹50 copies/ml whilst on cART

			Switch		No switch		P-value
All		N,% of total	1110	15.7	5961	84.3	
Gender	Male	N,%	843	76.0	4552	76.4	0.76
Race	White	N,%	960	86.5	5137	86.2	0.78
Exposure group	Homosexual	N,%	504	45.4	2654	44.5	0.50
	IDU		205	18.5	1114	18.7	
	Heterosexual		304	27.4	1733	29.1	
Region of Europe	South	N, %	269	24.2	1699	28.5	0.0007
	Central		274	24.7	1513	25.4	
	North		379	38.1	1670	28.0	
	East		155	14.0	881	14.8	
	Argentina		33	3.0	198	3.3	
Age		Median, IQR	41	36-49	41	35-48	0.11
Baseline CD4 count (/mm³)		Median, IQR	408	278-579	419	275-589	0.65
Nadir CD4 (/mm³)		Median, IQR	159	60-248	162	70-259	0.03
Peak viral load (log_{10}copies)		Median, IQR	4.7	3.6-5.2	4.8	3.8-5.3	0.0005
Baseline (month/year)		Median, IQR	7/03	2/00-9/05	9/03	1/00-9/05	‹.0001
Year since starting cART		Median, IQR	2.1	0.9-54	2.4	0.8-5.3	0.51

Figure 1

Kaplan-Meier probability of switch whilst virologically suppressed (VL ‹ 50 copies/ml)

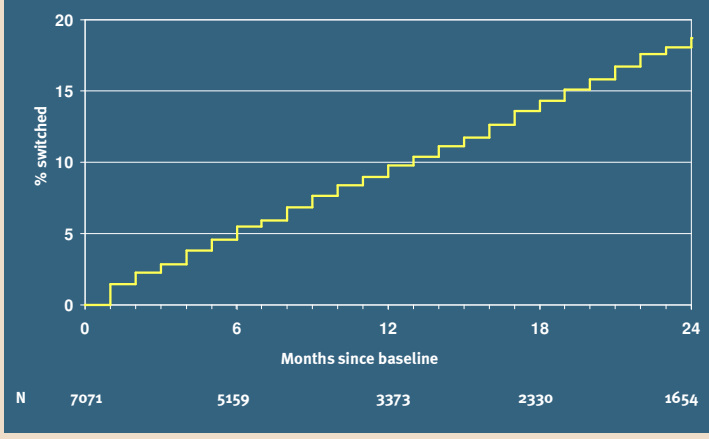


Table 2

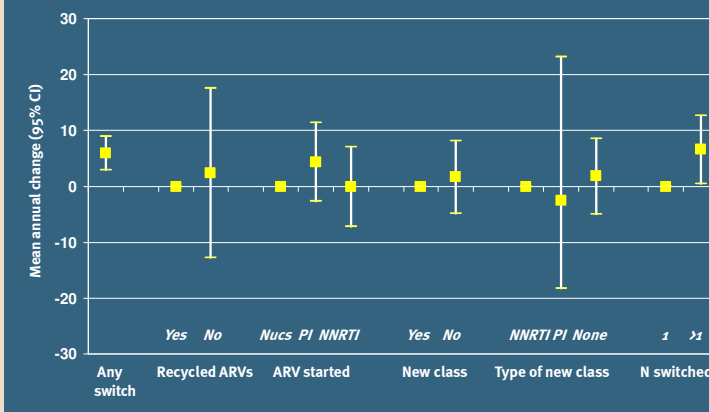
Antiretroviral used at baseline, after switch and reasons for stopping

	At baseline	On after switch	Total ARVs stopped	Reason		
				Patient/ physician choice	Toxicity	Treatment failure
Nucleoside pair N (%)						
zdv/lam	2312 (33)	2175 (30)	292 (37)	107 (37)	85 (29)	6 (2)
ddi/d4t	466 (7)	408 (6)	89 (11)	20 (22)	48 (54)	6 (7)
d4t/3TC	1347 (19)	1242 (17)	141 (18)	42 (30)	73 (52)	1 (1)
tdf+1	1587 (22)	1814 (26)	138 (17)	54 (39)	30 (22)	3 (2)
abc+1	866 (12)	959 (13)	66 (8)	34 (52)	17 (26)	0
other	493 (7)	473 (8)	70 (9)	31 (44)	14 (20)	3 (4)
Third drug N (%)						
Single PI	2419 (34)	2150 (30)	399 (64)	96 (24)	159 (40)	6 (1)
Boosted PI	1973 (28)	2041 (29)	125 (20)	31 (25)	52 (42)	1 (1)
NNRTI	2679 (38)	2880 (41)	100 (16)	25 (25)	53 (53)	0

Patients did not necessarily have to stop both ARVs in the nucleoside pair
zdv-zidovudine, ddi-didanosine, d4t-stavudine, 3TC-lamivudine, tdf-tenofivir, abc-abacavir

Figure 2

Adjusted CD4 count changes in patients with a treatment switch with VL ‹ 50 copies/ml



Adjustment for time since baseline, time since starting ARVs, age, date of baseline, risk group, gender, ethnic origin, region of Europe, AIDS before baseline, HBsAg status, HCV antibody status, AIDS during prospective follow-up, nucleoside pair and third drug at baseline, CD4 nadir, peak viremia before baseline and proportion of time prior to baseline with VL ‹ 500

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