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Predicting the CD4 slope in patients starting cART after 1 January 1999

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INTRODUCTION

Previous research has demonstrated that CD4 slope is a useful prognostic marker for clinical disease progression in patients starting cART (1).

AIMS

To determine predictors of CD4 slopes in patients starting cART after 1 January 1999.

PATIENTS

EuroSIDA patients satisfying the following criterion were included

- started cART after 1/1/99
- CD4 and VL measured in the 6 months prior to starting cART

cART was defined as treatment with exactly 2 nucleosides/ nucleotides plus exactly 1 PI, RTV-boosted-PI, NNRTI or abacavir. Triple class failure (TCF) was defined as previously within EuroSIDA and according to the PLATO definition (2).

METHODS

CD4 slopes were calculated for each successive 3 CD4s and changes in viral load over the same time determined using the viral load closest to the first and third CD4 count used to calculate the slope. Generalised-estimating-equations were used to investigate factors associated with CD4 slope.

RESULTS

1956 patients were included in analyses (**Table 1**). 21279 CD4 slopes were included in analyses, with a median of 10 per patient (IQR 6-17). The median time covered by the 3 CD4 counts used to derive the slopes was 6 months (IQR 5-8 months).

Figure 1 shows the ***unadjusted*** annual CD4 slope according to viral load change over the same time period. **Figure 2** shows the ***unadjusted*** CD4 slope according to treatment regimen in use at the first CD4 used to calculate each slope.

Table 2 shows the multivariate factors associated with annual change in CD4 slope:

- periods spent on no antiretrovirals had, on average, a 170/mm³ per year lower increase in CD4 counts compared to periods spent treated with a boosted PI regimen
- antiretroviral naïve patients had a 22/mm³ per year higher increase in CD4 compared to patients starting cART with prior nucleoside exposure
- the mean annual CD4 increase within the first 6 months of cART was 64/mm³ higher than the mean annual CD4 slope at 3-6 years after starting cART

In comparison to periods with virologic suppression

- periods where the VL decreased by › 2 log copies per year had a 123/mm³ per year higher increase in CD4
- periods where VL was increasing by 0.5-2 log copies per year had a 45/mm³ lower increase in annual CD4 count
- periods with VL increasing by more than 2 log copies per year had a 140/mm³ per year lower increase in annual CD4 count

CONCLUSIONS

- There were a number of predictors of CD4 slope in patients starting cART after 1 Janaury 1999
- After adjustment for other variables, the rate at which viral load was changing was a strong predictor of the rate of change in CD4 count
- There were some differences between CD4 slope for different cART regimens
- As expected, patients who stopped all ARVs had a rapidly declining CD4 slope
- After adjustment, development of triple class failure was not an independant predictor of CD4 slope

SUMMARY

There are a number of predictors of CD4 slope which will be useful to identify patients with rapidly decreasing CD4 and at the greatest risk of clinical disease progression.

Table 1

Characteristics of 1956 patients included in analyses

		N	%
Gender	Male / Female	1363 / 593	69.7 / 30.3
Ethnic Origin	White / Other	1720 / 236	87.9 / 12.1
Exposure	Hom. / Het. / IDU	743 / 404 / 678	38.0 / 20.7 / 34.7
Prior AIDS		75	19.2
cART	Single PI	488	25.0
Regimen	RTV-boosted PI	420	21.5
	NNRTI	960	49.1
	Abacavir	88	4.5
ARV naive		1408	72.0
		Median	IQR
CD4 at cART		231	120 – 360
VL at cART		4.80	4.03 – 5.32
Nadir CD4		188	90 – 287
Peak VL		4.96	4.38 – 5.44
Date started cART		1/01	1/00 – 6/03
Age		37.4	31.5 – 44.3

Figure 1

Unadjusted CD4 count increase stratified by VL suppression

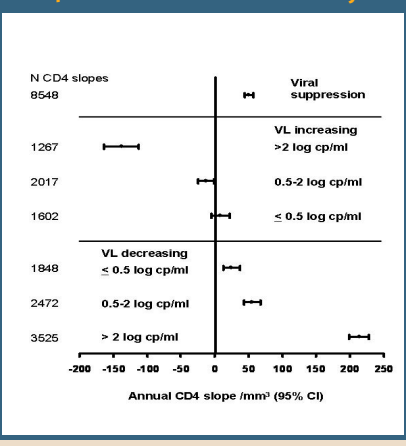

Figure 2

CD4 slope and cART regimens

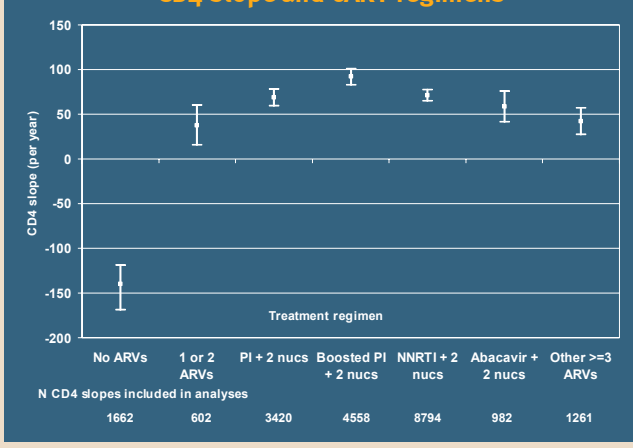

Table 2

Multivariate factors associated with CD4 slope

		Annual slope	95% CI	p
Treatment regimen	Off all ARVs	-169.7	-194.6 to -144.8	<0.0001
	1 or 2 ARVs	-20.9	-45.3 to 3.6	0.095
	PI + 2 nucs	-19.7	-32.5 to -7.0	0.0023
	Boosted PI + 2 nucs	0	-	-
	NNRTI + 2 nucs	-14.7	-25.0 to -4.3	0.0053
	Abacavir +2 nucs	-14.7	-33.8 to 4.5	0.13
	Other ≥ 3 ARVs	-18.4	-36.0 to -0.8	0.040
ARV naïve at cART		21.6	13.3 to 29.8	<0.0001
CD4 at cART	Per doubling	-0.32	-2.47 to 1.84	0.77
VL at cART	Per 1 log higher	1.67	-3.29 to 6.64	0.51
Current VL	Per 1 log higher	7.31	1.14 to 13.48	0.020
Time since cART	< 6 months	63.7	43.9 to 83.5	<0.0001
	6 months- 3 years	37.9	29.1 to 46.8	<0.0001
	3 – 6 years	0	-	-
	> 6 years	-6.7	-24.8 to 11.4	0.47
Change in VL	No change	0	-	-
	≤ 0.5 log decrease	-13.6	-28.0 to 0.8	0.065
	0.5 – 2 log decrease	-1.5	-17.1 to 14.1	0.85
	> 2 log decrease	123.0	101.9 to 144.2	<0.0001
	≤ 0.5 log increase	-22.3	-38.3 to -6.3	0.0063
	0.5 – 2 log increase	-45.1	-58.9 to -31.3	<0.0001
	>2 log increase	-140.3	-168.7 to -112.0	<0.0001
Develop TCF		-12.6	-27.5 to 2.4	0.10
Date started cART	Per 12 months later	-1.34	-3.91 to 1.24	0.31
Age	Per 10 years older	-4.7	-8.0 to -1.5	0.0040
IDU risk group	Vs other	-5.7	-14.4 to 3.1	0.20

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2 PLATO collaboration. Predictors of trends in CD4 positive T-cell count and mortality among HIV-1 infected individuals with virological failure to all three antiretroviral-drug classes. Lancet 2004;364:51-62.

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