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Patterns of viral suppression on cART as predictors of uncontrolled viremia after starting a new antiretroviral after 1st January 2003

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INTRODUCTION

HIV infected patients on combination antiretroviral therapy (cART) experience different patterns of viral suppression throughout antiretroviral treatment. Studies have found a variety of reasons why patients respond differently, such as resistance, adherence, toxicity, viral load and CD4 count at starting cART, and previous exposure to antiretrovirals (ARV).

However, little is known about how these previous patterns of viral suppression affect the risk of future virological failure in addition to traditional predictors.

AIM

To investigate whether the history of viral suppression after starting cART is predictive of future virological failure after starting a new antiretroviral.

METHODS

Inclusion Criteria

- All patients who had been on cART for at least 6 months who started at least 1 new ARV for any reason on or after 1/1/2003
- Patients must have achieved viral load <500 copies/ml on cART prior starting new ARV
- Patients must have at least 1 viral load measured after starting new ARV
- cART defined as being on exactly 2 nucleoside/nucleotides and either a PI, ritonavir-boosted PI or an NNRTI

Factors describing patterns of prior virological suppression

- Time to initial suppression from cART initiation
- Ever rebounded (viral load >500 copies/ml)
- Number of previous rebounds
- Total time with suppressed viral load
- % time on cART with viral load <500 copies/ml (any periods of time where the patient was off cART and the first 4 months after starting a new cART regimen were excluded)
- Size rebound
- Time since last rebound till starting new ARV
- Ever rebounded above viral load at starting cART

Statistical Methods

- Baseline is date of starting new ARV
- Virological failure was defined as one viral load measured above 500 copies/ml at least 6 months after starting a new antiretroviral
- Poisson regression analysis was used to identify the previous patterns of prior virological suppression predictive of virological failure after starting a new antiretroviral

RESULTS

The characteristics of the 1,917 patients included in the study are shown in **table 1**.

Prior to baseline

- Median time to first suppression 3.9 months, inter quartile range 1.6-11.6
- 1,195 (62%) experienced at least 1 rebound
- 569 (30%) had at least 1 rebound >10,000 copies/ml

After baseline whilst under follow-up

- 1,600 (83.5%) achieved suppression within the first six months after baseline
- 561 (29%) patients experienced virological failure after a baseline
- IR 12.5/100 PYFU, 95% confidence interval (11.5-13.9)

Figure 1

- Incidence rate of virological failure decreases with increasing percentage of time on cART suppressed prior to baseline

Figure 2

- Incidence rate of virological failure decreases with increasing time prior to baseline since last rebound
- There was no significant difference in virological failure rate in patients whose last rebound was more than 6 years prior to baseline and those who had never rebounded prior to baseline

Figure 3

- Patients had a 2.5, 2, 1.5 times higher virological failure rate if they were suppressed less than 30%, 30%-60%, 60%-90% of the time they were on cART respectively, compared to those suppressed more than 90% of the time
- Patients whose last rebound was less than 4 years prior to baseline had double the rate of future virological failure
- There was no significant difference in the rate of virological failure in a patient whose last rebound was more than 4 years prior to baseline and those that had never rebounded

CONCLUSION

- Patients with a higher percentage of time on cART suppressed prior to starting a new antiretroviral had a lower rate of future virological failure
- Patients who had rebounded in the 4 years prior to starting a new antiretroviral had a higher rate of virological failure
- After adjustment for these factors, time to initial suppression, number of rebounds, total time suppressed, size of rebound, were not significant with future virologic failure after starting a new ARV

DISCUSSION

- Future work will look into how the importance of these patterns is affected when resistance at baseline and number of active drugs in regimen are considered
- The history of patterns of viral response to cART regimens should be an integrated component in deciding monitoring strategies and adherence counseling for patients whenever a change in cART is made

Table 1

Baseline Characteristics

Baseline is date of starting new ARV N=1917

		N	%
Gender	Male	1446	75.4
Race	White	1638	85.4
Exposure group	Homosexual	870	45.4
	IDU	375	19.6
	Heterosexual	556	29.0
Region of Europe	South/Argentina	544	28.3
	Central	473	24.7
	North	709	37.0
	East	191	10.0
Age	Median, IQR	43	38-50
CD4 count (mm3)	Median, IQR	442	283-646
Viral load (copies/ml)	Median, IQR	1.76	1.30-3.59
Number ARV's exposed to	Median, IQR	7	5-9
Number new ARV's started	Median, IQR	1	1-3
Time since started cART	Median, IQR	6.3	4.8-7.4
Baseline	Median, IQR	06/04	09/03-06/05

Figure 1

Incidence Rate (IR) of virological failure

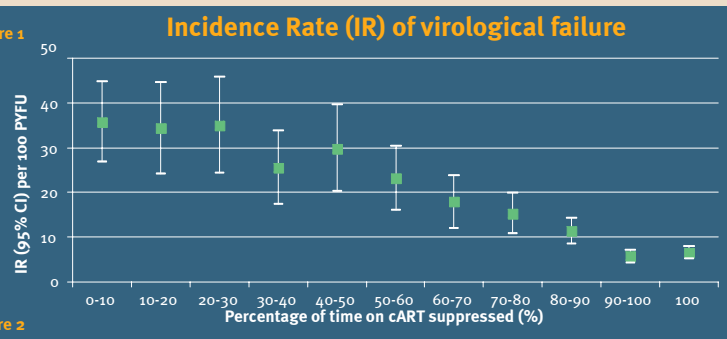


Figure 2

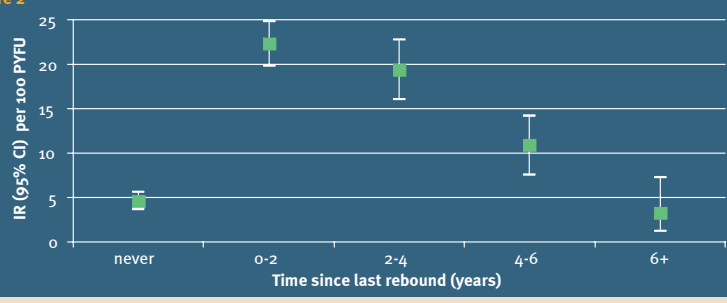
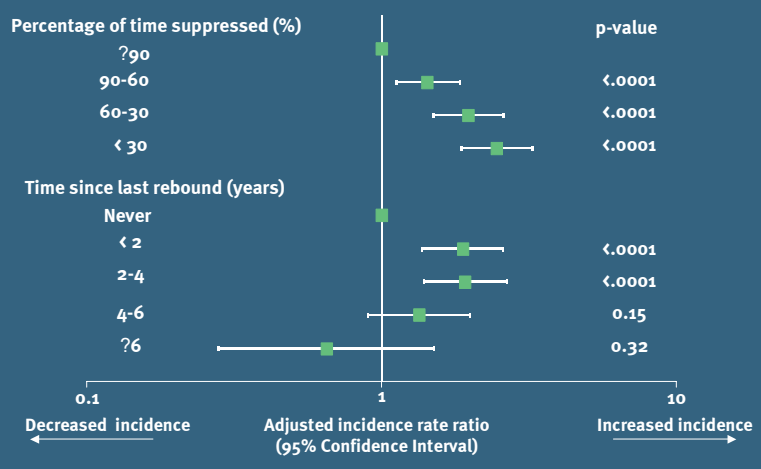


Figure 3

Factors predictive of future virological failure after baseline



Multivariate analysis adjusted for age, gender, race, exposure group, region of Europe, baseline treatment, naïve at starting cART, number ARV's previously exposed to, number new ARV's started, hepatitis B&C status, CD4 count & viral load at baseline, baseline date, time since starting cART and reason for treatment change

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