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Joanne Reekie
Research department of infection and population health
UCL Medical School, Royal Free Campus
Rowland Hill Street, London, UK, NW3 2PF
Tel: +44 (0)20 7830 2239
Fax: +44 (0)202 7472 6737
E-mail: j.reekie@ucl.ac.ukl

Fatal and Non-fatal AIDS and Non-AIDS Events in HIV-1 Infected Patients with High CD4 Counts According to Viral Load Strata

J Reekie[1], J Gatell[2], I Yust[3], E Bakowska[4], A Rachmanova[5], M Losso[6], M Krasnov[7], P Francioli[8], J Kowalska[9], A Mocroft[1] for the EuroSIDA study group

University College London Medical School, London, UK; [2]Hospital Clinic, Barcelona, Spain; [3]Ichilov Hospital, Tel Aviv, Israel; [4]Centrum Diagnostyki I Terapii AIDS, Warsaw, Poland; [5]Medical Academy Botkin Hospital, St Petersburg, Russia; [6]Hospital JM Ramos Mejia, Buenos Aires, Argentina; [7]Kharkov State Medical University, Kharkov, Ukraine; [8]Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; [9]Copenhagen HIV Programme, University of Copenhagen, Copenhagen, Denmark

INTRODUCTION

There is evidence that clinical progression to AIDS is associated with a low CD4 count, additionally, some non-AIDS events have been found at an increased rate in patients who are immune compromised. However, the risk of uncontrolled viral replication in HIV+ patients who are not immune compromised on the development of serious AIDS and non-AIDS events has not been fully investigated.

AIM

The aim of this study was to compare the incidence of fatal and non-fatal AIDS and non-AIDS events occurring in HIV infected patient with a CD4 count >350 cells/mm^3 in different viral load strata (<500, 500-10000, ≥10000 copies/ml)

METHODS

For a given month a patient contributed person years at risk if their most recent CD4 count was >350 cells/mm^3 in addition to a viral load measured

All EuroSIDA patients were eligible for inclusion into the analysis from
- 1/1/1997 for AIDS events
- 1/1/2001 for non-AIDS events, as non-AIDS events were only routinely collected in EuroSIDA after this date

Follow up was censored
- if there was no CD4 count or viral load measured in the previous 6 months
- if the patients CD4 count dropped below 350 cells/mm^3
- at the patients last recorded visit in EuroSIDA or death

Therefore person years were not necessarily consecutive, depending on the availability of viral load measurements, CD4 counts and whether they were greater than 350 cell/mm^3

All fatal and non-fatal AIDS and non-AIDS events occurring during follow-up were recorded and recurrences of the same diagnosis were excluded.
Person years were split into three different viral load strata (<500, 500-10000, ≥10000 copies/ml) and the incidence rate (IR) calculated as the number of events per 100 person years of follow-up (PYFU)
Poisson regression analysis was used to investigate the relationship between viremia and clinical events, after adjustment for confounding variables.

RESULTS

Table 1

- 10,998 patients contributed 43,524 PYFU to the fatal and non-fatal AIDS analysis, 379 AIDS events occurred during this time
- 10,278 patients contributed 35,252 PYFU to the fatal and non-fatal non-AIDS analysis, 476 non-AIDS events occurred during this time the most common were cardiovascular events (176), non-AIDS defining malignancies (163) and liver related events (32).

Figure 1

- Patients with a viral load ≥10000 copies/ml had a higher incidence rate of AIDS events, IR 2.38 per 100 PYFU, compared to those with a viral load <500 copies/ml, IR 0.69 per 100 PYFU
- This increased rate of AIDS events in patients with a higher viral load was observed in AIDS events of differing severity

Figure 2

- Patients with a viral load <500 copies/ml had a rate of non-AIDS events of 1.40 per 100 PYFU which was similar to the incidence rate in patients with a viral load between 500-10,000 copies/ml (IR 1.56 per 100 PYFU) and ≥10,000 copies/ml (IR 1.39 per 100 PYFU)
- A similar rate of cardiovascular events and non-AIDS defining malignancies was observed in different viral load strata

Figure 3

- After adjustment patients with a viral load ≥10,000 copies/ml had a 3 times higher rate of AIDS events than those with a viral load <500 copies/ml
- Compared to a viral load <500 copies/ml after adjustment, particularly for age, region of Europe and whether or not the patient was on cART, there was a 48% and 54% higher incidence of non-AIDS events in patients with a viral load between 500-10,000 copies/ml and ≥10,000 copies/ml
- The effects of viral load on the incidence of non-AIDS events were independent of CD4 count and were similar in different CD4 count strata (test for interaction p>0.05 for both endpoints)

CONCLUSIONS

In patients with a CD4 count >350 cells/mm^3 an increased incidence of fatal and non-fatal AIDS events was found in patients with uncontrolled viral replication, this association was consistent across AIDS of differing severity. The association between viral replication and fatal and non-fatal non-AIDS events was less clear. A slightly increased incidence of non-AIDS events was found with high replication, although this was only apparent after adjustment and no difference was found between intermediate and high viral replication. A larger dataset is need to fully investigate the relationship between viral replication and specific non-AIDS events in patients who are not immune compromised

Table 1

Follow-up characteristics

		AIDS events			Non-AIDS events		
		Viral load categories			Viral load categories		
		<500	500-10000	≥10000	<500	500-10000	≥10000
Total PYFU (% of total)		34676	5315	3533	29399	3335	2518
Percentage of total		80%	12%	8%	83%	10%	7%
Gender	Male	77%	72%	75%	77%	72%	74%
Ethnic origin	White	86%	88%	89%	86%	89%	90%
HIV exposure group	Homosexual	48%	43%	47%	48%	42%	46%
	IDU	17%	21%	19%	17%	20%	18%
	Heterosexual	28%	30%	28%	28%	32%	31%
On cart		91%	62%	37%	93%	65%	32%
CD4 count	<500	34%	49%	56%	32%	44%	52%
	500-750	41%	38%	34%	41%	40%	36%
	>750	25%	13%	10%	27%	16%	12%

For AIDS events patients were eligible for inclusion into the analysis from 1/1/1997
For non-AIDS events patients were eligible for inclusion into the analysis from 1/1/2001

Figure 1

Crude incidence rate of fatal and non-fatal AIDS events per 100 person years of follow up

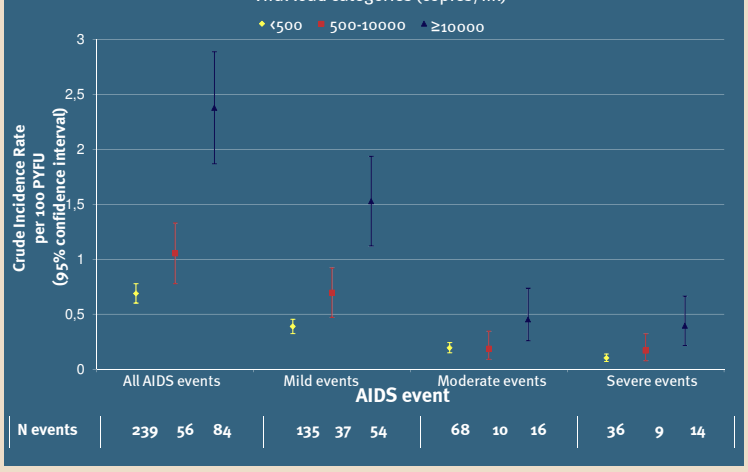


Figure 2

Crude incidence rate of fatal and non-fatal non-AIDS events per 100 person years of follow up

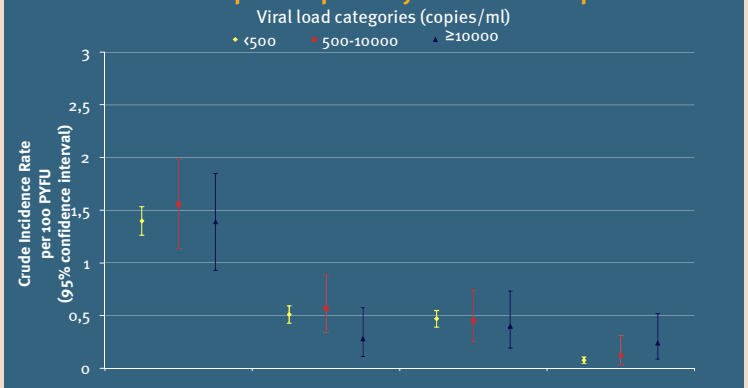
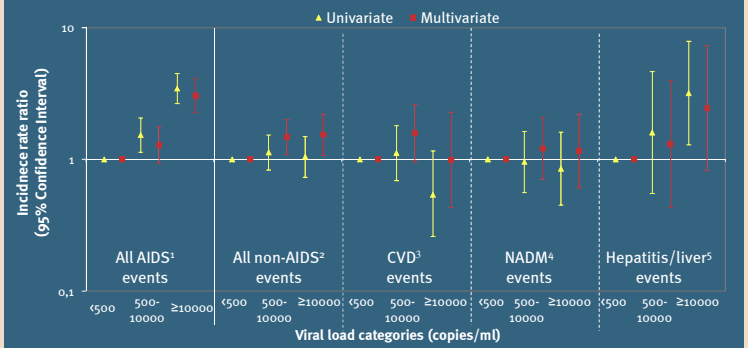


Figure 3

Adjusted incidence rate ratio by viral load categories



1 also adjusted for gender, HIV exposure group, region of Europe, hepatitis B and C status, smoking status, hypertension, year of follow-up, on cART, prior AIDS and CD4 count
2 also adjusted for peak viral load, age, HIV exposure group, region of Europe, hepatitis B and C status, diabetes, hypertension, smoking status, prior AIDS and on cART
3 also adjusted for peak viral load, CD4 nadir, age, ethnic origin, gender region of Europe, hepatitis B and C status, diabetes, hypertension, smoking status, on cART and year of follow-up
4 also adjusted for peak viral load, CD4 nadir, age, ethnic origin, HIV exposure group, gender, region of Europe, hepatitis B status, diabetes and prior AIDS diagnosis
5 also adjusted for HIV exposure group, hepatitis B and C status, smoking status and on cART

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