Poster #503

Episodes of HIV Viremia and the Risk of Non-AIDS Events among Successfully Treated Patients

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Background

The association between immunodeficiency and the risk of serious non-AIDS diseases in HIV-infected patients has been previously reported.

Objective

To investigate the additional impact of episodes of viremia during therapy and treatment interruptions, and CD4 counts on non-AIDS events in patients successfully treated with combination antiretroviral therapy (cART).

Methods

Patients

6440 patients were selected from the ATHENA observational cohort, if

- previously cART-naive
- initially treated successfully: RNA ≤ 50 copies/ml before 48 weeks of cART
- previously not diagnosed with non-AIDS events
- censored at one year with long interruption

Exposure

Since initial success onwards, four types of episodes were defined as:
viral suppression (RNA ≤ 50 copies/ml), low-level viremia (RNA 50-400), high-level (RNA>400) and treatment interruption.

Outcome

three types of clinical diagnosed non-AIDS endpoints (fatal and non-fatal) were considered:

1. cardiovascular disease (CVD, 102 events) : myocardial infarction, stroke, invasive coronary procedures
2. renal disease (72 events) : acute and chronic renal failure
3. liver disease (70 events) : fibrosis, cirrhosis

Statistical analyses

- Time-discrete proportional hazards model.
- Episodes of viremia and interruption and CD4 included as time-updated variables.
- Adjusted for age, gender, diabetes, HBV/HCV co-infection, CDC stage, transmission risk group, smoking, alcohol abuse.

Results

Characteristics of 4 types of episodes

- In total, 17364 episodes were observed, of which 10673 were viral suppression, accounting for 85.8% of total follow-up, 3353 low-level viremia, 1709 high-level viremia and 1629 interruptions.
- 74.6% low-level viremia consisted of only 1 RNA measurement in contrast with 17.3% viral suppression.
- Patients with interruption, of whom 578 (53.4%), was more often (p<0.001) than patients without interruptions, of whom 625 (11.7%), to experience high-level viremia.

Non-AIDS incidence rate

- To examine the association between CD4 counts and non-AIDS events, incidence rates were estimated across latest CD4 category (Figure 1a). The trend of overall incidence decreased from 2.2 when CD4<200 cells/mm^3 to 0.64 per 100 person-years when CD4 counts greater 500.
- Incidence rates did not differ across episodes of interruption, viral suppression, and viremia (Figure 1b)

Table 1. characteristics of the study population

N=6440	N (%) / median (IQR)	
gender, male	4864	75.3
transmission group		
homosexual contact	3347	52.0
heterosexual contact	2426	37.7
injection drug use	162	2.5
hepatitis B coinfection	419	6.5
hepatitis C coinfection	410	6.4
diabetes mellitus	138	2.1
disease stage at initial success		
CDC-B	1062	16.5
CDC-C	1683	26.1
	median	IQR
age at initial success (years)	39.0	32.4-46.1
follow-up time (years)	3.9	1.7-6.4
CD4 counts at start of cART* (cells/mm^3)	200	90-296
at initial success (cells/mm^3)	330	210-470
$\log_{10}$ RNA at start of cART** (copies/ml)	5.0	4.5-5.4

IQR: inter-quartile range; *CD4 counts at start of cART available for 5959 (92.5%) patients; **viral load at start of cART available for 5585 (86.8%) patients.

Figure 1a. Incidence rate of non-AIDS events across latest CD4 category

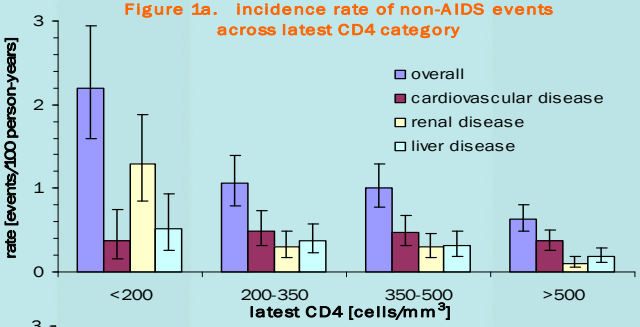
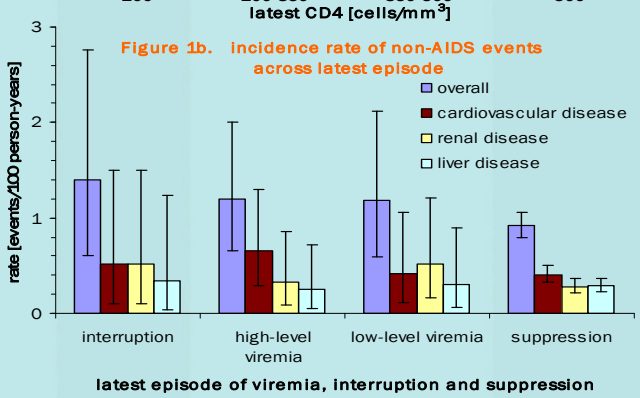


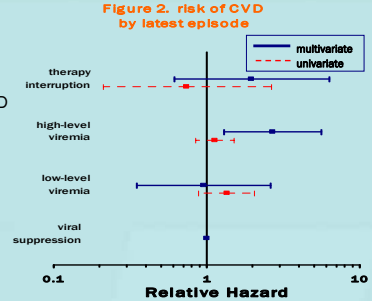
Figure 1b. Incidence rate of non-AIDS events across latest episode



non-AIDS events with latest episode of viremia, interruption or suppression

- In adjusted models we found a significant association of high-level viremia and the risk of CVD (RH 2.69, 95% CI 1.29-5.63), independent of latest CD4 counts when comparing to viral suppression.
- No association was found between high-level, low-level viremia or interruption with renal disease and liver disease.

Figure 2. risk of CVD by latest episode



non-AIDS events with latest CD4 counts

- Estimates of risk for CVD, renal disease and liver disease are plotted by per 100 cells/mm3 higher CD4 counts, log transformed CD4 and CD4 categories(CD4>500 as reference group).
- CD4 counts (Figure 3a) was not associated with CVD (0.96, 0.68-1.36 per logCD4).
- Higher CD4 counts (Figure 3b) was associated with lower risk of renal disease (0.36, 0.27-0.47 per logCD4).
- CD4 counts <200 cells/mm^3 (Figure 3c) had a 2.33 (1.04-5.25) times higher risk of liver disease when comparing to CD4 counts >500.

Figure 3a. risk of CVD by latest CD4

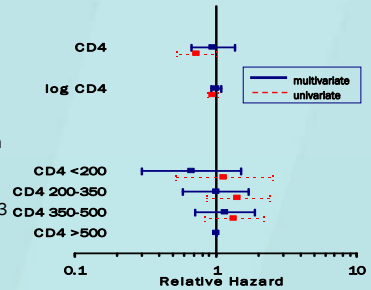


Figure 3b. risk of renal disease by latest CD4

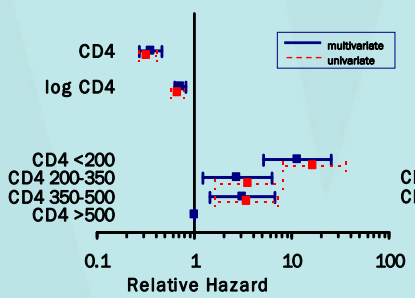
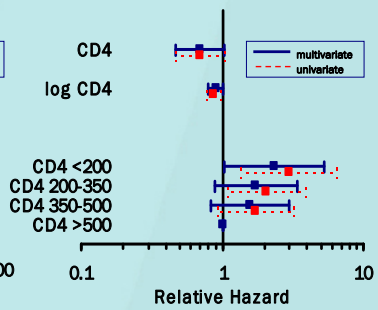


Figure 3c. risk of liver disease by latest CD4



Conclusion

- There appeared to be an independent association between high-level viremia and CVD. However, the power to detect an association of viremia may have been small given the limited amount of follow-up time spent in episodes of viremia.
- Lower CD4 counts were associated with an increased risk of renal and liver disease, but not CVD.