Poster #791

Initiation of cART for HIV Infection and the Risk of Non-AIDS Diseases

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Background

An association between immunodeficiency, HIV RNA level, and the risk of non-AIDS diseases has been previously reported for patients treated with combination antiretroviral therapy (cART).

But therapy could confound this association by increasing the risk via adverse effects and simultaneously reverse the harm by restoring immunity.

In addition, the range of RNA level is limited in treated patients.

Objective

to investigate whether the association between CD4 counts, RNA level and non-AIDS diseases before start of cART remains the same with after cART.

Methods

Patients

- 9777 patients, diagnosed with HIV in or after 1998, were selected from the ATHENA national cohort. Patients should have at least one CD4 count and RNA before cART.
- Follow-up started at the first available CD4 count and censored at either the occurrence of the events interested, or end of the follow-up.

Outcome

four newly diagnosed non-AIDS endpoints (fatal and non-fatal) were considered.

- cardiovascular disease (CVD): myocardial infarction, stroke, invasive coronary procedures
- Chronic renal failure (RRD): a confirmed (2 or more consecutive measurements, at least 3 months apart) estimated glomerular filtration rate (eGFR) ≤60 ml/min/1.73 m^2 if eGFR >60 at study entry, or else a confirmed 25% eGFR decline if baseline eGFR ≤60.
- liver disease (LRD): fibrosis, cirrhosis, hepatocellular carcinoma
- overall (All): combination of non-AIDS events abovementioned

Statistical analyses

- Poisson regression models were used to compare the effect of CD4 and RNA on non-AIDS events before and after cART.
- CD4 count, RNA level and age were included as time-updated variables.
- Both univariate and multivariate analyses were conducted; the latter were adjusted for age, gender, diabetes, HBV/HCV co-infection, CDC stage, smoking, alcohol abuse and hypertension.

Results

Characteristics of study population

- 9777 patients were included in the analysis with a total follow-up of 45232 person-years (Table 1). Of which, 2299 (23.5%) had never been on cART.
- Patients entered the study with CD4 count of 350 (IQR 170-550) and log10RNA of 4.8 (IQR 4.1-5.2) while initiating cART with lower CD4 (215, 101-310) and higher log10RNA (5.0, 4.5-5.4).
- The median follow-up time is much short with 0.4 years (IQR 0.1-2.1) before cART than after (3.5, IQR 1.5-6.6).

Non-AIDS incidence rate

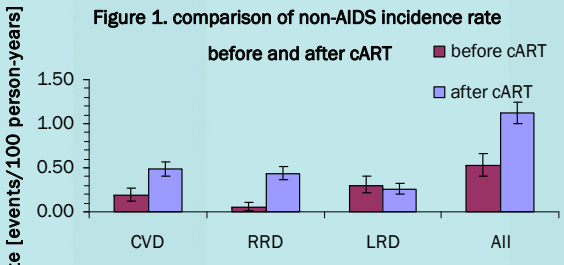
- Figure 1. showed the incidence before start of cART (0.52; 0.41-0.66, per 100 person-years) was lower than after start for overall (1.12; 1.00-1.25). It was mainly caused by CVD (0.18, 0.12-0.27 before cART vs. 0.49; 0.41-0.57 after) and RRD (0.05; 0.02-0.11 before cART vs. 0.43; 036-0.51 after).
- Due to short follow-up time before cART, there were 6 chronic renal failure before cART than 130 after cART.

Table 1. Characteristics of the study population

N=9777	N (%) / median (IQR)	
Gender, male	7732	79.1
Region of origin		
Netherlands	5487	56.1
Sub-Saharan Africa	1805	18.5
Disease stage at baseline		
CDC-B	622	6.4
CDC-C	934	9.6
Hepatitis B co-infection	404	4.1
Hepatitis C co-infection	249	2.5
Diabetes mellitus	158	1.6
History of alcohol abuse	529	5.4
Smoking status		
never	3125	32.0
current or former	4271	43.7
unknown	2381	24.4
Patients no. never on cART	2299	23.5
	at entry of study	at start of cART
Age (years) at entry	37.1 (30.2-44.3)	38.6 (31.8-45.9)
CD4 counts (cells/mm^3)	350 (170-550)	215 (101-310)
Log_{10}RNA plasma level	4.8 (4.1-5.2)	5.0 (4.5-5.4)
Follow-up time (years)	0.4 (0.1-2.1)	3.5 (1.5-6.6)

Non-AIDS incidence rates

Figure 1. comparison of non-AIDS incidence rate



non-AIDS events #	CVD	RRD	LRD	All
before cART	25	6	41	71
after cART	151	130	81	342

Non-AIDS events with latest CD4 counts

Figure 2. effect comparison of CD4 on non-AIDS events

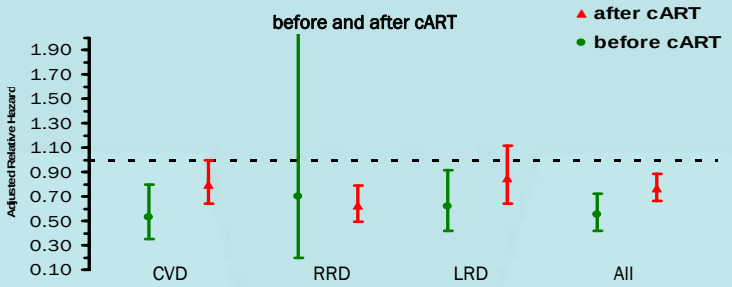


Figure 2. showed a lower log-transformed CD4 count was associated with higher risk of non-AIDS events. Besides the effect of CD4 before cART was stronger than that after cART.

Non-AIDS events with latest RNA level

Table2. Comparison of the effect of HIV RNA before and after on non-AIDS events.

		Adjusted Relative Risk (95% Confidence Interval)			
		cardiovascular disease	renal disease	liver disease	combined endpoint
latest RNA (copies/ml)					
After cART	≤10^3	0.98 (0.51-1.88)	2.31 (0.84-6.33)	0.55 (0.28-1.06)	0.96 (0.63-1.45)
	>10^5	2.40 (0.93-6.15)	2.49 (0.62-10.1)	1.69 (0.60-4.71)	1.69 (0.88-3.23)
	10^3-10^5	1	1	1	1
Before cART	≤10^3	-*	1.63 (0.18-14.2)	1.85 (0.76-4.50)	1.16 (0.34-2.57)
	>10^5	0.24 (0.05-1.04)	-*	1.26 (0.55-2.90)	0.71 (0.36-1.40)
	10^3-10^5	1	1	1	1

In adjusted models, there was no association between RNA level and non-AIDS events.

Conclusion

- Lower CD4 counts are more strongly related with higher risk of non-AIDS diseases before start of cART than thereafter.
- However, despite more variation in HIV RNA before cART, there was no significant association with incidence of non-AIDS events.
- The estimation precision is limited, presumably due to fewer events with short follow-up time before cART.