NON-AIDS DEFINING EVENTS IN HIV CONTROLLERS VS ART CONTROLLED PATIENTS

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BACKGROUND

- HIV controllers (HICs) are rare persons living with HIV who spontaneously maintain low or undetectable viremia. Low-grade chronic inflammation persisting in this population could lead to higher rates of non-AIDS defining events (nADEs) than in patients who achieve low or undetectable viremia on antiretroviral therapy (ART).

METHODS

- From the multicenter CODEX cohort, 315 HICs with a known HIV-1 infection ≥5 years, with at least 5 consecutive viral loads (VL) below 400 HIV-RNA copies/mL in the absence of ART were included.
- From the multicenter PRIMO Cohort, HIV-1 infected patients diagnosed during primary infection (≤3 months), 328 patients who initiated ART ≤1 month after the diagnosis, with undetectable VL ≤12 months following ART initiation and for at least 5 years (“ART-subjects”) were included .
- Incidence rates (IR) of first nADEs, i.e. malignancies, cardiovascular, pulmonary, hepatic, psychiatric or bone events were compared between HICs and ART-subjects; potential determinants were assessed by using Cox regression models.

Table 1: Characteristics* of the study population at the beginning of the control

	HICs (N=315)	ART patients (N=328)	p-value
Duration of control (years)	13.7 (9.7-18.4)	7.5 (6.2-11.4)	**0.0033**
Age (years)	34 (29-42)	37 (30-44)	**<0.0001**
Gender (male)	146 (46.3)	283 (86.3)	**<0.0001**
Race/Ethnicity			**<0.0001**
White	117 (37.1)	298 (90.9)	
Black	187 (59.4)	24 (7.3)	
Tobacco use	124 (39.4)	120 (36.6)	**0.0005**
Viral hepatitis coinfection			
HIV/HBV Co-infection	133 (42.2)	61 (18.6)	**<0.0001**
HIV/HCV Co-infection	7 (2.2)	3 (0.9)	
CD4 T cell count (cells/mm³)	796 (654-958)	624 (500-805)	**<0.0001**
200-350	4 (1.3)	28 (8.5)	
351-500	14 (4.4)	51 (15.6)	
501-750	105 (33.3)	139 (42.4)	
>750	164 (52.1)	107 (32.6)	
Nadir	531 (392-669)	505 (366-645)	0.83
Ratio CD4/CD8 < 1	98 (34.2)	185 (56.4)	**<0.0001**
Undetectable VL (n(%))	229 (72.7)	328 (100)	**<0.0001**

*Data are median (IQR) or n (%)

Key-messages:
HICs experienced two times less nADEs than virologically suppressed patients on ART. Age was the only other factor independently associated with nADEs occurrence, irrespective of immune or virologic parameters.

This study do not argue in favor of expanding the indication for ART in HICs subjects but rather a case-by-case approach considering clinical outcomes such as nADEs besides immune activation.

RESULTS

- The most common events observed in the 2 cohorts were non-AIDS related infections (36.9%), psychiatric events (17.2%), cardiovascular events (6.8%), and malignancies (6.1%), with no statistically significant differences in distribution between the 2 cohorts. Two and 4 non-AIDS related deaths were observed among HICs and ART subjects, respectively.
- All-cause nADEs incidence rates were 2.8 per 100 person-years (py) and 5.3 per 100 py among HICs and ART subjects, respectively (HR=0.53 [(95%CI), 0.40-0.71]. After adjustment for the cohort, demographic and immunological characteristics, the only other factor associated with all cause nADEs occurrence was age 36-43 (vs. 18-29) years at beginning of control (HR=1.56 [1.06-2.30]). Baseline CD4 T-cell count or nadir, CD4/CD8 ratio, history of viral blips, HBV/HCV co-infection and tobacco use, were not associated with an increased risk of nADEs.

Figure 1: Non AIDS defining events frequencies

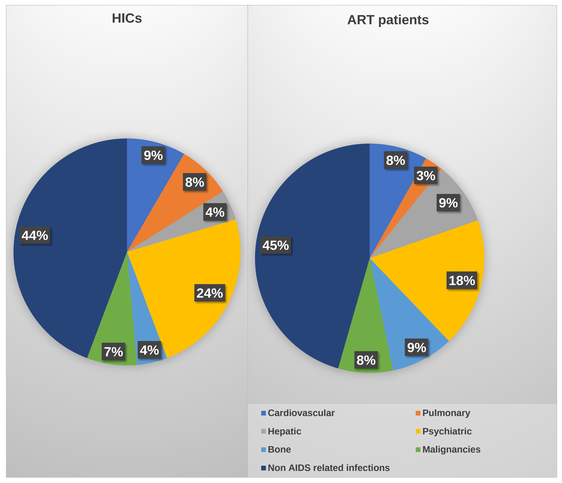


Table 2: All-cause and cause-specific incidence rates of nADEs by HIV control status

NADEs Category	HICs			ART patients			IRR [95%CI]
	m	PY	IR [95%CI]	m	PY	IR [95%CI]	
All-cause	107	3823.0	2.8 [2.3-3.3]	122	2313.0	5.3 [4.3-6.2]	1.9 [1.4-2.5]
Cardiovascular	12	4276.8	0.3 [0.1-0.4]	14	2995.1	0.5 [0.2-0.7]	1.7 [0.7-4.0]
Pulmonary	10	4314.8	0.2 [0.1-0.4]	8	3032.7	0.3 [0.1-0.5]	1.1 [0.4-3.2]
Hepatic	6	4312.8	0.1[0.0-0.3]	15	3011.0	0.5 [0.2-0.8]	3.6 [1.3-11.3]
Psychiatric	29	4161.3	0.7 [0.4-1.0]	25	2879.7	0.9 [0.5-1.2]	1.2 [0.7-2.2]
Malignancies	10	4315.3	0.2 [0.1-0.4]	13	3017.9	0.4 [0.2-0.7]	1.9 [0.8-4.7]
Bone	5	4310.4	0.1 [0.0-0.2]	14	3000.1	0.5 [0.2-0.7]	4.0 [1.4-14.3]
Non AIDS defining Infections	51	4171.3	1.2 [0.9-1.6]	62	2640.8	2.4 [1.8-2.9]	1.9 [1.3-2.8]

KEYWORDS

- HIV; controllers; non-AIDS defining events; ART; primary infection

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Table 3 : Factors associated with all-cause non AIDS defining events

	HR [95%CI]	p-value	HR [95%CI]	p-value
Characteristics	Bivariate		Multivariate	
HIV control satus				
HICs	0.46 [0.32-0.60]	**< 0.0001**	0.41 [0.27-0.61]	**< 0.0001**
ART	1		1	
Age (yrs)				
≤36	1	**0.002**	1	**0.04**
> 36	1.52 [1.17-1.98]		1.36 [1.02– 1.81]	
Gender				
Male	1	0.50	1	
Female	0.90 [0.66-1.22]		1.16 [0.82 – 1.66]	0.40
Ethnicity				
White	1	**0.02**	1	0.19
Black	0.58 [0.39-0.86]		0.68 [0.43 – 1.08]	
Viral hepatitis coinfection				
VIH mono infection	1		1	
VIH/VHB Co-infection	1.17 [0.88-1.57]	0.66	1.18 [0.85 – 1.61]	0.80
VIH/VHC Co-infection	1.43 [0.58-3.51]		1.09 [0.43 – 2.78]	
Tobacco use				
No	1	**0.02**	1	0.12
Yes	1.36 [1.05-1.78]		1.26 [0.93 – 1.70]	
CD4 T cell count				
200-350	1.24 [0.72-2.12]		1.41 [0.81 -2.48]	
351-500	0.79 [0.89-0.50]	0.15	0.93 [0.57 – 1.52]	0.20
501-750	0.77 [0.56-1.04]		0.81 [0.66 – 1.83]	
>750	1		1	