Reference Curves for CD4+ T Cell Count Response to Combination of Antiretroviral Treatment in HIV-1 Infected Naïve Patients

The Standard Reference Distribution of CD4 Response to HAART Project Team for the Collaboration of Observational HIV Epidemiological Research Europe (COHERE) in EuroCoord

Table 1. Baseline characteristics

.		Analysed population n=28,992	
Male	n (%)	21130	(72.9)
Age at cART initiation (years)	Median (IQR)	39	(33; 46)
Years of follow-up after initiating cART	Median (IQR)	2.3	(1.3; 3.5)
HIV transmission risk group	n (%)		
Heterosexual		11601	(40.0)
Men having sex with men		12547	(43.3)
Injecting drug use		1952	(6.7)
Other/unknown		2892	(10.0)
CDC stage C	n (%)		
No		21626	(74.6)
Yes		6144	(21.2)
Unknown		1222	(4.2)
HCV positive	n (%)	2250	(7.8)
HIV-1 RNA (copies/ml)	n (%)		
<50		2738	(9.4)

		Analysed population n=28,992	
50-9 999		4346	(15.0)
10 000-99 999		9730	(33.6)
≥100 000		8731	(30.1)
Unknown		3447	(11.9)
cART initiation year	n (%)		
2005		5342	(18.4)
2006		5864	(20.2)
2007		6266	(21.6)
2008		6958	(24.0)
2009		4562	(15.7)
Number of CD4 measures within [0-9] months	Median (IQR)	3	(2; 4)
CD4 mesure prior cART initiation (cells/mm^3)	Median (IQR)	249	(150; 336)
0-199	n (%)	9647	(35.6)
200-349	n (%)	11395	(42.1)
350-499	n (%)	3769	(13.9)
500 and above	n (%)	2286	(8.4)
Months from baseline to months 6 HIV-1 RNA in months	Median (IQR)	5.9	(5.1; 6.7)
Duration of 1st line regimen in months	Median (IQR)	13.5	(5.5; 26.5)
1st line cART regimen, n(%)	n (%)		
PI/r-based		12706	(43.8)
NNRTI-based		14665	(50.6)
PI- and NNRTI-based		328	(1.1)

		Analysed population n=28,992	
Unboosted PI-based		607	(2.1)
Other *		686	(2.4)

cART: combination of Antiretroviral Therapy, IQR: Interquartile Range, HIV: Human Immunodeficiency Virus, CDC: Center for Disease Control, HCV: Hepatitis C Virus, CD4: Cluster of Differentiation 4, RNA: Rubonucleic Acid, PI: Protease Inhibitor, NNRTI: Non-Nucleoside Reverse-Transcriptase Inhibitor

* Abacavir containing n=496, Integrase inhibitor containing n=151, Fusion inhibitor containing n=24, other combination n=15

Table 2. Factors associated with the CD4+ T cell count according to the 25th, 50th and 75thpercentile. Multivariate quantile regressions of CD4+ T cell count.

	25th percentile			50th percentile			75th percentile		
	Beta	[95%CI]	p	Beta	[95%CI]	p	Beta	[95%CI]	p
Female (ref : male)	13	[11; 16]	$<10^{-4}$	13	[11; 16]	$<10^{-4}$	10	[6; 13]	$<10^{-4}$
Age (for 10 years)	-8	[-9; -7]		-9	[-10; -8]	.	-9	[-10; -8]	$<10^{-4}$.
HIV transmission risk group (ref :MSM)			$<10^{-4}$			$<10^{-4}$			$<10^{-4}$
Heterosexual	-59	[-61; -57]	$<10^{-4}$	-60	[-62; -57]	$<10^{-4}$	-62	[-65; -58]	
Injecting drug use	-67	[-72; -62]	.	-66	[-71; -61]	.	-55	[-62; -48]	.
Other/unknown	-64	[-67; -60]	.	-61	[-65; -57]	.	-54	[-60; -49]	.
CDC stage C (ref : A/B)			$<10^{-4}$			$<10^{-4}$			$<10^{-4}$
Yes	-111	[-113;-109]		-115	[-117;-112]		-89	[-93; -86]	
Unknown	1	[-4; 6]	.	9	[4; 14]	.	11	[5; 18]	
HCV co-infection (ref : no)	-6	[-10; -3]	7.10^{-4}	-6	[-10; -3]	4.10^{-4}	-12	[-17; -7]	$<10^{-4}$
HIV-1 RNA (ref: <50cop/ml)			$<10^{-4}$			$<10^{-4}$			$<10^{-4}$
50-9 999	-32	[-36; -28]		-62	[-67; -58]	.	-105	[-111; -98]	
10 000-99 999	-42	[-46; -38]		-72	[-76; -68]	.	-122	[-128;-116]	
>=100 000	-69	[-72; -65]		-91	[-96; -87]	.	-126	[-132;-120]	
Unknown	-62	[-67; -58]		-79	[-84; -74]	.	-100	[-107; -92]	
1st line cART regimen (ref : PI/r-based)			$<10^{-4}$			$<10^{-4}$			$<10^{-4}$

	25th percentile			50th percentile			75th percentile		
	Beta	[95%CI]	p	Beta	[95%CI]	p	Beta	[95%CI]	p
NNRTI-based	8	[6; 10]		-2	[-5; -0]	.	-25	[-28; -22]	
PI- and NNRTI-based	40	[31; 50]		57	[47; 67]	.	103	[85; 121]	
Unboosted PI-based	32	[25; 40]		48	[39; 56]	.	56	[46; 66]	
Other *	52	[45; 59]		51	[43; 59]	.	49	[39; 58]	
Year of cART initiation (ref : 2009)			$<10^{-4}$			$<10^{-4}$			$<10^{-4}$
2005	-48	[-51; -45]		-65	[-68; -62]		-70	[-75; -66]	
2006	-36	[-39; -32]		-44	[-47; -41]		-45	[-50; -40]	
2007	-26	[-29; -23]		-38	[-41; -35]		-40	[-45; -36]	
2008	-21	[-25; -18]		-29	[-32; -25]		-31	[-36; -27]	

cART: combination of Antiretroviral Therapy,, HIV: Human Immunodeficiency Virus, CDC: Center for Disease Control, HCV: Hepatitis C Virus, RNA: Rubonucleic Acid, PI: Protease Inhibitor, NNRTI: Non-Nucleoside Reverse-Transcriptase Inhibitor, MSM: Men having Sex with Men

Figure 1. Flow chart of patient selection

Figure 2. Box plot of CD4+ T cell count at month 6 according to various baseline characteristics. Boxplots show respectively the 5th, 10th,25, 50th, 75th, 90th and 95th percentiles.

Figure 3. Percentiles (5th, 10th, 25th, 50th, 75th, 90th, 95th) of CD4+ T cell count over time from cART initiation. Two individual trajectories are added for illustration (one (purple line) is droping from the 82th percentile to the 61th percentile, the other (green line) is starting at the 18th percentile and reach the 12th percentile at 7 months.

Figure 4. Example of individual CD4 cell count responses (crude and adjusted) for two patients. Crude (dotted lines) and adjusted (solid lines) percentile at baseline (left) and during follow-up (right) are provided according to the measured CD4+ T cell count (dashed line).