

# Long-Term Changes of Inflammatory Biomarkers in Individuals on Suppressive Three-drug or Two-drug Antiretroviral Regimens

## Supplemental Materials

### Supplemental tables

**Table S1. Population baseline characteristics according to the ART regimen in the whole cohort.**

	Subjects remaining on 3DR <b>N=7665</b>	Subjects changing to 2DR <b>N=424</b>	Subjects changing to MT <b>N=327</b>	p value
<b>Age (mean, [SD])</b>	37 (30 – 44)	38 (31 – 45)	37 (30 – 45)	0.02
<b>Gender, n (%)</b>				0.009
Male	6480 (84.5)	323 (80.9)	260 (79.5)	
Female	1185 (15.5)	76 (19.1)	67 (20.5)	
<b>Mode of transmission, n(%)</b>				0.003
MSM	4698 (61.3)	236 (59.1)	166 (50.8)	
Heterosexual	466 (6.1)	25 (6.3)	32 (9.8)	
IDU	2235 (29.2)	118 (29.6)	116 (35.5)	
Unknown	266 (3.5)	20 (5.0)	13 (4.0)	
<b>Spanish Origin, n (%)</b>	4739 (61.8)	230 (54.2)	168 (51.4)	<0.001
<b>Education level, n (%)</b>				<0.001
No studies or compulsory	2217 (28.9)	148 (34.9)	111 (33.9)	
Upper secondary or university	4097 (53.5)	226 (53.3)	182 (55.7)	
Unknown	1351 (17.6)	50 (11.8)	34 (10.4)	
<b>AIDS diagnosis, n (%)</b>	873 (11.4)	48 (12.0)	46 (14.1)	0.31
<b>HCV positive ever, n (%)</b>	680 (8.9)	41 (10.3)	44 (13.5)	0.001
<b>Maximum HIV-1 RNA, n (%)</b>				0.04
<100000 copies/mL	4749 (62.0)	262 (61.8)	200 (61.2)	
≥100000 copies/mL	2580 (33.7)	153 (36.1)	120 (36.7)	
Unknown	336 (4.4)	9 (2.1)	7 (2.1)	
<b>Time from ART initiation to virologic suppression (years), median (IQR)</b>	0.3 (0.2 – 0.5)	0.3 (0.2 – 0.5)	0.3 (0.2 – 0.5)	0.03

<b>Time from virologic suppression (years) to ART switch, median (IQR)</b>	-	3.4 (1.8 – 5.9)	2.7 (1.3 – 4.2)	0.012
<b>Nadir CD4 cell count (cells/<math>\mu</math>L), median (IQR)</b>	321 (198 – 463)	290 (159 – 417)	270 (151 – 366)	<0.001
<b>Time from ART initiation to censoring, median [years (IQR)]</b>	3.8 (2.0 – 6.5)	6.0 (3.8 – 8.4)	7.3 (5.3-9.5)	<0.001
<b>Number of HIV RNA determinations from ART initiation to last study contact median (IQR)]</b>	13 (7 – 20)	20 (14 – 27)	23 (16 – 30)	<0.001

Abbreviations: 3DR, triple therapy; 2DR, 2-drug combinations; MT, monotherapy; ART, antiretroviral therapy; IDU, injecting drug use; MSM, men who have sex with men.

**Table S2. Rate of severe non-AIDS events during the follow-up**

	3DR	2DR	MT
	N=90	N=58	N=23
<b>Mortality</b>	0 (0)	0 (0)	0 (0)
<b>Cardiometabolic (N, %)</b>			
Diabetes	2 (2)	1 (2)	0 (0)
Myocardial infarction	1 (1)	0 (0)	1 (4)
Stroke	0 (0)	2 (3)	0 (0)
<b>Non-AIDS malignancies (N, %)</b>	0 (0)	2 (3)	0 (0)
<b>Visceral leishmaniasis (N, %)</b>	1 (1)	0 (0)	0 (0)

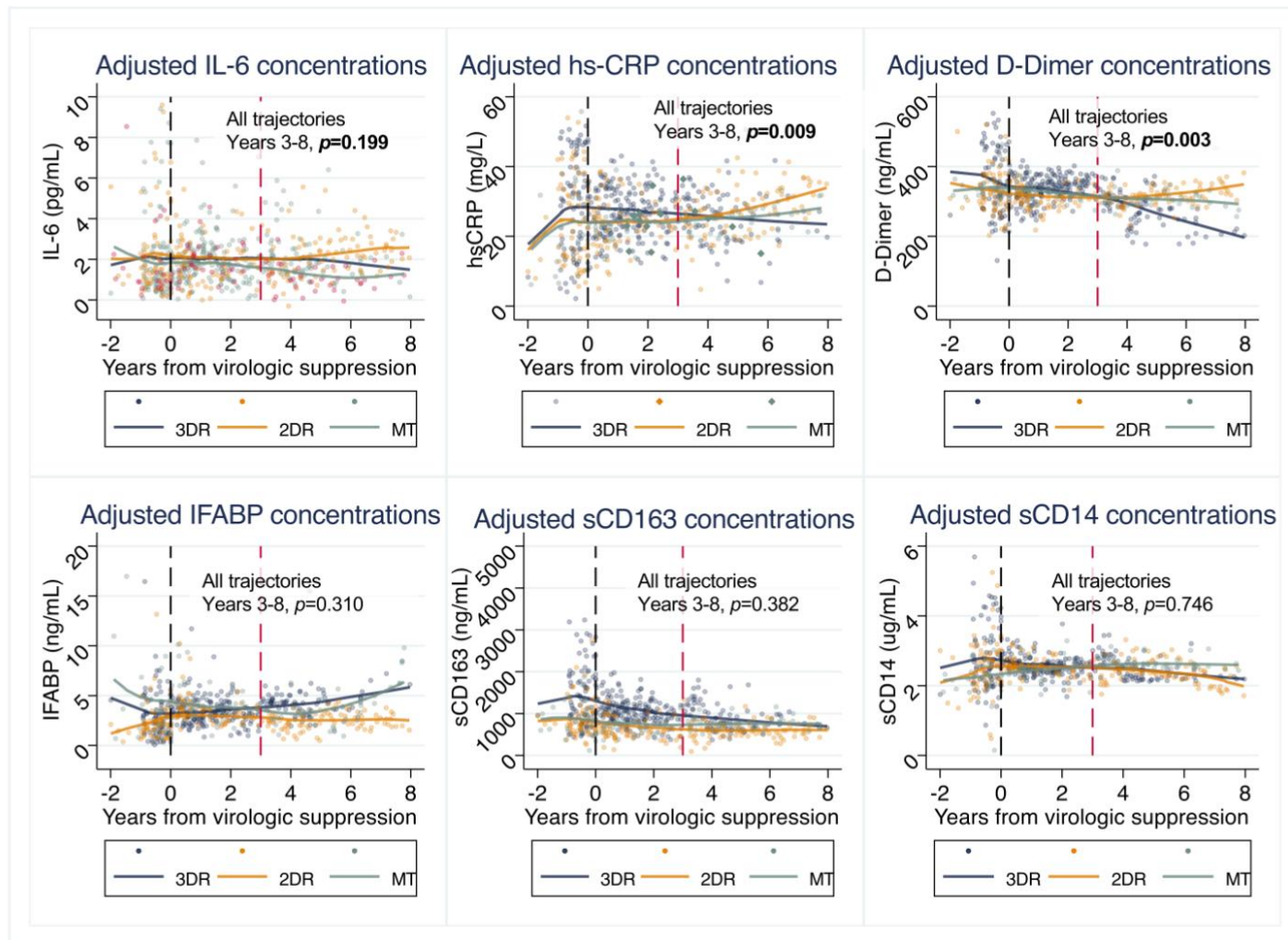
**Table S3. Adjusted coefficients of inflammatory biomarker changes by ART strategy (MT vs. 3DR) at year 0-3 and 3-8 from virologic suppression.**

	<b>Coefficient</b>	<b>95% CI</b>	<b>p</b>
<b>Years 0-3 of viral suppression</b>			
IL-6 (log10)	0.066	-0.036, 0.167	0.204
hs-CRP	0.067	-0.034, 0.170	0.194
D-dimers	-27.256	-45.877, -8.636	<b>0.004</b>
IFABP	-0.973	-2-23, 0.292	0.132
sCD163 (log10)	0.067	0.004, 0.131	0.038
sCD14	0.102	-0.122, 0.326	0.373
<b>Years 3-8 of viral suppression</b>			
IL-6 (log10)	-0.027	-0.159, 0.106	0.690
hs-CRP	0.052	0.051, 0.155	0.328
D-dimers	26.179	9.806	42.552
IFABP	0.453	0.598, 1.506	0.398
sCD163 (log10)	0.041	-0.022, 0.103	0.201
sCD14	0.114	0-069, 0.297	0.225

\*Reference category: MT

Abbreviations: ART, antiretroviral therapy; 3DR, triple therapy; MT, monotherapy; CI, confidence interval; INSTI, integrase strand transfer inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI, protease inhibitor

## Supplemental figures



**Figure S1. Effects of switch to MT on inflammatory biomarkers compared to remaining on 3DR.** Panels represent the values predicted in piecewise linear mixed models at intervals between years 0-1, 1-2, 3-4 and 4-8, adjusted for age, sex, country of origin, mode of transmission, educational level, maximum HIV RNA, previous AIDS, nadir CD4, and pre-ART biomarker value. Lines represent predicted mean values and dots the individual observations. The P values computed using Wald tests represent the global-group comparison of biomarker trajectories from year 3 to 8. The tables piecewise comparisons for the periods 0-3 and 3-8, are provided in **Table S2**.