

Dettaglio abstract

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Title: Body weight and plasma lipids changes in person living with HIV (PLWH) starting double or triple INSTI-based cART regimens

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Outcome in first-line regimens

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Abstract

Background: Data about associations between INSTI-based therapy, weight gain (WG) and lipids, as well as possible differences between dual and triple INSTI therapies are still limited. We aimed to compare WG and lipid modifications between first-line 3TC/DTG (2DR) vs FTC/TAF/BIC (3DR).

Material and Methods: Retrospective cohort study, including PLWH starting a 2DR or 3DR in ICONA (01/2016-01/2023), having available weight measurements and/or plasma lipids at T0 (cART start) and T12 (12 +/-3 months after cART start). Patients who switched cART regimen during the first year were included; we excluded patients with lipid lowering therapy during study period. Linear regressions were fitted to compare T0-T12 WG and lipids change by 2DR vs 3DR, controlling for: (i) baseline weight/lipids; (ii) baseline weight/lipids and time fixed baseline variables (age, sex, mode of HIV transmission, CD4 count and log-transformed HIV-RNA at cART start, glycemia, hemoglobin, ALT, AST and hypertension); (iii) baseline weight/lipids and a propensity score (PS) adjustment. PS was calculated as a probability from a logistic regression that had 3DR vs 2DR as the dependent variable and the same variables as covariates. Logistic regression was also fitted to correlate BMI category change by 2DR vs 3DR, adjusted for the same confounders.

Results: During the study period, 164/472 (35%) patients started 2DR and 308 (65%) started 3DR. Patients who started 2DR were younger and showed higher CD4 counts and lower HIV-RNA, compared to 3DR; baseline weight, total cholesterol and LDL were higher in 2DR vs 3DR (Table 1). 3DR patients presented higher T0-T12 WG compared to 2DR, but the weight difference was lost after controlling for confounders and baseline characteristics [adjusted mean WG 2DR 3.18 (SD 10.35); 3DR 4.03 Kg (SD 5.26) Kg, Table 2]. Similarly, a higher proportion of normal weight 3DR patients became overweight (32% vs 15%), but no therapy effect on BMI category change was observed in multivariable analyses (Table 3/4). 3DR patients displayed a worse T0-T12 lipid profile and were characterized by a trend towards a higher LDL increase, also after adjustment for confounders and baseline parameters, without differences in the proportion of patients that reached T12 LDL \geq 160 mg/dL (2DR 11/121, 9% vs 3DR 15/185, 8%); furthermore, no effect of 3DR vs 2DR was seen in total cholesterol/HDL ratio (Table 5).

Conclusions: PLWH starting 3DR showed higher WG after one year, compared with 2DR, but the association was largely attenuated after correction for baseline unbalanced characteristics. Despite proportion of patients who gained high LDL and total cholesterol/HDL ratio didn't differ between treatments after one year, LDL seems to increase more in patients starting 3DR, also in the weighted

analyses, suggesting a possible effect of TAF on serum lipids that was independent of weight; future studies are needed to explore a possible effect of 2DR vs 3DR on cardiovascular risk and IMT. This study was funded by ViiV Healthcare. The authors are solely responsible for final content and interpretation.

Table 1 Characteristics	2DR (DTG/3TC) N 164 (35%)	3DR (BIC/TAF/FTC) N 308 (65%)	p
Age (mean, SD)	38.51 (11.09)	42.81 (12.71)	<0.001
Males (n, %)	148 (90.2)	263 (85.4)	0.176
Foreigners (n, %)	36 (22.0)	66 (21.4)	0.989
Heterosexual	47 (28.7)	117 (38.0)	0.233
IDU	9 (5.5)	16 (5.2)	
MSM	100 (61.0)	160 (51.9)	
Other/Unknown	8 (4.9)	15 (4.9)	
Baseline log HIV-RNA cp/mL (mean, SD)	4.14 (1.03)	4.84 (1.14)	<0.001
Baseline CD4 count, cell/mm ³ (median [IQR])	489 [345, 685]	316 [116, 513]	<0.001
AIDS events (n, %)	1 (0.6)	37 (12.0)	<0.001
Cardiovascular diseases (n, %)	0 (0.0)	1 (0.3)	1
Cancer (n, %)	1 (0.6)	7 (2.3)	0.338
Diabetes (n, %)	5 (3.0)	9 (2.9)	1
HCV Ab (n, %)	7 (4.6)	12 (4.5)	1
Baseline weight, Kg (mean, SD)	74.19 (11.74)	70.93 (12.63)	0.019
BMI (mean, SD)	24.13 (3.57)	23.39 (3.44)	0.067
Total cholesterol, mg/dL (mean, SD)	171.26 (34.41)	163.06 (38.26)	0.025
Total cholesterol categories (n, %):			0.598
<200	128 (80.0)	234 (82.1)	
200-239	28 (17.5)	41 (14.4)	
≥240	4 (2.5)	10 (3.5)	
HDL, mg/dL (mean, SD)	43.81 (11.62)	41.93 (14.02)	0.157
HDL categories (n, %):			0.034
<40/65 mg/dL males; <40/80 mg/dL females	55 (34.8)	126 (47.7)	
40/65 mg/dL males; 40/80 mg/dL females	97 (61.4)	129 (48.9)	
≥40/65 mg/dL males; ≥40/80 mg/dL females	6 (3.8)	9 (3.4)	
LDL, mg/dL (mean, SD)	110.58 (29.94)	103.48 (33.20)	0.035
LDL categories (n, %):			0.067
<100	55 (36.7)	107 (47.6)	
100-129	57 (38.0)	75 (33.3)	
130-159	31 (20.7)	30 (13.3)	
160-189	7 (4.7)	9 (4.0)	
≥190	0 (0.0)	4 (1.8)	
Ratio total cholesterol/HDL, (mean, SD)	4.11 (1.17)	4.18 (1.5)	0.619
Ratio total cholesterol/HDL (n, %):			1
<5 males; <4.5 females	128 (81.5)	213 (81.9)	
≥5 males; ≥4.5 females	29 (18.5)	47 (18.1)	
Triglycerides, mg/dL (median [IQR])	87 [66, 131]	97 [69, 135]	0.324

Table 2 Effect of 2DR vs 3DR on weight gain	2DR	3DR	Model 1	Model 2	Model 3
	Mean (SD)	Mean (SD)	p-value	p-value	p-value
Weight gain (T12-T0)	2.64 (9.82) N=54	5.30 (6.68) N=104	0.056	0.914	0.590
BMI (T12-T0)	1.11 (3.01) N=52	1.77 (2.17) N=96	0.137	0.679	0.799
Table 3 BMI categories	2DR (N 34)	3DR (N 65)	Total (N 99)		p-value
<18.5	1 (2.94)	0 (0.00)	1 (1.01)		0.115
18.5-24.9	28 (82.35)	44 (67.69)	72 (72.73)		
25-29.9	5 (14.71)	19 (29.23)	24 (24.24)		
30-34.9	0 (0.00)	2 (3.08)	2 (2.02)		
Table 4	2DR	3DR	Model 1	Model 2	Model 3
Overweight vs normal weight	5 (15%) N 33	21 (32%) N 65	0.076	0.395	0.270
Table 5	2DR	3DR	Model 1	Model 2	Model 3
	Mean (SD)	Mean (SD)	p-value	p-value	p-value
Triglycerides T12-T0	9.09 (70.28) N 152	7.51 (73.79) N 263	0.816	0.594	0.459
Total cholesterol T12-T0	8.52 (24.93) N 152	20.91 (36.32) N 271	0.002	0.108	0.086
HDL T12-T0	2.90 (9.89) N 139	7.66 (14.23) N 244	0.002	0.244	0.282
LDL T12-T0	3.24 (20.99) N 127	11.28 (29.56) N 196	0.050	0.055	0.052
Total cholesterol/HDL ratio T12-T0	-0.05 (0.91) N 138	-0.28 (1.34) N 239	0.087	0.462	0.432

Linear regression analysis; Model 1: After controlling for the baseline value. Model 2: After controlling for the baseline values and time fixed baseline variables: age, sex, mode of HIV transmission, CD4 count and HIV-RNA (log-transformed), glycemia, hemoglobin, ALT, AST and hypertension. Model 3: After controlling for the corresponding baseline values and a propensity score (PS) adjustment.