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DIGITAL EDITION

Risk of weight gain (WG) according to type of switching strategy in a large cohort of HIV-infected individuals with stable suppressed HIV-RNA

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on behalf of the ICONA Foundation Study Group.

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Disclosures

Dr. Cicalini has relationships with commercial entities to disclose

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Background

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- There is growing evidence that the use of INSTIs could lead to an increase in body weight and even clinical obesity, although there are differences among various INSTIs, NRTI backbones and patient subsets.
- Dolutegravir has been associated with the greater risk in both observational and randomized studies, in naïve and experienced patients.
- Results from studies also suggest that there may be an additional effect of TAF on weight gain (WG).
- Whether INSTIs also contribute to increase in visceral adiposity or whether they increase the risk of diabetes and cardiovascular disease remains to be defined.
- At present, studies comparing differences in WG in virologically suppressed patients switching to a INSTI- or to a non-INSTI regimen are still limited.
- Aim of the study was to evaluate WG in virologically suppressed patients switching to INSTIs.

Methods-1

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This analysis included ARV-treated **patients in the Icona Foundation Cohort** who:

- had no history of virological failure;
- switched for the first time over 2009-2019 to an ARV regimen with anchor drug belonging to a drug class (INSTI or PI/b or NNRTI) to which they were currently naïve;
- had stable viral suppression (HIV-RNA<200 copies/mL).

Weight gain (WG) was defined as:

- An increase of ≥3 kg or ≥5% or BMI over 2 units from baseline (OUTCOME 1);
- An increase of weight ≥10% from baseline or BMI ≥30, identifying “greater gainers” and treatment-emergent obesity (OUTCOME 2); patients with BMI ≥30 at baseline were excluded.

Methods-2

- The follow-up accrued from the time of regimen switch (baseline) until to change/stop of drug class or last observation.
- Inverse Probability Weighted Cox regression was used to estimate causal hazard ratio (HR) of WG, adjusting for the main confounders: gender, age at baseline, time-updated CD4, duration of virological suppression, previous drug-class regimen, weight at baseline.
- A sensitivity analysis, excluding patients with BMI≥30 or ≤18.5 at baseline and patients receiving TAF was performed.
- Measurements of weight, lipids and glucose at baseline and 6 and 12 months after switch were compared according to third drug class started using ANOVA for inter-group comparison.

Results-1

Main characteristics of study population, overall and according to third drug class started after switch

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N=740 patients		All population	INSTI N=359, 48.5%	PI/b N=142, 19.2%	NNRTI N=239, 32.3%	P-value
Gender	M	582 (78.7%)	286 (79.7%)	112 (78.9%)	184 (77.0%)	0.734
	F	158 (21.4%)	73 (20.3%)	30 (21.1%)	55 (23.0%)	
Age, median (IQR)		44 (36-51)	45 (37-52)	43 (35-52)	42 (35-49)	**0.012**
Years of HIV infection, median (IQR)		2.9 (1.2-6.1)	3.9 (1.4-7.1)	2.0 (0.8-4.5)	2.6 (1.0-4.8)	**<0.001**
Weight at switch, kg, median (IQR)		71 (64-80)	72 (64-80)	72 (63-82)	70 (64-80)	0.939
BMI*	<18.5	20 (3.0%)	13 (4.0%)	2 (1.6%)	5 (2.3%)	0.218
*only 671 pts with height available	18.5-25	410 (61.1%)	191 (58.8%)	72 (57.1%)	147 (66.8%)	
	25-30	180 (26.8%)	89 (27.4%)	42 (33.3%)	49 (22.3%)	
	>30	61 (9.1%)	32 (9.9%)	10 (7.9%)	19 (8.6%)	
CD4 at switch, cell/mmc median (IQR)		568 (389-795)	592 (400-874)	525 (335-759)	549 (400-731)	**0.017**

Results-2

Main characteristics of study population, overall and according to third drug class started after switch

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N=740 patients		All population	INSTI N=359, 48.5%	PI/b N=142, 19.2%	NNRTI N=239, 32.3%	P-value
History of smoking before switch, n(%)	No	397 (53.7%)	196 (54.63%)	69 (48.6%)	132 (55.2%)	0.719
	Yes	325 (43.9%)	154 (42.9%)	70 (49.3%)	101 (42.3%)	
	Unknown	18 (2.4%)	9 (2.5%)	3 (2.1%)	6 (2.5%)	
Diabetes before switch, n(%)	No	708 (95.7%)	341 (95.0%)	134 (94.4%)	233 (97.5%)	0.234
	Yes	32 (4.3%)	18 (5.0%)	8 (5.6%)	6 (2.5%)	
TAF exposure, n(%)	No exposure	654 (88.4%)	307 (85.5%)	133 (93.7%)	214 (89.5%)	0.124
	TAF started as a new drug at switch	63 (8.5%)	38 (10.6%)	6 (4.2%)	19 (8.0%)	
	TAF continued	23 (3.1%)	14 (3.9%)	3 (2.1%)	6 (2.5%)	
Previous cART regimen	2NRTI+NNRTI	164(22.2%)	109 (30.4%)	55 (38.7%)	-	**<0.001**
	2NRTI+PIb	350 (47.3%)	178 (49.6%)	-	172 (72.0%)	
	2NRTI+INSTI	59 (8.0%)	-	23 (16.2%)	36 (15.0%)	
	Other	167 (22.6%)	72 (20.1%)	64 (45.1%)	31 (13.0%)	
Months of undetectable before switch, median (IQR)		19 (7-42)	28 (11-59)	10 (3-24)	16 (7-34)	**<0.001**
Duration of therapy yrs, median(IQR)		2.6 (1.3-4.6)	3.0 (1.4-4.6)	2.2 (1.0-3.2)	2.9 (1.7-5.3)	**0.017**

Results-3

Specific ARV agents started after switch

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	Overall	On TAF*
INSTIs	**359**	**38**
-RAL	78 (21.7%)	2 (5.3%)
-DTG	162 (45.1%)	3 (7.9%)
-EVG	119 (33.2%)	33 (86.8%)
b/PIs	**142**	**6**
-DRV/r or DRV/c	90 (63.4)	6 (100)
-ATV/r or ATV/c	42 (29.6)	0
-LPV/r	9 (6.3)	0
-FPV/r	1 (0.7)	0
NNRTIs	**239**	**19**
-RPV	144 (60.3%)	19 (100%)
-EFV	56 (23.4%)	0
-NVP	32 (13.4%)	0
-ETR	7 (2.9%)	0

*TAF started as a new drug at switch

Results-4

Comparison of weight and lipid values from baseline to 6 and 12 months after switch according to third drug class started

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Weight (kg)	N	BL	6 months	change	p-value	ANOVA	N	BL	12 months	change	p-value	ANOVA
		mean (SD)	mean (SD)			p-value		mean (SD)	mean (SD)			p-value
INSTI	225	73.3 (13.2)	73.8 (13.1)	0.5	0.045	0.263	255	73.0 (13.5)	73.9 (14.2)	1	0.007	0.298
PI/b	101	72.2 (12.8)	73.4 (13.7)	1.1	0.050		107	73.2 (12.8)	74.9 (13.8)	1.8	<0.001	
NNRTI	157	72.0 (11.8)	73.3 (11.6)	1.3	0.002		191	71.5 (12.7)	72.4 (12.2)	0.9	0.005	

Total cholesterol (mg/dl)	N	BL	6 months	change	p-value	ANOVA	N	BL	12 months	change	p-value	ANOVA
		mean (SD)	mean (SD)			p-value		mean (SD)	mean (SD)			
INSTI	242	197 (45)	194 (42)	-3	0.205	0.033	244	194 (44)	190 (39)	-3.5	0.167	0.035
PI/b	92	128 (45)	199 (48)	6.9	0.059		90	191 (47)	195 (43)	4.7	0.265	
NNRTI	174	192 (43)	184 (38)	-8.3	<0.001		186	193 (44)	185 (42)	-7.9	0.002	

TG (mg/dl)	N	BL	6 months	change	p-value	ANOVA	N	BL	12 months	change	p-value	ANOVA
		mean (SD)	mean (SD)			p-value		mean (SD)	mean (SD)			p-value
INSTI	231	151 (87)	150 (127)	-1.4	0.856	<0.001	239	144 (83)	136 (89)	-8.5	0.085	0.013
PI/b	92	164 (161)	172 (148)	8.4	0.606		88	181 (221)	182 (250)	1.5	0.962	
NNRTI	174	161 (117)	120 (78)	-41.8	<0.001		186	163 (115)	118 (96)	-44.4	<0.001	

- No difference was observed in LDL, HDL, total chol/HDL ratio and glucose values before, 6 and 12 months after switch
- **No difference was observed after stratification by type of INSTI used (RAL, DTG, EVG)**

Results-5

Comparison of weight and lipid values from baseline to 6 and 12 months after switch according to third drug class started in "greater gainers", N=104/610^ (17.5%)

^excluding pts with BMI ≥30 at baseline

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Weight (kg)*	N	BL	6 months	change	p-value	ANOVA	N	BL	12 months	change	p-value	ANOVA
INSTI	20	64.7 (11.2)	71.0 (13.7)	6.4	<0.001	0.348	34	68.8 (11.3)	75.6 (12.3)	6.8	<0.001	0.508
PI/b	17	68.8 (15.1)	76.0 (18.4)	7.3	0.002		16	69.3 (13.5)	76.4 (16.4)	7.1	<0.001	
NNRTI	28	66.8 (11.5)	71.4 (13.4)	4.5	<0.001		28	64.0 (11.3)	69.0 (12.1)	5.0	<0.001	

*Evaluated in pts with both measurements

- Trend of lipid and glucose values in "greater gainers" before and after switch were similar to those observed in overall population;
- Percentage of patients initiating TAF after switch was similar among the three groups (INSTIs 9%; PIs 5%; NNRTIs 13%; p=0.8);

- **No difference was observed after stratification by type of INSTI used (RAL, DTG, EVG).**

Results-6

Crude and adjusted hazard ratios (AHR) of experiencing weight gain (WG) after switching to a new ARV drug-class.

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OUTCOME 1

WG = increase of ≥3 kg or ≥5% or BMI over 2 units from BL, N=287/740 (38.8%)

Overall analysis	HR	95%CI		p	AHR*	95%CI		p
INSTIs vs b/PIs	0.87	0.59	1.28	0.473	0.91	0.63	1.31	0.619
INSTIs vs NNRTIs	0.99	0.75	1.32	0.951	1.00	0.76	1.32	0.982
Sensitivity analysis^	**HR**	**95%CI**		**p**	**AHR***	**95%CI**		**p**
INSTIs vs b/PIs	0.85	0.54	1.34	0.485	0.89	0.59	1.35	0.577
INSTIs vs NNRTIs	1.05	0.76	1.45	0.783	1.09	0.78	1.51	0.613

*adjusted for **gender, age at baseline, time-updated CD4, duration of virological suppression, previous drug-class regimen, weight at baseline**

^ excluding patients with BMI≥30 or ≤18.5 at baseline and patients receiving TAF

- **No different risk was observed after stratification by type of INSTI used (RAL, DTG, EVG)**

Results-7

Crude and adjusted hazard ratios (AHR) of experiencing WG after switching to a new ARV drug-class

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OUTCOME 2

WG = increase of weight ≥10% respect baseline or BMI ≥30, N=104/610 (17.5%)

Overall analysis	HR	95%CI		p	AHR*	95%CI		p
INSTIs vs b/PIs	0.70	0.30	1.65	0.415	0.77	0.38	1.53	0.448
INSTIs vs NNRTIs	1.29	0.81	2.03	0.280	1.31	0.83	2.08	0.245
Sensitivity analysis^	**HR**	**95%CI**		**p**	**AHR***	**95%CI**		**p**
INSTIs vs b/PIs	0.76	0.30	1.92	0.559	0.81	0.38	1.74	0.594
INSTIs vs NNRTIs	1.87	1.12	3.11	**0.017**	1.95	1.16	3.27	**0.012**

*adjusted for **gender, age at baseline, time-updated CD4, duration of virological suppression, previous drug-class regimen, weight at baseline**

^ excluding patients with BMI≥30 ≤18.5 at baseline and patients receiving TAF

- **No different risk was observed after stratification by type of INSTI used (RAL, DTG, EVG)**

Conclusions

- No clear evidence of WG after switching to INSTIs was observed in overall population, also when considering type of INSTI used.
- No difference in glucose and lipid profile was observed after switching to INSTIs.
- However, when **considering great weight gain (≥10%) or obesity as outcome**, an increased risk was found in those switching to INSTIs compared to NNRTIs.

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