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Determinants of switching to TAF-based cART or dual combinations (DC) from TDF-based regimens in a cohort of HIV-infected individuals with controlled viral load ≤50 copies/mL

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on behalf of ICONA Foundation Study Group

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BACKGROUND AND AIMS

Switching to a TAF-based or to TDF-sparing (dual combination, DC) regimens is considered as safer than continuing to take TDF-containing regimens, particularly for bone/kidney health. The main aim of this analysis was to evaluate the possible impact of recent results from randomised studies, which led to a change in treatment guidelines, on the observed rate of switch from TDF to TAF-based regimens or TDF-sparing DC in real-life and to identify the determinants of switch separately for the two strategies, with focus on current eGFR v

STUDY DESIGN AND METHODS

HIV-1 positive and HBsAg-negative patients in the Icona Cohort, who achieved a VL≤50 copies/ml for the first time on a TDF-based regimen after January 2016 are included. Kaplan-Meier (KM) curves and (unweighted and weighted) Cox regression models were used to separately estimate the time to switch from TDF to either TAF or DC. A competing KM risk analysis was conducted to jointly model both switches. The main association of interest was between eGFR and the probability of switching after controlling for confounding factors. The switch to TAF-based cART outcome was defined not counting switches to TAF/F/EVG/c as events as they could be triggered by reasons not strictly related to renal toxicity.

RESULTS I

General characteristics of study population are shown on Table 1. Briefly, a total of 1,436 participants were included, 21% female, median (IQR) age of 36 (30-42) years, CKD-EPI eGFR 99.7 (86.2-111.3) mL/min/1.73m², 86% acquired HIV through unprotected sex. At baseline, the most commonly used anchor drugs were RPV(27%), EVG/c(26%), DTG(20%) and DRV/b (13%).

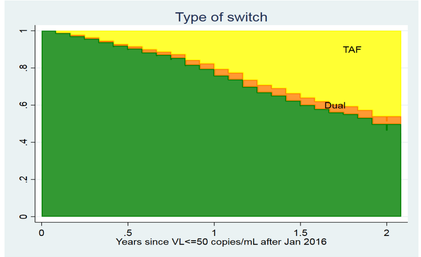
Table 1 – General characteristics of study population, according to anchor drug class used in TDF regimen

Anchor drug in TDF-regimen					
Characteristics	NNRTI	PI/b	INSTI	p-value*	Total
	N= 408	N= 244	N= 784		N= 1436
Time from HIV diagnosis to date of starting cART, months				**<.001**	
Median (IQR)	10 (5, 41)	8 (5, 15)	5 (3, 11)		7 (4, 17)
Nationality, n(%)				**<.001**	
Not Italian	145 (35.5%)	99 (40.6%)	239 (30.5%)		483 (33.6%)
AIDS diagnosis, n(%)				**<.001**	
Yes	11 (2.7%)	43 (17.6%)	128 (16.3%)		182 (12.7%)
Hepatitis co-infection', n(%)				**0.013**	
No	315 (77.2%)	191 (78.3%)	557 (71.0%)		1063 (74%)
Yes	27 (6.6%)	17 (7.0%)	46 (5.9%)		90 (6.3%)
Not tested	66 (16.2%)	36 (14.8%)	181 (23.1%)		283 (19.7%)
CD4 count, cells/mmc				**<.001**	
Median (IQR)	628 (470, 843)	393 (228, 581)	483 (266, 696)		514 (310, 738)
CD4 count nadir, cells/mmc				**<.001**	
Median (IQR)	464 (338, 621)	222 (96, 412)	310 (121, 510)		356 (168, 537)
Viral load, log10 copies/mL				0.553	
Median (IQR)	1.56 (0.00, 1.59)	1.51 (1.20, 1.60)	1.56 (0.00, 1.60)		1.56 (0.00, 1.60)
Diabetes, n(%)				**0.004**	
Yes	3 (0.7%)	3 (1.2%)	28 (3.6%)		34 (2.4%)
Total cholesterol, mg/dL				**<.001**	
Median (IQR)	162 (140, 187)	177 (152, 203)	166 (140, 192)		166 (142, 192)
Use of statins, n(%)				**0.030**	
Yes	7 (1.7%)	3 (1.2%)	30 (3.8%)		40 (2.8%)
Use of blood pressure lowering drugs, n(%)				0.677	
Yes	20 (4.9%)	10 (4.1%)	43 (5.5%)		73 (5.1%)
Follow-up, months				**<.001**	
Median (IQR)	19 (10, 25)	13 (6, 21)	13 (6, 19)		14 (7, 22)

*Chi-square or Kruskal-Wallis test as appropriate

By 2 years from baseline, the probability of switching was 3.1% (95%CI 2.2-4.3) to DC and 29.8% (95%CI 27.0-32.6) to TAF-based cART (Figure 1).

Figure 1 – Kaplan Meier plot of time to therapy switch (competing risk analysis)



RESULTS II

In the unadjusted analysis of the time to switch to TAF-based cART (EVG/c-based regimens not counted as events), patients with an eGFR <60 ml/min/1.73m² were not at higher risk of switching to TAF-based regimen (p=0.664;Figure 2). Concerning switch to DC, still in the unadjusted analysis, a higher probability of switch was found in people treated with TDF/FTC/PI/b (8.8%;95%CI 5%-13%, p<0.001) and with an eGFR <60 ml/min/1.73m² (20.9%; 95%CI 4.3%-37.6%, p<0.001)(Figure 3).

Figure 2 – Kaplan Meier plot of time to TAF initiation- EVG/c not countend as an event by baseline eGFR

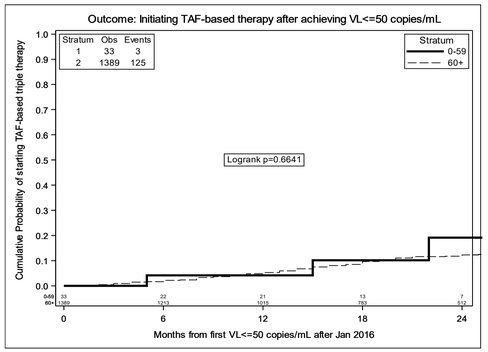
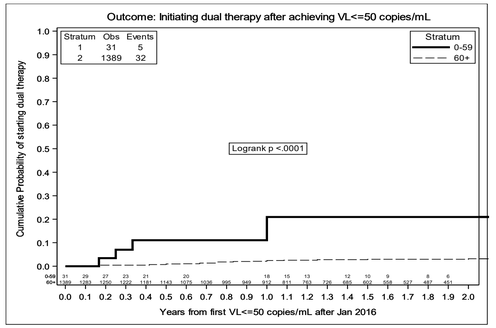


Figure 3 – Kaplan Meier plot of time to DC initiation by baseline eGFR



eGFR<60 ml/min/1.73m² both as time-fixed at baseline or as current value, was associated with a higher probability of switching to DC but not to TAF-based cART, after controlling for confounding factors (Table 2).

Table 2 –Hazard Ratios of TAF-based therapy initiation after excluding people switching to EVG/c (left panel) and DC (right panel) from fitting a Cox regression model- association with baseline and time-dependent eGFR.

Hazard Ratios of switching to TAF-based regimens - TAF/F/EVG/c not counted as an event			
	Hazard Ratio (95% CI) p-value		
	Unadjusted	Adjusted[1]	Adjusted[2]
eGFR (mL/min/1.73 m²)			
Baseline value			
60+	1.00	1.00	
0-59	1.29 (0.42, 3.97)	0.83 (0.25, 2.73)	
	0.662	0.756	
Most recent value			
60+	1.00		1.00
0-59	1.77 (0.79, 3.96)		1.20 (0.51, 2.82)
	0.167		0.679

Hazard Ratios of switching to DC regimens			
	Hazard Ratio (95% CI) p-value		
	Unadjusted	Adjusted[1]	Adjusted[2]
eGFR (mL/min/1.73 m²)			
Baseline value			
60+	1.00	1.00	
0-59	6.91 (2.65, 18.03)	3.83 (1.33, 11.00)	
	<.001	**0.013**	
Most recent value			
60+	1.00		1.00
0-59	7.78 (3.38, 17.92)		4.89 (1.94, 12.31)
	<.001		**<.001**

*(1)Adjusted for age, calendar year of cART initiation, number of concomitant comorbidities, number of drugs failed prior to baseline, baseline CD4 count, type of anchor drug of TDF-based regimen and current CD4 count fitted as time dependent
*(2)Adjusted for age, calendar year of cART initiation, number of concomitant comorbidities, number of drugs failed prior to baseline, baseline CD4 count, type of anchor drug of TDF-based regimen and current CD4 count using inverse probability of weighting

LIMITATIONS

I) Observational setting: unmeasured and residual confounding bias is likely to be an issue; II) eGFR can be modified by a number of different ways and, according to some, the key condition for the identifiability of causal effects from observational data does not hold; III) Renal function was evaluated solely by eGFR, as no other markers of renal impairment were available; IV) cART switches could also be triggered by bone health data, which are not collected in our database.

CONCLUSIONS

A consistent proportion of people with a VL≤50copies/mL in recent years in Italy have been switched from TDF to alternative strategies .The switch to a TAF-based cART was much more common, with a rate of 29% vs. 3% by 2 years of people switching to DC. eGFR, both at entry in this study and the most recently observed value, appears to trigger switches to DC but not those to TAF-based cART regimens.

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