

## Title

### ART switch for pro-active, re-active or cost-saving reasons: a real world evaluation of the determinants over the period 2017-2020 in the Veneto Region

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## Background

ART is for life and with the advent of simpler and more tolerated regimens in recent years an increasing proportion of persons living with HIV (PLWH) undergo treatment switches (TSw). Generally, TSw occur for “pro-active” reasons, such as to prevent long-term toxicity, reduce drug-drug interactions, simplify therapy, and improve adherence, or for re-active reasons typically driven by ongoing toxicities or treatment failure. In addition, ART may be switched for cost saving reasons in absence of other triggers. We aimed to identify patients’ profiles more frequently associated with pro-active or re-active TSw vs. those due to cost-saving reasons.

## Materials and Methods

We included a random samples of patients who underwent a TSw in 6 outpatient’s clinic for HIV care in the Veneto Region over 2017-2020. For PLWH who underwent more than one TSw in the same calendar period, only the first of these TSw was included. TSw were classified as i) pro-active (TSw-1), ii) re-active (TSw-2) and iii) cost-saving (TSw-3). The proportion of type of TSw by calendar period were described. We also calculated the frequency of TSw according to participants’ characteristics at time of switch and compared them using a chi-square test. A multinomial logistic regression was used to evaluate the association between a selected number of participants’ characteristics and the probability of switching for pro-active or re-active vs. cost-saving reasons. Separate multivariable models were fitted for each of the characteristics after controlling model-specific confounding variables.

## Results

We included 405 TSw occurring in the same number of unique PLWH. Demographic and clinical characteristics are reported in Table 1. TSw-3 were more prevalent in 2019-2020 (29%) vs. 2017-2018 (17%) when the TSw-1 were more frequent (34% vs. 22%) ( $p=0.004$ ). The most prevalent TSw regimen was 3TC-DTG (33% of TSw-3, 31% of the TSw-1 and 12% of TSw-2). In the TSw-2 group, 14% switched to TAF/FTC/RPV, 12% to ABC/3TC/DTG and 10% to TAF/FTC/DRV/Coc. Compared to TSw-3, factors associated with TSw-1 were: dyslipidaemia (30% vs. 7%,  $p<0.001$ ), TDF in previous regimen (40% vs 18%) and DTG in previous regimen (21% vs. 43%). Of note, 53% of PLWH previously on TDF were switched to a Descovy-based regimen and 55% of those previously on ABC were switched to 3TC-DTG for cost-saving reasons. Factors associated with TSw-2 vs. TSw-3 were: no. of tablets in previous regimen (2 vs. 1), ABC in previous regimen (23% vs 43%) and DTG in previous regimen (12% vs. 43%, Table 1). Associations remained strong after controlling for confounding factors (Table 2).

## Conclusions

In our analysis, cost-saving TSw appeared to be most prevalent in recent years. Pro-active TSw appeared to be mainly driven by detection of dyslipidaemia and previous use of TDF (50% were switched to TAF). In contrast, use of DTG very infrequently led to pro-active or re-active changes and ABC was mainly replaced with the aim of reducing costs.

**Table 1 Participants characteristics at time of switch by main reason for switch**

Characteristics	Reason for therapy switch				Total N= 405
	Cost-saving N= 93	Pro-active N= 112	Re-active N= 200	P- value*	
<b>Age, years</b>				0.093	
Median (IQR)	49 (40, 56)	51 (45, 57)	52 (43, 57)		51 (43, 57)
<b>Gender, n(%)</b>				0.477	
Female	24 (25.8%)	32 (28.6%)	65 (32.5%)		121 (29.9%)
<b>Mode of HIV Transmission, n(%)</b>				0.136	
IDU	11 (11.8%)	14 (12.5%)	46 (23.0%)		71 (17.5%)
Homosexual contacts	42 (45.2%)	46 (41.1%)	60 (30.0%)		148 (36.5%)
Heterosexual contacts	34 (36.6%)	46 (41.1%)	83 (41.5%)		163 (40.2%)
Other/Unknown	6 (6.5%)	6 (5.4%)	11 (5.5%)		23 (5.7%)
<b>Nationality, n(%)</b>				0.402	
Not Italian	20 (21.5%)	22 (19.6%)	52 (26.0%)		94 (23.2%)
<b>Comorbidities, n(%)</b>				<.001	
Dyslipidemia	6 (6.5%)	34 (30.4%)	37 (18.5%)		77 (19.0%)
<b>Calendar period of switch</b>				0.179	
2017-2018	33 (35.5%)	66 (58.9%)	98 (49.0%)		197 (48.6%)
2019-2020	60 (64.5%)	46 (41.1%)	102 (51.0%)		208 (51.4%)
<b>Current HIV-RNA, log<sub>10</sub> copies/mL</b>				0.002	
Median (IQR)	0.0 (0.0, 2.0)	0.0 (0.0, 0.0)	1.7 (0.0, 2.2)		0.0 (0.0, 2.0)
0-50	28 (77.8%)	37 (88.1%)	66 (62.9%)	0.021	131 (71.6%)
50-1000	7 (19.4%)	4 (9.5%)	26 (24.8%)		37 (20.2%)
1000+	1 (2.8%)	1 (2.4%)	13 (12.4%)		15 (8.2%)
<b>Nadir CD4 count, cells/mm<sup>3</sup></b>				0.063	
Median (IQR)	270 (110, 390)	276 (150, 380)	210 (66, 347)		243 (88, 363)
0-200	37 (40.7%)	34 (32.1%)	84 (47.5%)	0.145	155 (41.4%)
200-500	43 (47.3%)	60 (56.6%)	75 (42.4%)		178 (47.6%)
500+	11 (12.1%)	12 (11.3%)	18 (10.2%)		41 (11.0%)
<b>Time from last therapy change, months</b>				0.002	
Median (IQR)	21 (13, 35)	30 (18, 68)	26 (13, 57)		26 (15, 49)
<b>No. of previous therapy lines</b>				0.080	
Median (IQR)	2 (1, 3)	2 (1, 3)	2 (2, 3)		2 (1, 3)
<b>Previous regimen</b>				0.183	
No. molecules, Median (IQR)	3 (3, 4)	3 (3, 3)	3 (3, 3)		3 (3, 4)
No. tablets, Median (IQR)	1 (1, 2)	2 (1, 2)	2 (2, 3)	<.001	2 (1, 2)
No. drugs, Median (IQR)	2 (1, 2)	2 (1, 2)	2 (2, 2)	0.002	2 (1, 2)
<b>Individual drugs, n(%)</b>				0.001	
TDF	17 (18.3%)	45 (40.2%)	50 (25.0%)		112 (27.7%)
Abacavir	40 (43.0%)	32 (28.6%)	46 (23.0%)	0.002	118 (29.1%)
Dolutegravir	40 (43.0%)	23 (20.5%)	25 (12.5%)	<.001	88 (21.7%)
PI/r	32 (34.4%)	42 (37.5%)	93 (46.5%)	0.09	167 (41.2%)

\*Chi-square or Kruskal-Wallis test as appropriate

**Table 2 Adjusted ORs from fitting a multinomial logistic regression model (cost saving switches as comparator)**

Factors	Reason for therapy switch				
	Cost-saving Comparator	Pro-active Adjusted OR 95% CI	p- value	Re-active Adjusted OR 95% CI	p- value
<b>Dyslipidemia<sup>1</sup></b>	1	5.43 (2.14, 13.79)	<.001	3.08 (1.24, 7.67)	0.015
<b>Nadir CD4 count<sup>2</sup>, below 200 cells/mm<sup>3</sup></b>	1	0.60 (0.28, 1.29)	0.190	1.34 (0.70, 2.56)	0.370
<b>No. tablets previous regimen<sup>3</sup>, &gt;1</b>	1	2.07 (1.11, 3.87)	0.022	4.40 (2.46, 7.87)	<.001
<b>TDF in previous regimen<sup>4</sup></b>	1	3.36 (1.75, 6.47)	<.001	1.58 (0.85, 2.94)	0.148
<b>Abacavir in previous regimen<sup>5</sup></b>	1	0.48 (0.26, 0.86)	0.014	0.36 (0.21, 0.62)	<.001
<b>DTG in previous regimen<sup>6</sup></b>	1	0.32 (0.17, 0.60)	<.001	0.18 (0.10, 0.33)	<.001
<b>PI/r in previous regimen<sup>7</sup></b>	1	1.16 (0.65, 2.07)	0.613	1.66 (0.99, 2.77)	0.055

<sup>1</sup>adjusted for age, gender, hepatitis, time from lasttherapy change and PI/r or TAF in previous regimen

<sup>2</sup>adjusted for age, AIDS diagnosis, no. previous regimens used

<sup>3</sup>adjusted for age, AIDS diagnosis, no. previous regimens used, >=2 comorbidities

<sup>4</sup>adjusted for age, gender

<sup>5</sup>adjusted for age, gender

<sup>6</sup>adjusted for age, gender

<sup>7</sup>adjusted for age, gender