# DETERMINANTS OF SWITCHING TO TWO-DRUG COMBINATIONS WITH HIV-RNA ≤50 COPIES/ML IN A COHORT OF HIV-INFECTED INDIVIDUALS SEEN FOR CARE IN ITALY

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## BACKGROUND

- Although some two-drug combinations (2DC) are now recommended as alternative in guidelines for use in specific contexts, there is little data documenting how frequently and in which patients these regimens are used in clinical practice in people with a viral load (VL)≤50 copies/mL

## AIMS

- To describe the main characteristics of a population of HIV-infected persons who switched from triple cART regimen to another triple combination (TT) or to a dolutegravir(DTG)-based or PI-based with a viral load(VL) was ≤50 copies/mL, regardless of the reason.

- To identify factors associated with the probability of switching to each of the 2DC regimens, as opposed to a standard switch to triple therapy.

## STUDY DESIGN AND METHODS

- The study includes data of HIV patients in the Icona Foundation Study cohort who switched to TT or to a DTG- or PI-based 2DC. Index date for this cross-sectional analysis was the date of first undergoing a therapy switch with the specific regimens of interest after achieving VL≤50 copies/mL over the period Jan 2004-Jun 2018.

- Only three type of switches were considered (first time ever occurring): i) a switch to another standard TT; ii) a switch to a DTG-based 2DC (including 3TC+DTG or RPV+DTG) and iii) a switch to a PI-based 2DC (including 3TC+DRV+r or cobicistat, 3TC+LPV+r and 3TC+ATV±r).

- Chi-square test was used to compare categorical factors and Kruskal-Wallis test to compare medians across the three switch groups.

- Multinomial logistic regression was used to identify factors associated with the probability of switching to DTG-, PI-2DC vs. TT. For factors with global p ≤0.5 specific contrasts (DTG-2DC vs. TT and PI-2DC vs. TT) were also calculated.

- Framingham CHD score and D.A.D. CKD scores were evaluated in the model. Therefore, all factors used to calculate such scores were not individually included.

- Potential confounding mechanisms were investigated.

## RESULTS

- A total of 3,859 switches were included. Four percent switched to DTG-2DC (3% 3TC+DTG, 1% RPV+DTG) and 7% to PI-2DC (3% 3TC+DRV+r or cobi, 1% 3TC+LPV+r, 3% 3TC+ATV±r).
- Median age of patients was 43 years, baseline CD4 571 cells/mm$^3$, 21% female, 14% of foreign origins.
- In the unadjusted analysis (Table 1), compared to patients switched to TT those on DTG-2DC and PI-2DC were older, had longer exposure to ART, had higher CD4 at switch, had switched more recently, had higher cardiovascular disease and CHD risk, had higher ESRD and higher CKD risk.

**Table 1 – Main characteristics of participants**

| Characteristics | Triple N= 3380 | DTG-based* N= 191 | PIr-based& N= 288 | p-value |
|---|---|---|---|---|
| Gender, Female | 22% | 23% | 22% | 0.833 |
| Age, Median (IQR), years | 43 (36, 49) | 49 (40, 57) | 48 (41, 54) | <.001 |
| >50, n(%) | 23% | 47% | 39% | |
| Mode of HIV transmission | | | | 0.029 |
| Heterosexual contacts | 41% | 42% | 41% | |
| PWID | 12% | 7% | 15% | |
| MSM | 40% | 48% | 38% | |
| Other/unknown | 7% | 3% | 7% | |
| Origin, Foreign | 14% | 8% | 13% | 0.082 |
| HBsAg+, n(%) | 5% | 5% | 2% | 0.067 |
| HCVAb+, n(%) | 21% | 23% | 29% | 0.017 |
| CD4 count, cells/mmc | | | | <.001 |
| 350+ | 81% | 92% | 90% | |
| 201-350 | 13% | 6% | 9% | |
| 0-200 | 6% | 3% | 1% | |
| Nadir CD4 count, cells/mmc | | | | 0.054 |
| 350+ | 30% | 38% | 30% | |
| 201-350 | 36% | 37% | 34% | |
| 0-200 | 35% | 25% | 36% | |
| Year of switch, >2010 | 68% | 100% | 94% | <.001 |
| Smoking | | | | 0.610 |
| No | 50% | 53% | 49% | |
| Yes | 41% | 37% | 40% | |
| Unknown | 9% | 9% | 11% | |
| CHD Framingham score, Median (IQR) | 9 (5, 17) | 12 (7, 27) | 14 (8, 26) | <.001 |
| Low | 43% | 34% | 31% | |
| Moderate | 23% | 23% | 29% | |
| High | 15% | 27% | 28% | |
| Unknown | 20% | 17% | 13% | |
| Exposure to ART, Median (IQR),years | 3 (1, 5) | 4 (2, 10) | 4 (2, 9) | <.001 |
| >5, n(%) | 23% | 37% | 43% | |
| Number of ARVs previously failed, Median (IQR)# | 3 (3, 4) | 3 (2, 5) | 3 (2, 5) | 0.043 |
| >3, n(%) | 5% | 5% | 8% | |
| Number of ARVs previously used, Median (IQR) | 3 (2, 4) | 4 (2, 6) | 4 (3, 7) | <.001 |
| >3, n(%) | 27% | 58% | 61% | |
| Hypertension | 56% | 54% | 63% | 0.054 |
| AIDS | 14%) | 9% | 12% | 0.059 |
| Diabetes | 3% | 6% | 4% | 0.083 |
| Cardiovascular disease | 14% | 24% | 24% | <.001 |
| ESLD | 0.1% | 1% | 1% | 0.087 |
| ESRD | 3% | 15% | 10% | <.001 |
| eGFR, CKD-Epi | | | | <.001 |
| 90+ | 65% | 38% | 43% | |
| 60-90 | 32% | 47% | 47% | |
| <60 | 3% | 15% | 10% | |
| CKD D.A.D. score | | | | <.001 |
| Low | 47% | 28% | 30% | |
| Moderate | 27% | 24% | 20% | |
| High | 26% | 48% | 50% | |

*3TC-DTG or RPV-DTG
&3TC-DRV-cobi or 3TC-LPV-r or 3TC-ATV
#in those with >1 failure

**Table 2 – Adjusted OR of switching to 2DC regimens instead of another triple from fitting a multinomial logistic regression analysis**

| Characteristics | DTG-based* | PI-based& | p-value |
|---|---|---|---|
| Origin Foreign vs. Italian | 0.60 (0.34, 1.05) | 1.20 (0.80, 1.80) | 0.110 |
| HBsAg+ vs. HBsAg-neg, n(%) | 0.93 (0.43, 1.97) | 0.37 (0.15, 0.92) | 0.101 |
| CD4 count, cells/mmc | | | 0.006 |
| 201-350 vs. 350+ | 0.49 (0.25, 0.96) | 0.57 (0.36, 0.93) | |
| 0-200 vs. 350+ | 0.56 (0.21, 1.53) | 0.27 (0.10, 0.76) | |
| p-value** | 0.018 | 0.002 | |
| Year of switch, per year more recent | 1.87 (1.66, 2.10) | 1.16 (1.11, 1.21) | <.001 |
| p-value** | <.001 | <.001 | |
| Exposure to ART, per 5 years longer | 0.60 (0.34, 1.05) | 1.20 (0.80, 1.80) | 0.110 |
| Number of ARVs previously failed, per 3 additional | 0.65 (0.54, 0.77) | 0.68 (0.60, 0.77) | <.001 |
| p-value** | <.001 | <.001 | |
| Previous CVD (Yes vs. No) | 1.22 (0.79, 1.90) | 1.00 (0.70, 1.43) | 0.656 |
| AIDS (Yes vs. No) | 0.51 (0.29, 0.91) | 0.68 (0.45, 1.03) | 0.025 |
| p-value** | 0.016 | 0.041 | |
| Framingham CHD score | | | 0.629 |
| Moderate vs. Low | 0.79 (0.50, 1.24) | 1.23 (0.86, 1.75) | |
| High vs. Low | 0.87 (0.52, 1.44) | 1.28 (0.85, 1.94) | |
| N/A vs. Low | 1.12 (0.70, 1.78) | 1.04 (0.68, 1.57) | |
| p-value** | 0.890 | 0.690 | |
| DAD CKD score | | | <.001 |
| Moderate vs. Low | 1.43 (0.92, 2.22) | 0.99 (0.68, 1.45) | |
| High vs. Low | 2.06 (1.33, 3.20) | 2.01 (1.41, 2.86) | |
| p-value** | 0.004 | <.001 | |

*3TC-DTG or RPV-DTG
&3TC-DRV-cobi or 3TC-LPV-r or 3TC-ATV
$Adjusted for all factors shown in table
**Contrasts Chi-square p-values

- In the unadjusted analysis people with an history of >3 virological failures before baseline appeared to have greater chance of switching to PI-based 2DC as opposed to TT (unadjusted odds ratio (OR)=1.76; p=0.01). However, this association was confounded by total duration of exposure to ART before baseline (adjusted (aOR)=0.61, p=0.06).

- In the adjusted analysis (Table 2), compared to TT, switches to 2DC occurred more frequently in recent years, older participants, those with higher CD4 and still free from AIDS, those with less extensive history of virological failure before baseline and higher estimated risk of renal disease.

- For all these factors, the strength of the association was similar regardless of the type of 2DC regimen (Table 2).

## CONCLUSIONS

***Although switches to 2DC occurred more frequently in recent years, over 80% of participants with a VL ≤50 copies/mL in our analysis switched to another standard TT. In our study population of people seen for care in Italy, patients appear to be selected for 2DC strategies based on older age, less evidence of previous virological failure, more stable HIV disease and higher risk for renal complications. Further research is necessary to prospectively assess the virological and clinical outcomes of these strategies.***

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