Efficacy and safety of switching to co-formulated DOR/TDF/3TC in virologically suppressed HIV-1-infected patients: early experience from a single Italian center

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Background:

Doravirine (DOR) belongs to the class of non-nucleoside reverse transcriptase inhibitors (NNRTI) and is also available co-formulated with tenofovir disoproxil (TDF) and lamivudine (3TC). Real-life data on DOR is lacking. The study aims to evaluate the efficacy and safety of switching to DOR/TDF/3TC in a cohort of HIV-living persons treated in a single center in Florence, Italy.

Materials and methods:

This is a retrospective-monocentric cohort study. From 01/01/2020 to 31/12/2021, we included all HIV-1 positive, ART-experienced people switching to DOR/TDF/3TC with HIV-RNA <50 copies/mL. Study entry was the date of drug initiation; exit was the date of discontinuation, virologic failure (VF), or the end of follow-up (FU) (30/05/2022).

Results:

We included 53 patients (median FU: 1.3 years). The majority were male (n=43; 81.3%) and Italian- born (n=35; 66%). Baseline characteristics are summarized in table 1. Most had at least one comorbidity (n=46; 86%): dyslipidemia (24.5%), cardiovascular diseases (16.9%) and mental disorders (9.4%). Pre-switch regimen was mainly NNRTI-based (n=30; 56.6%) and INSTI-based regimen (n=14; 26.4%). Historical genotype was available in 31 out of 53 patients. According to Stanford algorithm, low-level TDF resistance was reported in 1 case, potential low-level/low-level DOR resistance in 4 cases, and 3TC high-level resistance in 3 cases. Overall, we observed 7 discontinuations: 6 due to grade 1-2 adverse events (mainly gastrointestinal 3 out of 7) and 1 due to virologic failure [Table 1]. No baseline or acquired resistance was identified in the VF patients. The 48-week probability of remaining free of discontinuation was 88.6% (95%CI 74.6-95.1). The discontinuation rate was 11.1 x 100 py [5.3-23.3]. A lower, although not significant, discontinuation rate for adverse events was observed in people who came from an NNRTI-based regimen compared to an INSTI-based regimen (RR 0.25 [95% CI 0.04-1.62]; p = 0.1473). No difference in total CD4 count, cholesterol, or triglycerides was observed at the end of FU.

Table 1. Clinical/demographic characteristics and outcome of HIV-1 infected patients, ART experienced with HIV-RNA level <50 copies/mL switching to DOR/TDF/3TC at the Infectious and Tropical diseases unit in a tertiary teaching hospital in Florence, Italy.

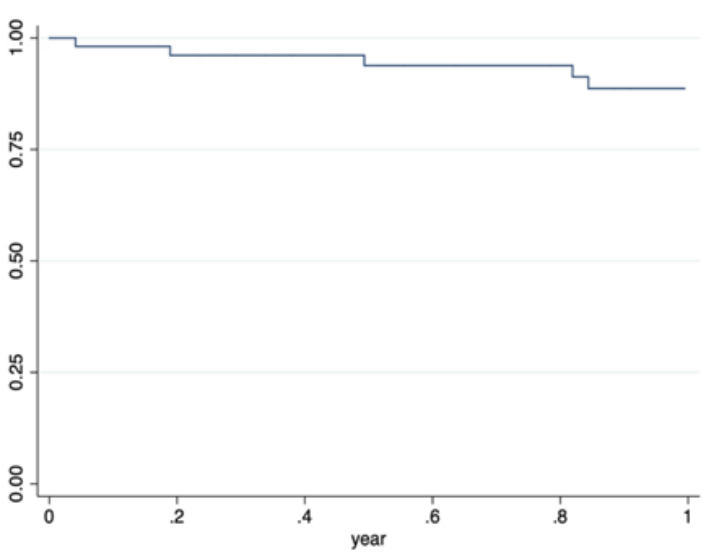
	DOR/TDF/3TC (N=53)	
Italians, n (%)	35	66.0
Gender, n (%)		
• Female	4	7.5
• Male	43	81.3
• Transgender	6	11.3
Age at entry, median [IQR]	52	44-58
Risk of HIV transmission, n (%)		
• Heterosexual	15	28.3
• MSM	31	58.5
• *IVDU*	3	5.7
• Other/not known	4	7.5
Cardiovascular disease	9	16.9
Diabetes	4	7.5
Dyslipidemia	13	24.5
Mental disorders	5	9.4
No comorbidity	7	13.2
Years of undetectable viremia, median [IQR]	6	[2-9]
AIDS diagnosis, n (%)	15	28.3
Previous virologic failure	3	5.7
HBsAg positivity, n (%)	3	5.7
HIV-RNA Zenit, Log_{10} copies/mL, median [IQR]]	5.0	4.6-5.4
CD4 Nadir (cells/mL), median [IQR]	350	131-477
Years of HIV, median [IQR]	10	4-18
Years of antiretroviral therapy, median [IQR]	9	4-16
CD4+ T cells at baseline/µL, median [IQR]	697	525-923
Type of pre-switch regimen		
• NNRTI	30	56.6
• PI	5	9.4
• INSTI	14	26.4
• Other	4	7.5
Number of previous ART regimens, median [IQR]	3	2-5
Type of pre-swicth backbone		
• 3TC/ABC	3	5.6
• FTC/TAF	34	64.1
• FTC/TDF	12	22.6
• 3TC	3	5.7
• No backbone	1	1.9
Major drug resistance on historical genotype*		
• Low-level resistance TDF	1 / 31	3.23
• Low-level/potential low-level resistance DOR	4 / 31	12.9
• High-level resistance 3TC	3 / 31	9.7
Discontinuation for all causes	7	13.2
• Virologic failure	1	
• Gastrointestinal toxicity	3	
• Itch	2	
• Rash	1	

ART: antiretroviral treatment; TDF: Tenofovir disoproxil fumarate; 3TC: Lamivudine; FTC: emtricitabine; MSM: males who have sex with males; IVDU: intravenous- drug users; PI: Protease inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitor; INSTI: integrase strand transfer inhibitor

*Historical genotype available in 31 / 53 patients.

Conclusions:

The switch to DOR / TDF / 3TC maintained virologic suppression with a low risk of VF. The discontinuation rate for adverse events seemed lower when the previous regimen was NNRTI-based. Larger cohort studies are needed to confirm these findings.



One year probability of remaining free from treatment discontinuation for all causes in HIV-1 infected patients, ART experienced with HIV-RNA level <50 copies/mL switching to DOR/TDF/FTC at the Infectious and Tropical diseases unit in a tertiary teaching hospital in Florence, Italy.