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P 5
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Improved lipid profiles in adults living with HIV receiving doravirine-based regimens: week 52 analysis

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Introduction

- Doravirine (DOR), a non-nucleoside reverse transcriptase inhibitor (NNRTI) with improved genetic barrier, was approved in 2018 for the treatment of HIV-1 in Europe and North America. It is available alone or coformulated with tenofovir disoproxil fumarate (TDF) and lamivudine (3TC) as a single tablet regimen. ART-naïve and -switch studies demonstrated the non-inferior efficacy of DOR-based regimens (vs. darunavir/ritonavir or efavirenz) and an overall favorable safety profile including improved blood lipids.[1,2,3]

Methods

- We retrospectively studied an adult cohort in follow-up at Tor Vergata University Hospital who started a DOR-based regimen between 2016 and February 2024. We collected demographic, clinical and laboratory data at the start of DOR (T0), and after 12 (T12), 24 (T24) and 52 (T52) weeks. Paired t-test was used to compare parameters at T0 vs. T52. We used the Systemic Coronary Risk Estimation algorithm (SCORE2) to estimate 10-year fatal and non-fatal cardiovascular disease (CVD) risk in individuals without previous CVD or diabetes aged 40–69 years.

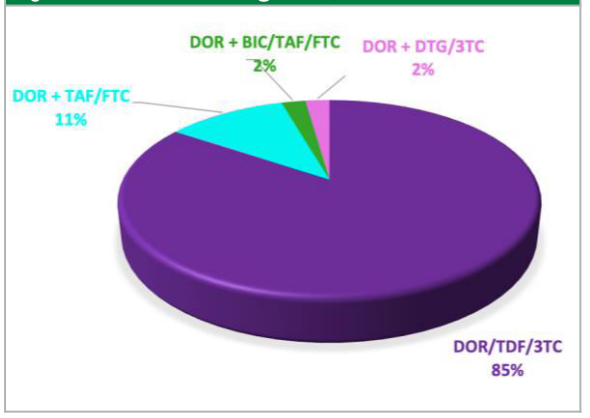
Table 1. Characteristics of the study population

Total number		45
Sex at birth, n (%)	Male	35 (77.8)
	Female	10 (22.2)
Age, median years (IQR)		54 (42 – 62)
Country of origin, n (%)	Italy	34 (75.8)
	Azerbaijan	1 (2.2)
	Brasil	1 (2.2)
	Bangladesh	1 (2.2)
	Cape Verde	2 (4.4)
	Colombia	1 (2.2)
	Dominican Republic	1 (2.2)
	Guinea	1 (2.2)
	Ivory Coast	1 (2.2)
	Poland	1 (2.2)
	Russia	1 (2.2)
Transmission group, n (%)	Heterosexual	18 (40)
	MSM	16 (35.6)
	IDU	4 (8.9)
	Other / not reported	7 (15.5)
CD4 nadir, median cells/mm³ (IQR)		148 (54 – 381)
Zenith HIV-1 RNA, median log_{10} copies/mL (IQR)		5.4 (4.8– 5.1)
HIV-1 RNA at DOR start, n (%)	<50 copies/mL	38 (84.4)
	>200 copies/mL	7 (15.6)
CD4 at DOR start, median cells/mm³		652 (451- 984)

Results

- The cohort comprised 45 participants (Table 1). At T0, most (38/45, 84.4%) were virologically suppressed (<50 copies/mL), 3 were ART-naïve, and 4 were experiencing virological failure (confirmed viral load ≥ 200 copies/mL). 24 patients experienced a prior NNRTI regimen but none of them had a prior history of NNRTI failure or documented NNRTI resistance. DOR-based regimens are represented in Figure 1, while baseline regimens are summarised in Table 2. The most frequent reasons to start DOR were dyslipidaemia or weight gain (n=16), followed by proactive switch (n=12), toxicity (n=6), virological failure (n=4), unknown (n=3), and DDIs (n=1). Overall, 30/45 (66.7%) participants had dyslipidaemia before starting DOR and 10/30 (33%) were receiving lipid-lowering agents.

Figure 1 **DOR-based regimens**



Results of 2

- Over median 77 weeks of follow-up (IQR 34-110), 6/45 (13.3%) participants discontinued DOR (after a median of 12 weeks); reason included paradoxical dyslipidaemia (n=2), gastrointestinal symptoms (n=2), inability to swallow the pill (n=1), and osteoporosis (n=1, on TDF). All patients maintained or achieved virological suppression after the introduction of DOR, with a significant increase in the CD4/CD8 ratio between T0 and T52 (mean difference 0.1 ±0.2; p=0.01).

Results of 3

- Between T0 and T52, there were significant decreases in total cholesterol by mean -38 mg/dL (±41, p<0.001), LDL cholesterol by mean -26 mg/dL (±42, p<0.001) and triglycerides by mean -48 mg/dL (±107, p=0.01). SCORE2 values showed a significant reduction by mean 0.8 (±2.1, p=0.04). eGFR values remained stable both in the overall cohort and in the subgroup who started TDF. There were no apparent differences in blood pressure, weight, BMI or HDL cholesterol when comparing T0 and T52.

Table 2. Baseline ART regimens

	Number/total (%)
NNRTI-based	
RPV/TAF/FTC	7/45 (15.5%)
EFV/TDF/FTC	5/45 (11.1%)
EFV + ABC/3TC	2/45 (4.5%)
RPV/TDF/FTC	2/45 (4.5%)
ETV + TDF/FTC	1/45 (2.2%)
NVP + TAF/FTC	1/45 (2.2%)
INSTI-based	
BIC/TAF/FTC	4/45 (8.9%)
RAL + ABC/3TC	2/45 (4.5%)
RAL + TAF/FTC	2/45 (4.5%)
DTG/3TC	1/45 (2.2%)
DTG/ABC/3TC	1/45 (2.2%)
DTG + TAF/FTC	1/45 (2.2%)
PI-based	
DRV/c/TAF/FTC	3/45 (6.7%)
ATV/c + 3TC	1/45 (2.2%)
ATV/c + TAF/FTC	1/45 (2.2%)
ATV/c + ABC/3TC	1/45 (2.2%)
ATV/r + ABC/3TC	1/45 (2.2%)
DRV/c + 3TC	1/45 (2.2%)
Other	
NVP + RAL	2/45 (4.5%)
DTG + DRV/r + 3TC	1/45 (2.2%)
DTG/RPV	1/45 (2.2%)
Not available	1/45 (2.2%)
None	3/45 (6.7%)

Conclusion

- DOR-based regimens represented a valid choice in this cohort with a high baseline prevalence of dyslipidaemia, achieving excellent virological and immunological efficacy, improving blood lipids, and reducing cardiovascular risk.

References

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