Metabolic and hepatic safety in ART experienced PLWH switching to a DOR-based regimen vs rilpivirine. Data from a real-life setting.

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BACKGROUND

Doravirine (DOR) is a newly approved antiretroviral belonging to the class of non-nucleoside reverse transcriptase inhibitors (NNRTIs). In the phase 3 trial DRIVE-AHEAD, DOR in combination with 3TC and TDF showed minimal changes in lipidic profile compared with EFV/FTC/TDF. In the phase 3 DRIVE SHIFT trial the switch to DOR/3TC/TDF showed reduction in fasting lipids.

AIM

Our aim was to investigate the role of switching to a doravirine DOR-based regimen on metabolic and hepatic safety in a real-life setting. We compared DOR patients with a cohort of subjects switching to rilpivirine based regimen.

PATIENTS & METHODS

459 consecutive experienced PLWH,enrolled in the SCOLTA project, starting DOR-based or RPV-based regimens, with at least one visit after enrollment were evaluated. T0 and T1 were defined as the baseline and 6-month follow-up respectively. Comparisons were performed using chi-square, paired t-test, or analysis of variance as appropriate.

RESULTS

128 and 331 subjects were enrolled, respectively, in the DOR and RPV cohorts (Table).55 (43.0%) patients on DOR were on 3TC/TDF/DOR regimen (DOR1), and the remaining were in other DOR-based regimens (DOR2).The mean age of patients in DOR1 was lower (46.7 vs 59.5), and they were less frequently switching from integrase inhibitors (36% vs 57%). At baseline, DOR patients were older, with higher BMI, and more frequently treated with lipid-lowering drugs and switching from PI and INI. In the first year of observation, 12(9.3%) patients on DOR interrupted the treatment vs 39 (11.7%) on RPV. Changes from baseline to T1 showed significantly decreasing total cholesterol (TC), LDL-c, TC/HDL-c ratio, and triglycerides, both in all patients and in those not on lipid-lowering treatment. A more marked improvement in lipid profile in the DOR group is suggested by the deeper TC/HDL-c ratio decrease seen in this group.Patients in DOR1 showed a significant reduction in TC and LDL-c. Weight did not change. Both DOR and RPV subjects showed a slight increase in ALT, when baseline levels were <40 UI/dL. On the contrary, when ALT was>40 UI/l,the DOR group significantly reduced ALT levels.

TABLE 1

Variables at enrollment	Doravirine n=128 Mean SD or n (%) or Median (IQR)	Rilpivirine n=331 Mean SD or n (%) or Median (IQR)	P
Age, years	53.6 ± 12.4	42.3 ±9.3	<0.0001
Sex M	91 (71.1%)	237 (71.6%)	0.91
BMI Kg/m^2	26.2 ±5.5	24.4 ±3.8	0.0002
Weight, Kg	77.3 ±17.6	81.7 ±14.3	0.0007
Caucasian	117 (91.4%)	304 (91.8%)	0.88
Risk factor for HIV acquisition Sexual IDU Other/ND	 89 (69.5%) 24 (18.8%) 15 (11.7%)	 244 (73.7%) 66 (19.9%) 21 (6.3%)	 0.16
HBV coinfection (n=102/321)	8 (7.8%)	20 (6.2%)	0.57
HCV coinfection (n=107/329)	26 (24.3%)	76 (23.1%)	0.80
Detectable HIVRNA	16 (12.5%)	50 (15.1%)	0.48
Previous ART PI INI NNRTI	 29 (22.7%) 62 (48.4%) 47 (36.7%)	 152 (45.9%) 17 (5.1%) 151 (45.6%)	 <0.0001 <0.0001 0.08
CD4, cells/mm3	685 (493-955)	624 (443-820)	0.02
Total cholesterol, mg/dL	198± 45	189 ±42	0.06
HDL-cholesterol, mg/dL	51± 15	48 ±16	0.08
LDL-cholesterol, mg/dL	118± 38	112± 38	0.12
Triglycerides, mg/dL	114 (85-153)	120 (85-172)	0.56
On lipid-lowering drugs	25 (19.5%)	29 (8.8%)	0.001
AST, UI/dL	21 (18-29)	24 (19-31)	0.008
ALT, UI/dL	24 (17-32)	28 (21-42)	0.0007

CONCLUSIONS

In both groups (DOR and RPV), patients showed a significant reduction in TC, LDL-c, TC/HDL-c ratio, and triglycerides. A deeper TC/HDL-c ratio decrease was observed in the DOR group. Patients in DOR1 showed a significant reduction in TC and LDL-c with respect to DOR2. Moreover, the DOR group showed a significant reduction in ALT levels when ALT were >40 UI/l at baseline

REFERENCE
Mazzitelli M., Antoni MD, Castelli F., et al. Real life use of Doravirine in treatment-experienced people living with HIV: A multicenter Italian study. Medicine, 101, e29855. https://doi.org/10.1136/gutjnl-2019-318372.

DISCLOSURES

The authors declare to have no conflicts of interest.

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