Dettaglio abstract

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Title: Reasons for choosing a doravirine (DOR) based versus an INSTI-based regimen in ART-naïve and ART-experienced patients in real-world setting: data from the Icona Cohort

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Authors: A. Saracino[1], M. Ponzano[2], F. Bovis[2], E. Quiros-Roldan[3], M. Fabbiani[4], N. Squillace[5], S. Rusconi[6], M. Ferrara[7], S. Lo Caputo[8], A. Tavelli[9], A. Antinori[10], A. d'Arminio Monforte[9]

Affiliation: [1]Clinic of Infectious Diseases, Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University of Bari "Aldo Moro", Bari, Italy, [2]Biostatistics Unit, Department of Health Sciences, University of Genoa, Genoa, Italy, [3]Clinic of Infectious Diseases, University of Brescia, Brescia, Italy, [4]Clinic of Infectious Diseases, Azienda Ospedaliera Universitaria Senese, Siena, Italy, [5]Infectious Diseases Clinic, Fondazione IRCCS San Gerardo dei Tintori, University of Milano-Bicocca, Monza, Italy, [6]Infectious Diseases Unit, Ospedale Civile di Legnano, ASST Ovest Milanese, and DIBIC Luigi Sacco, Università degli Studi di Milano, Legnano, Italy, [7]Department of Infectious Diseases, University of Torino and "Amedeo di Savoia" Hospital, Turin, Italy, [8]Infectious Diseases Unit, Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy, [9]Icona Foundation, Milan, Italy, [10]Clinical and Research Infectious Diseases Department, National Institute of Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy

Abstract
Background: Doravirine (DOR), the most recent antiretroviral drug of the NNRTI lass, demonstrated to overcome limitations of previous NNRTIs including low genetic barrier, CNS toxicity, food requirement, and showed a favourable safety profile, especially on metabolic side effects. However, as a direct comparison of DOR versus INSTI regimens in randomized trials is lacking, the clinical characteristics of PLWH assigned to different regimens is crucial and could affect outcomes in real world.
Aim of the study was to investigate the sociodemographic and clinical drivers of starting or switching to a doravirine (DOR) versus an INSTI-based regimen.
Methods: All PLWH enrolled in the Icona cohort, who after January 2020 (date of DOR availability in Italy) started a first line DOR- or INSTI-based 3 drug regimens (DR) (Naïve Group) or switched for the first time to DOR or a 3DR/2DR INSTI-based regimen while on virological suppression (Experienced Group), were included in this observational study. Demographic and clinical data were compared according to different groups. Chi-square or U-Mann-Whitney or one-way ANOVA tests were used to compare baseline characteristics. A logistic regression model was used to explore factors associated with DOR start and a multinomial logistic analysis was used to explore factors associated to switch to INSTI vs DOR regimen.
Results: The baseline characteristics of 62 naive PLWH starting 3DR DOR and 1,341 starting 3DR INSTI were compared; features associated with DOR use were intravenous drug use, smoking, higher CD4 count and CD4:CD8 ratio, lower HIV-RNA and nadir CD4 count, higher BMI and LDL levels, and a longer disease duration (Table 1). In adjusted multivariate models, higher CD4 (AOR 1,43, 95%CI1,09-1,86,) and not Italians remained significantly associated with DOR use (Italians vs non Italian DOR use: AOR 0,20, 95%CI 0,05-0,91).
In the experienced group, DOR, 2DR INSTI and 3DR INSTI regimens were initiated in 308, 1,594 and 1,134 PLWH, respectively, whose characteristics were differently distributed as shown in Table 2.
12.8% of DOR group were switching from a PI-based, 18.3% from an INSTI-based, and 64.0% from another NNRTI-based regimen, 4.9% from other regimens.
Independent factors of prescribing DOR were being females and diabetes (only vs 2DR-INSTI), older age (vs 3DR-INSTI), high tryglicerides, high HDL and disease duration (vs both 2DR-and 3DR-INSTI).
Conclusions: DOR is preferentially used by clinicians for ART-naïve PLWH with less advanced HIV disease, and, in case of switching with suppressed viral load, in females and older dyslipidemic PLWH.

Overall, clinicians’ choices were in agreements with guidelines and were in line with the lower toxicity of doravirine-regimen.

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Table 1. Baseline characteristics of 62 PLWH starting a 3DR DOR regimen and 1,341 starting a 3DR INSTI regimen in the ICONA Cohort.

		DOR	INSTI	p
n		62	1341	
age years, mean (SD)		41.29 (10.46)	42.48 (12.61)	0,485
female gender (%)		10 (16.1)	221 (16.5)	0,05
Italian nationality (%)		42 (75.0)	934 (72.2)	0,764
mode_of_hiv_transmission (%)	HS	20 (32.3)	505 (37.7)	0,053
	IDU	6 (9.7)	65 (4.8)	
	MSM	24 (38.7)	595 (44.4)	
	Other/UK	6 (9.7)	128 (9.5)	
Smokers (%)		26 (63.4)	451 (42.6)	<0.001
hiv rna >5log (%)		13 (25.0)	650 (52.6)	<0.001
cd4, median [IQR]		406 [300, 549]	293 [99, 485]	0,001
cd4_cat (%)	<200	8 (15.4)	461 (37.3)	0,002
nadir_cd4, median [IQR]		396 [303, 531]	284 [91, 471]	0,001
nadir_cd4_cat (%)	<200	8 (15.4)	487 (38.7)	0,001
cd4_cd8_ratio, median [IQR]		0.47 [0.29, 0.68]	0.33 [0.16, 0.59]	0,007
Bmi, mean (SD)		25.78 (6.28)	23.67 (4.21)	0,021
BMI cat (%)	<25	13 (21.0)	538 (40.1)	0,001
	25-30	5 (8.1)	184 (13.7)	
	>=30	5 (8.1)	42 (3.1)	
	UK	39 (62.9)	577 (43.0)	
weight Kg, mean (SD)		78.20 (21.26)	71.83 (14.88)	0,046
egfr_ckd_epi, mean (SD)		109.31 (16.86)	104.55 (20.12)	0,1
hbsag_status (%)		1 (2.4)	36 (3.6)	1
hcvab_status (%)		4 (9.5)	51 (5.0)	0,351
hdl, mean (SD)		40.90 (11.29)	40.06 (13.57)	0,698
ldl, mean (SD)		116.26 (32.68)	102.88 (32.95)	0,015
triglycerides, median [IQR]		110.50 [78.75, 140.50]	100.00 [72.00, 144.00]	0,348
glycemia, median [IQR]		88 [80, 97]	86 [80, 95]	0,684
hb g/dl, median [IQR]		14.60 [12.75, 15.25]	13.60 [12.00, 14.90]	0,016
alt, median [IQR]		23 [16, 32]	25 [18, 41]	0,221
ast, median [IQR]		21 [17, 30]	27 [20, 37]	0,001
aids (%)		3 (4.8)	168 (12.5)	0,107
cvd (%)		0 (0.0)	5 (0.4)	1
esld (%)		62 (100.0)	1341 (100.0)	NA
cancer (%)		1 (1.6)	24 (1.8)	1
hypertension (%)		1 (1.6)	109 (8.1)	
dm (%)		1 (1.6)	28 (2.1)	
dyslipidemia (%)		16 (25.8)	288 (21.5)	0,515
framingham_10yrs_risk%, median [IQR]		6.30 [2.94, 14.88]	5.02 [1.94, 10.91]	0,68
disease duration, median [IQR]		24.50 [11.75, 41.25]	17.00 [8.00, 31.00]	0,058

Table 2. Characteristics of experienced PLWH switching to DOR, 2DR INSTI and 3DR INSTI in the ICONA Cohort.

		3DR_DOR	2DR_INSTI	3DR_INSTI	p
n		308	1594	1134	
age, mean (SD)		48.00 (10.14)	47.80 (12.11)	48.27 (12.19)	0,592
female gender (%)		62 (20.1)	266 (16.7)	238 (21.0)	0,014
italian (%)		41 (13.3)	206 (12.9)	202 (17.8)	0,001
hiv_transmission mode (%)	HS	131 (42.5)	557 (34.9)	479 (42.2)	<0.001
	IDU	23 (7.5)	111 (7.0)	106 (9.3)	
	MSM	146 (47.4)	828 (51.9)	488 (43.0)	
	Other/UK	8 (2.6)	98 (6.1)	61 (5.4)	
smoker_active (%)		122 (42.4)	596 (39.5)	492 (46.3)	0,003
log_hiv-rna, mean (SD)		4.59 (0.98)	4.64 (1.01)	4.74 (1.01)	0,015
hiv-rna >5log (%)		101 (33.6)	567 (36.5)	477 (43.4)	<0.001
cd4, median [IQR]		340 [192, 494]	353 [200, 519]	304 [131- 475]	<0.001
cd4, cat (%)	<200	79 (26.1)	388 (24.9)	377 (34.1)	<0.001
nadir_cd4, median [IQR]		298 [167, 441]	306 [171-455]	261 [109-411]	<0.001
cd4_bl, median [IQR]		729 [569, 912]	749 [570, 974]	708 [505-926]	<0.001
cd4_bl_cat (%)	<200	8 (2.6)	22 (1.4)	40 (3.5)	
bmi, mean (SD)		25.23 (4.38)	24.83 (4.10)	25.23 (4.65)	0,071
bmi cat (%)	<25	142 (54.8)	768 (59.2)	496 (56.4)	0,523
	25-30	89 (34.4)	403 (31.0)	283 (32.2)	
	>=30	28 (10.8)	127 (9.8)	100 (11.4)	
weight, mean (SD)		75.29 (15.12)	74.78 (13.53)	75.21 (15.06)	0,741
egfr_ckd_epi, mean (SD)		91.14 (15.63)	85.80 (20.03)	89.58 (19.55)	<0.001
hbsag_status (%)		23 (8.0)	14 (1.0)	58 (5.5)	<0.001
hcvab_status (%)		32 (10.7)	138 (9.0)	136 (12.7)	
hdl, mean (SD)		47.48 (14.20)	50.27 (15.53)	50.26 (15.14)	0,011
ldl, mean (SD)		120 (35)	117 (35)	120 (34)	0,064
triglycerides, median [IQR]		107 [72, 157]	108 [7, 151]	115 [82-166]	<0.001
glycemia, median [IQR]		86 [78, 94]	89 [81, 97]	89 [82- 98]	<0.001
hb, median [IQR]		15.2 [14.3-16.0]	15.0 [14.2-15.8]	14.8 [13.8-15.7]	<0.001
alt, median [IQR]		24 [18, 38]	23 [17, 32]	23 [16- 32]	0,006
ast, median [IQR]		24 [20, 30]	23 [19, 28]	23 [18- 28]	0,023
aids (%)		36 (11.7)	189 (11.9)	220 (19.4)	
cvd (%)		3 (1.0)	23 (1.4)	29 (2.6)	0,05
esld (%)		0 (0.0)	1 (0.1)	1 (0.1)	0,865
cancer (%)		10 (3.2)	62 (3.9)	42 (3.7)	0,857
hypertension (%)		76 (24.7)	470 (29.5)	344 (30.3)	0,15
dm (%)		17 (5.5)	77 (4.8)	83 (7.3)	0,023
dyslipidemia (%)		240 (77.9)	1162 (72.9)	870 (76.7)	0,032
framingham_10yrs_risk%, median [IQR]		7.1 [3.6, 15.8]	6.5 [2.9, 15.3]	8.0 [3.1, 16.8]	0,031
disease years] median [IQR])		9.6 [5.8, 14.3]	7.3 [4.0, 12.0]	6.7 [3.5, 11.6]	<0.001
n ART lines, median [IQR])		2 [1, 3.]	2 [1, 3]	2 [2, 4]	<0.001
virological failure_cat (%)		31 (10.1)	114 (7.2)	126 (11.1)	0,001