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OC 91 **Impact of transmitted drug resistance in naïve-patients starting 2 NRTI plus a boosted protease-inhibitor (PI) or integrase-inhibitor (INSTI)**

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Abstract:

Background: The role of transmitted drug resistance (TDR) in predicting outcomes of initial antiretroviral therapy including PI or INSTI has not been fully explored.

Methods: From the ARCA database we selected adult naïve HIV-1 infected patients starting first-line 3-drugs therapy including INSTI or PI, from 1/2008 to 6/2016, with baseline resistance genotype and at least 1 HIV-1 RNA during follow up. TDR was defined as the detection of at least one mutation among those included in the WHO-recommended SDRM list (Bennett 2009). The primary endopoints were: virological failure (VF, defined as an HIV-RNA, VL, > 200 copies/ml after week 24) and treatment failure (TF, defined as VF or treatment change for any reason). Survival analysis was used to investigate predictors of TF and VF.

Results: 1147 pts were analyzed: 1031 (89.9%) treated with PI and 116 (10.1%) with INSTI. Baseline characteristics are shown in table. In the PI-group baseline VL was higher while CD4+ cells count was lower than in INSTI. Overall TDR were 4.7% for NRTI, 4.4% NNRTI, 1.5% PI without significant differences between groups.

During a median observation time of 57 wks (IQR 26-107) TF occurred in 771 treatments in PI-group, with an estimated probability at 48 wks of 36% (CI 34.5-37.5) and in 46 in INSTI-group with an estimated probability at 48 wks of 31% (26.2-35.8); during a median observation time of 55 wks (26-107) VF occurred in 161 treatments in PI-group, with an estimated probability at 48 wks of 12% (10.8-13.1) and in 11 in INSTI-group with an estimated probability at 48 wks of 12% (8.5-15.5).

After adjusting for gender, nationality, TDF/FTC use and viral subtype, independent predictor of VF was AZT/3TC use (vs other backbones HR 3.8, CI 95% 2.2-6.3, p<0.001); adjusting for nationality and viral subtype, independent predictors of TF were geographic area (Southern vs Northern Italy, HR 0.8, 0.6-0.9, p=0.04), baseline VL (+ 1 log10 HR 1.1, 1.0-1.2, p=0.03) and AZT/3TC (versus other backbones HR 2.1, 1.5-2.8, p=<0.001). Third drug class was not associated with VF or TF. In the INSTI-group, but not in the PI-group, the presence of any NRTI TDR was predictor of VF (HR 7.1, 1.8-28.2, p=0.005) after adjusting for nadir CD4 cells count and TF (HR 2.7, 1.1-7.0, p=0.03). Among patients in the INSTI-group with VF, 3 presented NRTI TDR (2 M41L and 1 M184V). In the PI-group, adjusting for gender, nationality, geographic area, viral subtype, TDF/FTC use, baseline and nadir CD4 cells count, independent predictor of VF was AZT/3TC use (HR 3.4, 1.8-6.2, p<0.001); adjusting for nationality and viral subtype, independent predictor of TF was AZT/3TC use (vs other backbones HR 2.3, 1.7-3.1, p<0.001).

Conclusions: PI and INSTI based first-line regimens show high efficacy in the real practice; despite the low incidence of TDR, our data support the need of pre-treatment genotyping to optimize therapy in patients starting INSTI-therapy. Further studies are required to confirm our suggestions.

Table. Comparison of baseline characteristics between PI-group and INSTI-group

Characteristics	Overall	PI-group	INSTI-group	P-value*
	N= 1147	N= 1031	N= 116	
Male, n (%)	852/1133 (75.2)	759/1017 (74.6)	93 (80.2)	0.21
Age (year), median (IQR)	40 (33-48)	40 (33-48)	40 (31- 49)	0.98
Italian, n (%)	840/1053 (79.8)	768/966 (79.5)	72/87 (82.8)	0.57
Risk factor, n (%):				<0.001
Heterosexual	379 (33)	350 (33.9)	29 (25)	
Homo/bisexual	227 (19.8)	210 (20.4)	17 (14.7)	
Injection drug users	88 (7.7)	81 (7.9)	7 (6)	
Other/Unknown	453 (39.5)	390 (37.8)	63 (54.3)	
Geographical Area, n (%):				<0.001
Northern Italy	478 (41.7)	446 (43.3)	32 (27.6)	
Central Italy	445 (38.8)	402 (39)	43 (37.1)	
Southern Italy and Islands	224 (19.5)	183 (17.7)	41 (35.3)	
Time from HIV diagnosis (YY), median (IQR)	0.3 (0.1-2.4)	0.2 (0.1-2.4)	0.4 (0.1-2.7)	0.38
Baseline plasma HIV-1 RNA (log_{10} copies/mL), median (IQR)	4.9 (4.3-5.4)	5 (4.4-5.4)	4.6 (4-5.3)	0.002
Baseline CD4 cell count (cells/mm^3), median (IQR)	250 (99.8-378.3)	235 (94-362)	388 (206-554)	<0.001
CD4 nadir cell count (cells/mm^3), median (IQR)	226 (94-342)	216 (89-332)	328 (167-496)	<0.001
Subtype, n (%):				
B	790 (68.9)	712 (69.1)	78 (67.2)	0.67
non B	357 (31.1)	319 (30.9)	38 (32.8)	
Patients with transmitted drug resistance, n (%):				
NRTI	54 (4.7)	47 (4.6)	7 (6)	0.48
NNRTI	51 (4.4)	48 (4.7)	3 (2.6)	0.47
PI	17 (1.5)	14 (1.4)	3 (2.6)	0.24
INSTI	0	0	0	
Backbone, n (%):				
TDF/FTC	858 (74.8)	773 (75)	85 (73.3)	0.73
ABC/3TC	192 (16.7)	163 (15.8)	29 (25)	0.02
AZT/3TC	87 (7.6)	87 (8.4)	0 (0)	<0.001
others	10 (0.9)	8 (0.8)	2 (1.7)	0.26
Third drug				
DRV/r		287 (27.8)		
LPV/r		435 (42.2)		
ATV/r		309 (30)		
RAL			50 (43.1)	
EVG			28 (24.1)	
DTG			38 (32.8)	

*Potential differences between the two groups were evaluated by Chi-Squared test for categorical variables and by t-Student test for continuous variables.