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SWITCHING LA CBG/RPV IN VIROLOGICALLY SUPPRESSED PLHIV. DOES KNOWING PREVIOUS GENOTYPING REALLY MATTER? A SUBSTUDY FROM THE RELATIVITY COHORT

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BACKGROUND

Resistance associated mutations (RAMs) to RPV and/or INSTI, along with BMI>30 and HIV subtype A1/A6, increase the risk of CBG/RPV-associated virological failure. The aim of the current substudy is to compare efficacy outcomes in real life in virologically suppressed PLHIV who switched to CBG/RPV according to whether previous genotyping was available or not at the time of switching.

MATERIAL AND METHODS

The relativity cohort is a nationwide Spanish cohort of PLHIV older than 18 years old treated with CBG/RPV. Patients coming from CBG/RPV clinical trials are not included. 1285 cases from 37 institutions are described. Quantitative variables are compared using the U-Mann Whitney test and qualitative variables using Chi-Square and/or Fisher´s exact test.

RESULTS

The group in which previous genotyping results were available comprised 675/1285 cases (52.5%) (see table 1). PLHIV within this group, were more frequently spanish, (74% vs 67.7%; p-value=0.012), older (46.0 years old [37.0, 56.0] vs 44.0 [37.0, 52.0]; p= 0.012) and had more psychiatric disorders (11.1% vs 7.0%; p=0.015); Besides, blips (33.0% vs 15.0%; p=0.005) and documented virological failures with any oral ART before switching (5.9% vs 3.2%; p<0.001) were more frequent in it. Time on oral ART until switch to LA CBG/RPV was significantly shorter in this group (9.0 [5.0, 12.0] vs 10.0 [6.0, 18.0] years; p-value <0.001), as was the length of the period with undetectable viral load in plasma before switching (73.0 [37.2, 117.0] vs 96.0 [45.0, 156.0] months; p-value<0.001). The median follow-up was 7.6 [5 – 11] months Switching from DTG/RPV (26.0%vs 19.7%; p<0.001) or DRV-based regimens (6.4% vs 2.3%, p<0.001) (figure 2) was more frequent when genotyping was unavailable. There were no statistically significant differences in time of follow-up, CD4 T cell count at the time of switch and abandon rate. Surprisingly, there was trend regarding the development of virological failure favouring the group of unknown genotype (tables 1 and 2).

	Known genotype N = 675/1285	Unknown genotype N = 610/185	p-value
Age (years) (median [IQR])	44.0 [37.0, 52.0]	46.0 [37.0, 56.0]	**0.012**
Sex, n (%)			
Female	89 (13.2)	94 (15.5)	0.288
Male	583 (86.8)	513 (84.5)	0.288
Nationality, n (%)			
Spaniards	497 (74.0)	405 (67.7)	**0.017**
Migrants	175 (26.0)	193 (32.3)	**0.017**
CD4 nadir (cells/mm3), median [IQR]	346.0 [201.0, 500.0]	329.0 [198.5, 480.0]	0.298
HIV diagnosis viral load (copies/ml) (median [IQR])	65755.0 [19200.0, 215050.0]	49630.5 [9723.5, 156895.0]	**0.005**
Months from diagnosis to start of first ART (median [IQR])	2.0 [0.0, 12.0]	3.0 [1.0, 22.0]	**<0.001**
AIDS, n (%)	78 (11.6)	83 (13.6)	0.322
Years of ART from treatment start to beginning of CBG/RPV (median [IQR])	9.0 [5.0, 12.0]	10.0 [6.0, 18.0]	**<0.001**
Months of undetectability until start of CAB+RPV (median [IQR])	73.0 [37.2, 117.0]	96.0 [45.0, 156.0]	**<0.001**
Previous virological failure on any ART regimen (%)	39 (5.8)	19 (3.1)	**<0.001**
Which third drug was involved in the failure?, n (%)			
INI	9 (1.3)	7 (1.1)	0.702
NNRTI	9 (1.3)	4 (0.7)	0.393
PIs	17 (2.5)	3 (0.5)	0.073
Not available	4 (0.6)	5 (0.8)	1
Number of BLIPS in the 5 years prior to CBG/RPV treatment, n (%)			
0	508 (77.0)	500 (85.0)	**<0.001**
1	102 (15.5)	55 (9.4)	0.281
2	23 (3.5)	19 (3.2)	0.788
3	12 (1.8)	8 (1.4)	0.52
More than 3	15 (2.3)	6 (1.0)	0.076
Baseline genotipying previous to switch, n (%)	675 (100.0)	-	
Basal genotype type B	312 (79.8)	-	
Basal genotype type A1/A2	21 (5.4)	-	
Basal genotype F/CRF	21 (5.4)	-	
Basal genotype other	37 (9.5)	-	
Not available	284		
Wild type without mutations, n (%)	451 (66.8)	-	
PLHIV harbouirng virus with RAMs to NRTI, n (%)	63 (9.3)	-	
184V	13 (1.9)	-	
Others	65 (9.6)	-	
PLHIV harbouirng virus with RAMs to NNRTI, n (%)	63 (9.3)	-	
K103N	18 (2.7)	-	
E138A	3 (0.4)	-	
Others	37 (5.5)	-	
PLHIV harbouirng virus with RAMs to INSTI, n (%)	5 (0.7)	-	
L74M/I/F	1 (0.1)	-	
T97A	2 (0.3)	-	
Others	7 (1.0)	-	
Treatment discontinuation, n (%)	32 (4.7)	33 (5.4)	1
Days of treatment discontinuation (median [IQR])	216.0 [86.5, 279.0]	113.0 [78.0, 207.0]	**0.06**
Systemic adverse effects, n (%)	5 (0.7)	3 (0.5)	0.678
Related to local injection site reaction, n (%)	9 (1.3)	11 (1.8)	0.17
Virological failure, n (%)	5 (0.7)	1 (0.2)	**0.09**
Other, n (%)	13 (1.9)	18 (3)	0.432
Type of toxicity, n (%)			
Dizziness	0 (0.0)	0 (0.0)	-
Headache	1 (20.0)	0 (0.0)	1
Dysthermia	0 (0.0)	0 (0.0)	-
Fever	1 (20.0)	2 (66.7)	1
Nausea	0 (0.0)	0 (0.0)	-
Others	3 (60.0)	1 (33.3)	1

Table 1. Basal characteristics of both groups of the cohort according to genotype availability

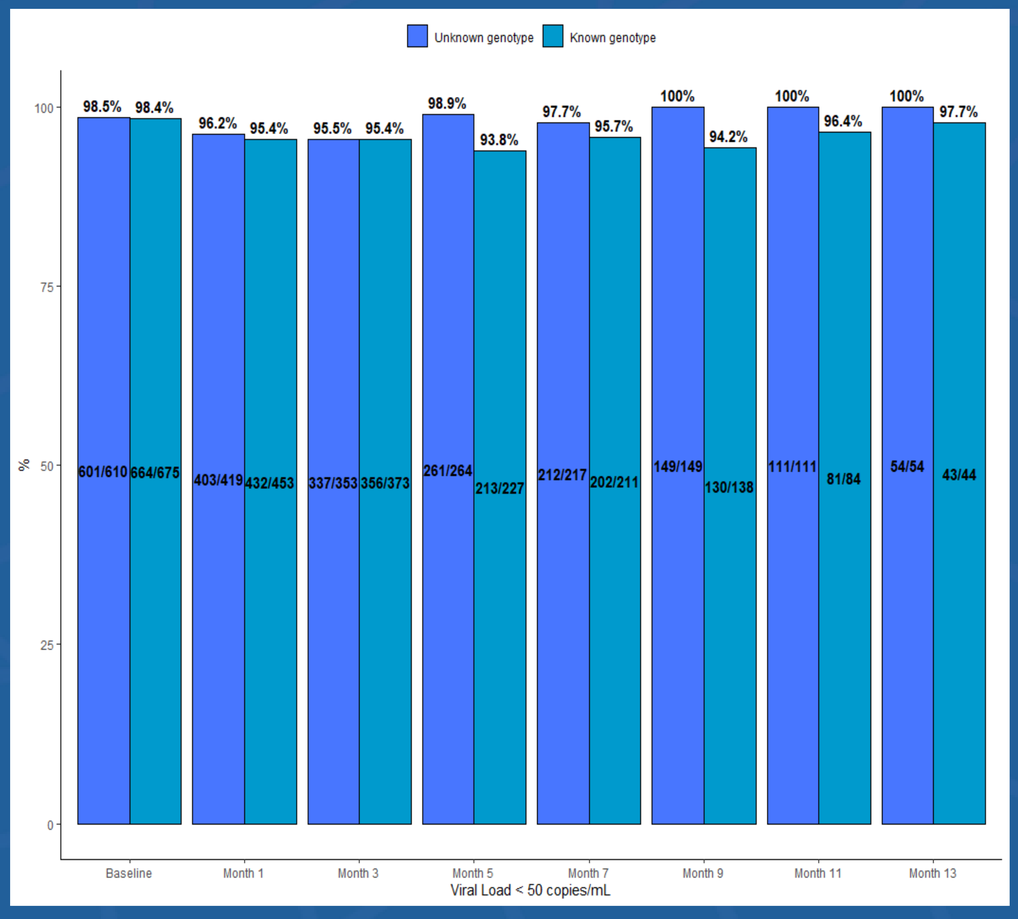

Figure 1: Percentage of PLHIV with VL<50 copies/mL in both subgroups throughout the different follow up periods

	1	2*	3	4**	5	6***
Sex	Male	Male	Male	Male	Female	Male
Age (years)	49	45	40	50	52	49
Body Mass Index (Kg/m^2)	22.5	29.3	24.3	33.9	36.3	27.5
Previous treatment	BIC/FTC/TAF	DTG/3TC	DTG/3TC	DTG/3TC	DTG/RPV	BIC/FTC/TAF
Month of discontinuation	7	7	9	9	1	9
Viral Load at discontinuation	3140	44000	289	128000	362	217
Previous mutations	Wild type without mutations	-	Wild type without mutations	INSTI: Q148K; Q148R; E157Q; NNRTI: G140S; L74M/I/F; T97A	184V; K103N	Wild type without mutations
New resistance mutations	No	INSTI: E138K, Q148R, L74LM and NNRTI: K103N, Y188L	No	INSTI: L100I; K103N	No	INSTI: Y143YS; Q148R
Oral ART after VF	DTG/3TC	DRVc/FTC/TAF	BIC/FTC/TAF	DRVc/FTC/TAF	DRVc/FTC/TAF	DRVc/FTC/TAF
VL supression	Yes	No	Yes	Yes	Yes	Yes

Table 2. Description of cases with confirmed virologic failure.*Screening failure. Previous VF with probable RAMs against INSTI unnoticed; **Patient with baseline mutations not known at the moment of switch *** Patient undetectable at the time of switch to oral ART. Two previous viral loads>200, last 217. In spite of it, resistances to INSTI were detected.

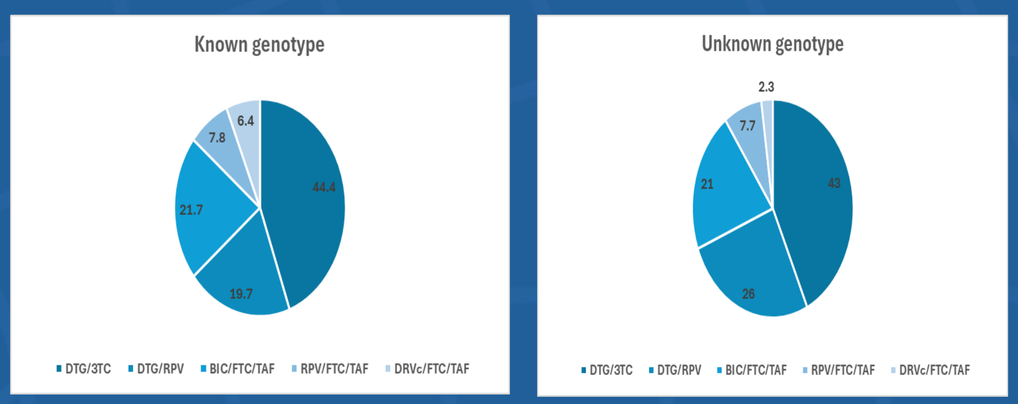

Figure 2: Oral ART previous to switch in both groups

CONCLUSIONS

Our results suggest that unavailability of previous genotyping doesn´t seem to increase the risk of virological failure in virologically suppressed PLHIV who switch to LA CBG/RPV. These seems to line up with the results of the CARES study. Nevertheless, a longer follow up is required to reach solid conclusions.

RELATIVITY