Single-center study of trends in HIV drug resistance

Perren-Llerena G[1], García-Deltoro M[2], Rosas ME[3], Rubio-Cordova C[4], Lopez-Lam P, Ortega-González E[2]

[1] Luzerner Kantonsspital [2] Consorcio Hospital General Universitario Valencia [3] Applied Statistics Center, Peru [4] Universitat València

Category n(%)	Patients n(%)	Risk Group			
		IDU	MSM	Heterosexuals	Unknown
Patients	852 (100)	334 (100)	235 (100)	159 (100)	124 (100)
Origin					
Africa	33 (3.9)	2 (0.6)	0	29 (18.2)	2 (1.6)
Europe	659 (77.3)	316 (94.6)	182 (77.4)	106 (66.7)	55 (44.4)
Latinamerica	63 (7.4)	1 (0.3)	43 (18.3)	17 (10.7)	2 (1.6)
Unknown	97 (11.4)	15 (4.5)	10 (4.3)	7 (4.4)	65 (52.4)
Sex					
Men	637 (74.8)	257 (76.9)	234 (99.6)	61 (38.4)	88 (71.0)
Women	206 (24.2)	74 (22.2)	0	99 (62.3)	27 (21.8)
Antiretroviral therapy (ART)					
Naïve	366 (43.0)	99 (29.6)	158 (67.2)	102 (64.2)	7 (5.6)
Experienced	417 (48.9)	229 (68.6)	74 (31.5)	55 (34.6)	117 (94.4)
HIV Subtype					
B	762 (89.4)	316 (94.6)	212 (90.2)	117 (73.6)	117 (94.4)
Non-B	69 (8.1)	11 (3.3)	15 (6.4)	38 (23.9)	5 (4.0)

Table 1. Study Population

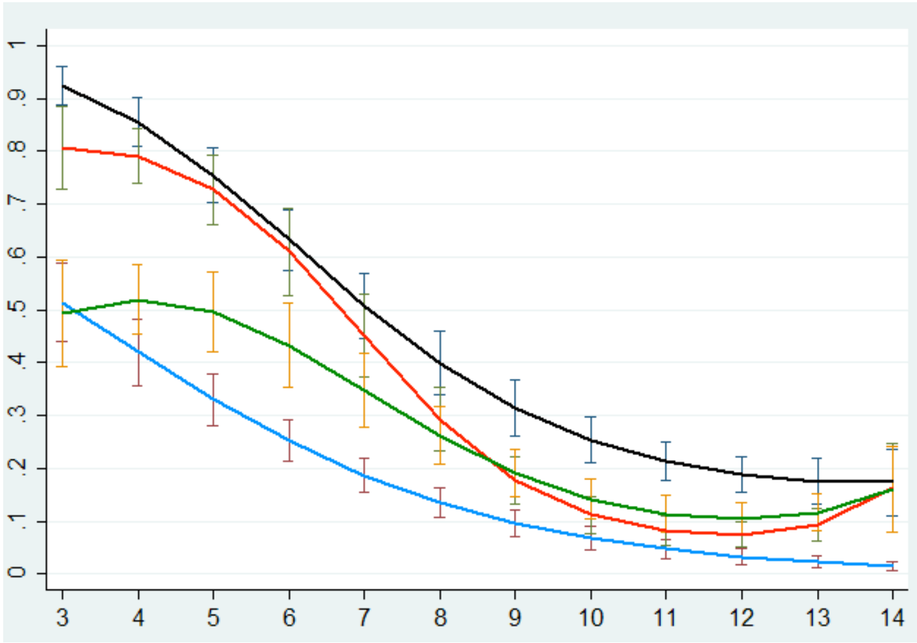

Figure 1. Overall trends of drug resistance rate (black line) according to antiretroviral classes. NRTI (red line); NNRTI (Green line); and PI (blue line). Significant increasing trend for NRTI and NNRTI resistance from 2012 to 2014 ($p<0.05$)

Introduction and Purpose:

HIV major drug resistance mutations compromise the success of ART. Genotyping them enables adjusted therapeutic decisions. Our objective was to describe the trends in drug resistance mutations to PI, NRTI and NNRTI among a University Hospital in Spain over the years 2003 and 2014.

Methods:

This is a transversal observational study. Treatment histories, viral sequences, demographic and clinical data were retrieved from our center database. All patients with a genotypic resistance test (GRT) were included (N=852), ART-naïve and ART-experienced patients were compared according to risk groups and calendar year. We collected all mutations according to the HIV-1 RT and PR Mutations for Drug-Resistance Surveillance of the Stanford HIV Drug Resistance Database.

Results:

A description of our population is summarized on table 1.

The overall rate of mutations was 40.73%. The rate in the ART-naïve and ART-experienced patients was 11% and 68.89% respectively.

We could appreciate a higher proportion of transmitted drug resistance mutations in the MSM group (19, 47.5%), compared to IDU (14, 35%) and heterosexuals (7, 17.5%).

A declining trend of the overall mutation rate was found (OR 0.38; IC95%: 0.28-0.51; p=0.000); however, after analysing the trends according to antiretroviral classes, we found a significant increasing trend for NRTI resistance (OR 1.01; IC95%: 1.00-1.02; p=0.013) and NNRTI resistance (OR 0.80; IC95%: 0.66-0.95; p=0.012) from 2012 to 2014 (Figure 1). We did not find differences in the ART-naïve group, probably because of a low number of positive GRT in this group. The ART-experienced group showed a very similar trend to the global rate, probably because it represented the major population of the study. Table 2 shows overall mutations with statistical significance according to risk groups. We excluded 124 patients with unknown risk group.

Overall double and triple class resistance mutations are also shown in table 2. In the ART-experienced group we found not only a significantly increased double class resistance for PI and NNRTI in the MSM group (18.84%, p=0.040), but also a significantly increased triple class resistance in this group (18.84%, p=0.009).

Mutation n(%)	Patients n(%)	Risk Group			
		IDU	MSM	Heterosexuals	*P*
Patients	852 (100)	334 (100)	235 (100)	159 (100)	
PI-Resistance					
D30N	10 (1.2)	8 (2.4)	0	0	0.01
M46IL	56 (6.6)	19 (5.7)	12 (5.1)	2 (1.3)	0.047
V82A	32 (3.8)	15 (4.5)	6 (2.6)	0	0.01
N88D	12 (1.4)	7 (2.1)	0	0	0.023
L90M	58 (6.8)	24 (7.2)	9 (3.8)	3 (1. 9)	0.023
NRTI-Resistance					
K70R	43 (5.1)	16 (4.8)	13 (5.5)	1 (0.6)	0.019
M184VI	177 (20.8)	85 (25.5)	26 (11.1)	17 (10.7)	0.000
NNRTI-Resistance					
K103N	120 (14.1)	55 (16.5)	25 (10.6)	14 (8.8)	0.031
Double class resistance					
PI+NNRTI	42 (4.9)	26 (7.8)	14 (6.0)	2 (1.3)	0.007
NRTI+NNRTI	106 (12.4)	60 (18.0)	33 (14.0)	13 (8.2)	0.014
PI+NRTI	78 (9.2)	56 (16.8)	17 (5.1)	5 (3.1)	0.000
Triple class resistance					
PI+NRTI+NNRTI	38 (4.5)	23 (6.9)	14 (6.0)	1 (0.6)	0.003

Table 2. Frequency of mutations according to risk group

Conclusions:

We observed an overall decreasing trend of HIV resistance. We think that the increasing pattern of NRTI and NNRTI resistance could be explained by the high amount of treatments with NRTI and NNRTI that were approved since 2000.

Our study population had a major group of IDU and the significance of mutations in this group was probably overestimated; however, we did not only found a higher proportion of transmitted drug resistance mutations in the MSM group compared to IDU and heterosexuals, but also a significantly steep frequency of double and triple class acquired resistance.

We found a very low frequency of HIV transmitted mutations. This shows that the risk for multiresistance transmission is still very low.

References:

García F et al. Transmission of HIV drug resistance and non-B subtype distribution in the Spanish cohort of antiretroviral treatment naïve HIV-infected individuals (CoRIS). Antiviral Res. 2011 Aug;91(2):150–3.

Ortega-González E et al. Trend of the prevalence of HIV-1 resistance mutations in the Valencian Autonomous Region (2004-2011), and its relation with the antiretroviral usage patterns. The RUVEN study (SEICV-VIH-2012-01).

Yebra G et al. Different trends of transmitted HIV-1 drug resistance in Madrid, Spain, among risk groups in the last decade. Arch Virol. 2014 May;159(5):1079–987.

giollerenag@gmail.com