Transmitted drug resistance in Spain (Coris) during 2019-2021

CoRIS Cohorte de la Red de Investigación en Sida

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P054

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Background & Aim

Testing for transmitted drug resistance (TDR) in the reverse transcriptase (RT) and protease (Pro) in newly diagnosed patients with HIV is recommended by clinical guidelines, as a part of the initial clinical assessment. On the other hand, INSTI baseline resistance is not recommended by clinical guidelines, so surveillance programs offering these data in real time are needed.

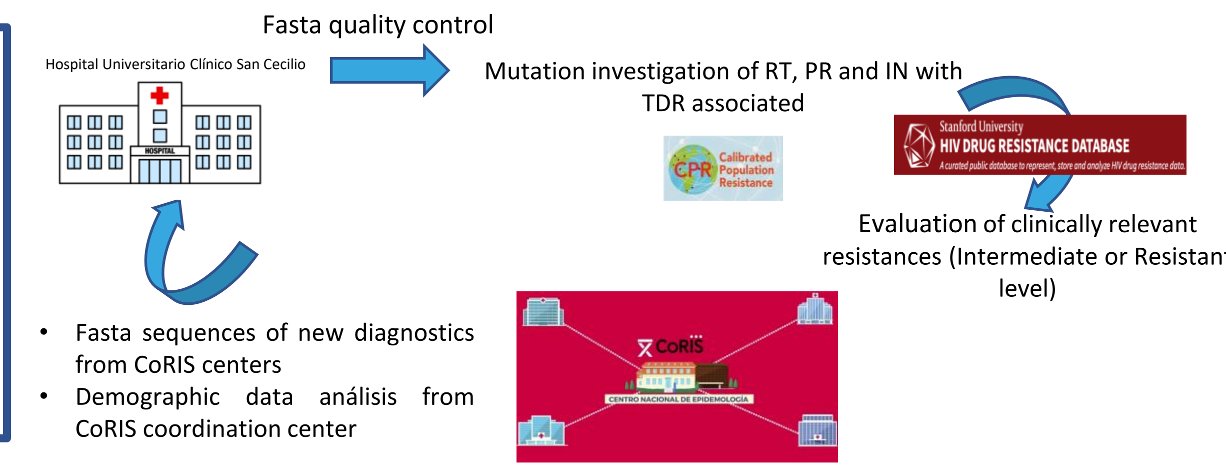
CoRIS program a platform for HIV research in people living with HIV, was established in 2004 and the transmitted drug resistance (TDR) work package begun in 2007.

The aims of our study are:

- ✓ To update TDR data in newly diagnosed patients from CoRIS for the period 2019-2021
- ✓ To present results on transmitted resistance with clinical relevance to drugs included in ART recommended as first line treatment in Spain

Methods

- We analyzed RT and Pro fasta sequences of HIV new diagnostics from 22 CoRIS centers. As integrase is not part of routine testing in NAÏVE patients in Spain, we analyzed only a subset of available integrase sequences.
- After fasta quality control, mutations in RT, Pro and integrase associated with TDR were investigated using the CPR-Stanford tool.
- To evaluate clinically relevant resistance (Intermediate or Resistant level) to the drugs currently recommended as first-line treatment in the GESIDA guidelines, as well as to the NNRTIs EFV, DOR and RPV, we used the Stanford v.9.1 HIVDB Algorithm.



Results

A total of **1859** patients were analyzed, 758 (2019), 567 (2020) and 534 (2021); of these, integrase data were available in **651** patients, 264 (2019), 167 (2020) and 220 (2021).

Most of the patients were MSM, aged 26-45, with high school or university education. Half of them presented with less than 10^5 c/ml HIV-RNA and/or more than 350 CD4 count.

Characteristics	Class	n (%)
Age	<=25	18%
	26-35	43%
	36-45	20%
	46-55	12%
	>55	6,70%
Education	no studies	0,20%
	primary school	8,80%
	secondary school	43,90%
	university	28,80%
	other/unknown	18,30%
Gender	male	91%
	female	8,90%
Origin	Spain	43,60%
	Europe (not-Spain)	4,30%
	Africa	4,60%
	Latin/Central America	46,40%
Transmission route	MSM	75,30%
	PWID	0,30%
	MSW	19%
	other/unknown	5,40%
CD4 counts (cells/mm3) (%)	<200	21.1%
	200-350	25.1%
	350-1000	54.1%
	>1000	1.4%
	Unknown	1.2%
Viral Load (copies/mL) (%)	<100.000	50.6%
	100.000-500.000	29.2%
	>500.000	17.6%
	Unknown	2.3%%
HBV coinfection (%)	Yes	1.8%
	No	70%
	Unknown	28.1%
HCV coinfection (%)	Yes	2.5%
	No	91.4%
	Unknown	6%

* Demographic data from 2021 are not included

Transmitted drug resistance (TDR) in the period 2019-2021 was: 3.7% for NRTIs, 6.02% for NNRTIs, 0.97% for PIs, and 0.15% for INIs. Of interest, most of the patients with TDR carried singletons

Nº of mutations	NRTIs	NNRTIs*	PIs	INIs**
1 mut	47 (3.4%)	90 (6.6%)	17 (1.2%)	1 (0.15%)
2 mut	13 (1.5%)	22 (1.6%)	1 (0.08%)	-
≥3 mut	3 (0.2%)	-	-	-
Prevalence	3.7%	6.02%	0.97%	0.15%

*E138A not included at WHO list

A detailed description of the most relevant TDR mutations included in current SDRM lists is shown below

	Mutation	n (%)
NRTIs	M41L	22 (1.6%)
	M184IV	14 (1.02%)
	L210W	12 (0.87%)
	Others*	21 (1.5%)
PIs	M46IL	9 (0.65%)
	I47V	2 (0.15%)
	I85V	2 (0.15%)
	Others**	6 (0.4%)
NNRTIs	K103NS	91 (6.6%)
	K101EP	13 (0.95%)
	G190AES	13 (0.95%)
	P225H	5 (0.4%)
	Others***	8 (0.6%)
INIs	E92Q	1 (0.15%)

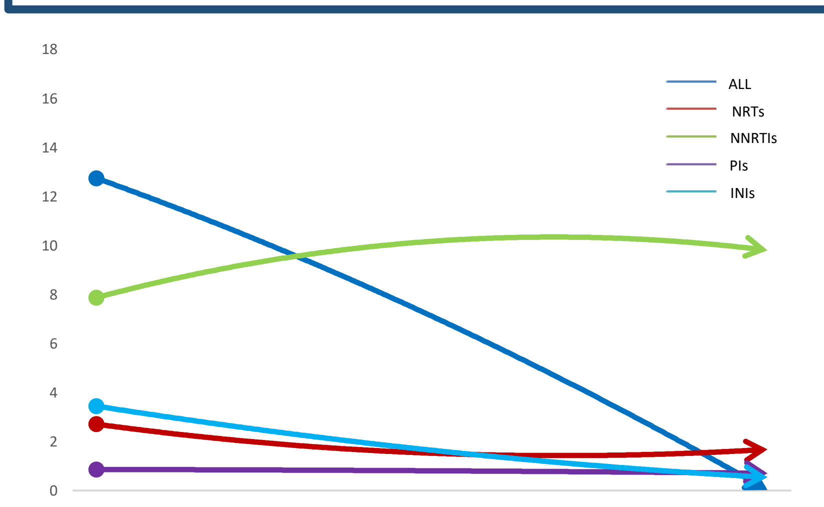
*D67NG, K219QENR, K70E, T215SDYQEI, L74IV, T69D; **D30N, N88D, F35Y, G73C, L90M, V82A
***Y188CL, L100I, V179F, Y181C

Clinically relevant resistance to first-line drugs in the period 2019-2021 was 1.3% for TDF (of which 1.2% were Intermediates), 2% for ABCs, 0.8% for 3TC/FTCs, 6.5% for EFVs, 2.6% for DOR (1.5% I), 7.1% for RPV, 0.7% for RAL (all Intermediate), 0.05 % for BIC, DTG (n=1, S153F) and DRV

		n	Prevalence (IC 95%)
NRTIs	Tenofovir	25	1.3 (0.9-1.9)
	3TC/FTC	15	0.8 (0.5-1.3)
	Abacavir	39	2.1 (1.5-2.8)
NNRTIs	Efavirenz	120	6.5 (5.3-7.7)
	Rilpivirine	132	7.1 (5.9-8.4)
	Doravirine	48	2.6 (1.9-3.4)

		n	Prevalence (IC 95%)
PIs	Lopinavir	4	0.2 (0.06-0.5)
	Atazanavir	2	0.1 (0.01-0.4)
	Darunavir	1	0.05 (0.0013-0.3)
INIs	Dolutegravir	1	0.05 (0.0013-0.3)
	Raltegravir	13	0.7 (0.4-1.2)
	Bictegravir	1	0.05 (0.0013-0.3)

From 2007, we have assisted to a decrease in clinically relevant resistance (CRR) to all drug classes except for NNRTIs, driven by the introduction of second generation integrase inhibitors as preferred drugs for first line regimens



Conclusions

As in previous years, the highest prevalence of transmitted resistance occurred for NNRTIs, with doravirine being the drug in this family with the lowest levels of TDR. Transmitted resistance to PIs, INIs, and 3TC/FTC continues at very low levels, with no patient presenting full resistance to 2nd generation integrase inhibitors or darunavir.

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