TRANSMITTED DRUG RESISTANCE TO INTEGRASE BASED FIRST-LINE TREATMENT IN EUROPE

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BACKGROUND

- Integrase strand-transfer inhibitors (INSTIs) based regimens are recommended regimens for first-line antiretroviral therapy.
- Currently, there is a growing interest on rapid initiation of first-line therapy.
- Monitoring of transmitted drug resistance in real time is needed.
- Our objective has been to study the prevalence of transmitted drug resistance to the INSTIs and the NRTI backbone in newly diagnosed patients that are naïve to antiretroviral therapy (ART).

METHODS

- MeditRes HIV is a consortium that includes ART naïve people living with HIV that have been newly diagnosed in France, Greece, Italy, Portugal and Spain during the years 2018-2021.
- Reverse transcriptase (RT), protease (Pro) and Integrase were sequenced following standard methodologies in use at the participating centers.
- To evaluate the prevalence of surveillance drug resistance mutations (SDRM) we used the Calibrated Population Resistance (CPR) tools (integrase and RT-Pro) available at Stanford HIV website.
- To evaluate clinically relevant transmitted resistance, we used the Stanford v.9.0 HIVDB Algorithm.

CONCLUSIONS

- Here we describe the most recent data on transmitted drug resistance to integrase based first-line regimens in Mediterranean Europe.
- Given the low prevalence of clinically relevant resistance to second generation INSTIs and to first-line NRTIs, in the years 2018-2021 it is very unlikely that a newly diagnosed patient in MeditRes countries would present with baseline resistance to a first-line regimen based on second generation INSTIs.

RESULTS

Characteristic	Class	(%)
Gender (%)	Male	72.2%
	Female	17.5%
	Transgender/Other	0.5%
	Unknown	9.9%
Age, years (%)	<30	21.1%
	30-50	45.3%
	>50	23.4%
	Unknown	10.2%
Origin (%)	Europe	47.2%
	Africa	17.5%
	Asia/Oceania	2.8%
	America (South/Central)	9.2%
	Other/unknown	23.2%
Transmission Route (%)	PWID	1.3%
	MSM	43.0%
	MSW	27.4%
	Other/unknown	28.3%
CD4 counts (cells/mm^3) (%)	<200	24.7%
	200-350	20.2%
	350-1000	36.7%
	>1000	1.3%
	Unknown	17.1%
Viral Load (copies/mL) (%)	<100,000	40.5%
	100,000-500,000	25.3%
	>500,000	18.9%
	Unknown	15.3%
Viral subtype (%)	B	56.3%
	CRF02_AG	16.3%
	A	5.9%
	C	5.2%
	F	4.6%
	Others	11.7%
HBV coinfection (%)	Yes	5.7%
	No	71.2%
	Unknown	23.1%
HCV coinfection (%)	Yes	2.4%
	No	75.2%
	Unknown	22.4%

PWID, people who inject drugs; MSW, men who have sex with women; MSM, men who have sex with men.

- Overall, we included 2705 patients with integrase and RT data available.
- The prevalence of **INSTI SDRMs** was **0.23%**, while for **NRTI SDRMs** was **3.73%**.
- **Clinically relevant resistance (CRR)**, defined as any resistance level for Stanford interpretation >= 3, was **2.42% for INSTIs** and **1.76%** to the components of the **NRTI** backbones.

Mutation	n (%)
M184V	23 (0.85)
M184I	5 (0.18)
K65R	1 (0.04)
Any TAM	72 (2.66)

Prevalence of NRTI SDRM

Mutation	n (%)
T66I	1 (0.04)
T66A	1 (0.04)
E138T/K	2 (0.08)
E92Q	1 (0.04)
R263K	1 (0.04)

Prevalence of INSTI SDRM

Drug	n (%)
TDF/TAF	24 (0.89)
Abacavir	49 (1.81)
3TC/FTC	31 (1.15)

Prevalence of NRTI CRR

Drug	n (%)
Raltegravir	62 (2.29)
Elvitegravir	63 (2.33)
Bictegravir	5 (0.18)
Dolutegravir	5 (0.18)

Prevalence of INSTIs CRR

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