Impact of NGS-Detected Viral Mutations on HIV Viral Decay in Patients Initiating a BIC/TAF/FTC Regimen

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Background: Integrase inhibitors (INIs) are recommended as a component of initial HIV treatment in most clinical guidelines. Next-generation-sequencing (NGS) has the capability to identify low-abundance drug-resistant HIV-1 variants within the viral quasi-species at levels lower than 20%. The objective of our study is to evaluate the impact of minor transmitted resistance mutations in viral decay in a group of people newly diagnosed with HIV and starting a first regimen with BIC/F/TAF.

Materials and methods: In our study we enrolled 48 patients newly diagnosed with HIV infection and who started a regimen containing BIC/TAF/FTC. A resistance test was performed on all patients using the NGS method, together with the determination of HIV viremia and $CD4^+$ lymphocyte count and the CD4/CD8 ratio. HIV-RNA viremia and $CD4^+$ determination were repeated 4 and 12 weeks after antiretroviral start.

Results: Table 1 shows the characteristics of the population under analysis. 36 PLWH showed no resistance to NGS testing, whereas 12 PLWH showed ≥ 1 mutation on the reverse transcriptase/integrase class. Table 2 shows the mutations found with the NGS method. The analysis of the nucleotide sequences was carried out by positioning the resistance threshold at 5%, 10% and 20%. After 4 and 12 weeks, the determination of HIV-1 viremia and lymphocyte typing was repeated in both analyzed groups.

Table 1. Characteristics of the groups analyzed

	Population (n=48)	Wild type (n=36)	Non-Wild type (n=12)
Male	42 (87.5%)	30 (83.3%)	12 (100%)
Female	5 (10.4%)	5 (13.9%)	-
MtF	1 (2.1%)	1 (2.8%)	-
Age (min-max)	46.40 (23-78)	44,17 (23-78)	53,08 (23-73)
Weeks of HIV (min-max)	96.46 (22-168)	96,89 (22-168)	95,15 (55-125)
CDC C Stage at diagnosis (%)	20 (41.7%)	16 (44.5%)	4 (33.3%)
HIV-RNA at diagnosis, copies/mL	1103614	914231	1655983
AIDS event	18 (37.5%)	15 (41.7%)	3 (25%)
% of HIV-RNA >100.000 at diagnosis	33 (68.8%)	24 (66.7%)	9 (75.5%)
% of HIV-RNA >500.000 at diagnosis	19 (39.6%)	13 (36.1%)	6 (50%)
CD4+ at diagnosis	243.83 (4-654)	250 (9-598)	225 (4-654)
CD4/CD8 at diagnosis	.3077 (.00-1.40)	.3186 (.00-1.40)	.2750 (.00-.90)
HCV Ig positive	1 (2.1%)	1 (2.8%)	0
CMV Ig positive	38 (79.2%)	28 (77.8%)	10 (83.3%)
HIV-1 Subtypes			
A1	2 (4.2%)	2 (5.6%)	-
B	22 (45.8%)	15 (41.7%)	7 (58.3)
C	1 (2.1%)	1 (2.8%)	-
CRF	19 (39.6%)	15 (41.7%)	4 (33.3%)
F1	3 (6.3%)	3 (8.3%)	-
G	1 (2.1%)	-	1 (83.3)

The analysis (Table 3) did not highlight any statistically significant difference regarding viremia and $CD4^+$ values between the two groups during the entire observation period. The wild-type group took 12.73 weeks to achieve HIV 1-RNA viremia below 50 copies/mL, whereas the transmitted resistance group took 19.92 weeks to achieve viral suppression (p=.037)

Table 2. Mutations found with the NGS method

	RT 20%	RT 10%	RT 5%
K70Q			1 (2,08%)
V106I	3 (6,25%)	2 (4,16%)	
T215S/D/E/DE	3 (6,25%)	1 (2,08%)	
L210W	1 (2,08%)		4 (8,34%)
M41L	1 (2,08%)		
E138A	1 (2,08%)		
T69 N/D	1 (2,08%)		
A98G	1 (2,08%)		
K103NT/T	2 (4,16%)		
K219R			1 (2,08%)
F227C			1 (2,08%)
F227V			1 (2,08%)
N348I	1 (2,08%)		
L100V			1 (2,08%)
I54S			1 (2,08%)
Q58E	3 (6,25%)		
K43T	1 (2,08%)		
Q148H/K	1 (2,08%)		
Q148R			1 (2,08%)
L74M	1 (2,08%)		
Y143S			4 (8,34%)
Y143H		1 (2,08%)	3 (6,25%)
S147G			2 (4,16%)
S147R			2 (4,16%)
N155D			1 (2,08%)
E157Q	1 (2,08%)	1 (2,08%)	1 (2,08%)
S153Y			1 (2,08%)

Table 3. Results.

	Wild type (n=36)	Non-Wild type (n=12)	p
HIV-RNA at diagnosis, copies/mL	914231	1655983	.913
HIV-RNA 4 weeks (± 2 ww), copies/mL	382.2	374.6	.973
HIV-RNA 12 weeks (± 2 ww), copies/mL	42.9	267.7	.212
$CD4^+$ at diagnosis, cell/mmc	250	225	.520
$CD4^+$ 4 weeks (± 2 ww), cell/mmc	341	301	.505
$CD4^+$ 12 weeks (± 2 ww), cell/mmc	398	345	.572
CD4/CD8 at diagnosis	.28	.32	.856
CD4/CD8 4 weeks (± 2 ww)	.43	.43	.675
CD4/CD8 12 weeks (± 2 ww)	.31	.52	.354
Weeks to obtain HIV 1-RNA <50 cp/mL	12,73	19,92	*.037*

Conclusions: The availability of high genetic barrier regimens such as BIC/F/TAF allows the clinician to obtain successful virological results even in scenarios in which the resistance test conducted with the NGS method detects minor resistance to classes such as NRTIs or even INIs. The data presented in this real-life study aims to strengthen the safety of a regimen such as BIC/F/TAF even in conditions in which it is not possible to obtain the results of the resistance test before starting antiretroviral therapy.