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High Prevalence of Baseline NRTI Resistance in PWH Switched from Second-line PI/r to B/F/TAF

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BACKGROUND

Patients on PI/r-based regimens in resource-limited settings have high rates of NRTI resistance, but testing is rarely available.

METHODS

In this open-label prospective trial conducted at GHESKIO in Haiti, virologically suppressed adults on second-line PI/r-based ART were randomized to continue current regimen vs. switch to B/F/TAF. The primary endpoint was the proportion with HIV-1 RNA ≥200 copies/mL at week 48 using the FDA snapshot algorithm. Proviral DNA genotype testing (GenoSure Archive, Monogram Biosciences) was performed on baseline samples for all participants randomized to B/F/TAF, HIV RNA genotyping was done for participants with virologic failure (VF), and results were interpreted using IAS-USA resistance associated mutations (RAMs) and Stanford HIVdb version 9.7.

RESULTS

Study cohort and baseline characteristics- Between October 2020 and April 2023, of 436 patients screened, 301 were randomized and treated (B/F/TAF: 153; PI/r: 148).

	B/F/TAF	bPI
Age—median (IQR)	49.5 (43.6, 56.2)	48.0 (40.5, 57.4)
Female—n (%)	90 (58.8)	83 (56.1)
Total duration of ART (years)—median (IQR)	10·8 (8.0, 12.8)	9·6 (7.1, 12.0)
Duration of ritonavir-boosted PI regimen (years)—median (IQR)	3.4 (1.9, 5.5)	4.1 (2.5, 6.2)
Ritonavir-boosted Protease Inhibitor—n (%)		
Atazanavir	63 (41.2)	58 (39.2)
Lopinavir	90 (58.8)	90 (60.8)
NRTIs—n (%)		
TDF+FTC/3TC	118 (77.1)	116 (78.4)
AZT+3TC	30 (19.6)	24 (16.2)
ABC+3TC	5 (3.3)	8 (5.4)

All were taking lamivudine or emtricitabine.

Primary outcome- At week 48, the proportion with HIV-1 RNA ≥200 copies/mL was 0.7% (1/153) and 4.1% (6/148) in the B/F/TAF and PI/r groups, respectively. 145 (94.8%) and 132 (89.2%), respectively, had 48-week HIV-1 RNA <200 copies/mL.

Switching virally suppressed adults **with or without NRTI resistance** from a second-line PI/r regimen to B/F/TAF was non-inferior to continuing a PI/r regimen, suggesting this switch can be done without baseline or historical drug resistance testing in regions where INSTI resistance is uncommon.

TABLE 1. Proviral DNA Genotyping NRTI RAMs at Baseline in Participants Randomized to B/F/TAF

RAM or RAM pattern	Number (n=149)	Prevalence
Any NRTI resistance	79	53.0%
M184V/I	76	51.0%
K65R	24	16.1%
M184V/I + K65R	21	14.1%
K70E	5	3.4%
L74I/V	7	4.7%
M184V/I + ≥3 TAMs	14	9.4%
M184V/I + M41L + L210W + T215Y	3	2.0%

TABLE 2. Proviral DNA Genotyping Baseline Resistance to INSTIs and PIs

Bictegravir and Dolutegravir	n=149 (%)
Potential Low-level resistance (G140R: n=3; E138K: n=2)	5 (3.4%)
Intermediate-level resistance (L74M, R263K)	1 (0.7%)
Atazanavir-ritonavir	
Potential low-level or Low-level resistance (M46I/L: n=5; G73S: n=2; N88D, N83D, I54L, I54T, V82C/F, V82A, V32I: n=1 each)	14 (9.4%)
Intermediate-level resistance (V32I+I47V)	1 (0.7%)
High-level resistance (M46I+I54V+I84V)	1 (0.7%)
Lopinavir-ritonavir	
Potential low-level or low-level resistance (M46I/L: n=5, I54L, I54T, V32: n=1 each)	8 (5.4%)
Intermediate-level resistance (I50V, V82C/F, V82A, V32I+I47V: n=1 each)	4 (2.7%)
High-level resistance (M46I+I54V+I84V)	1 (0.7%)

RESULTS CONTINUED

Resistance analysis- Of 153 participants randomized to B/F/TAF, 149 had baseline proviral genotype results. NRTI RAMs were common; 76 (51.0%) had M184V/I conferring resistance to 3TC and FTC; 24 (16.1%) had K65R which results in reduced susceptibility to TDF, ABC and 3TC/FTC; and 21 (14.1%) had both M184V/I and K65R mutations (Table 1). There were 109 (73.1%) with RAMs to at least one major ARV class (NRTI, NNRTI, PI or INSTI) at baseline, of which 68 (45.6%) had 2-class resistance and 9 (6.0%) had 3-class resistance (Table 3). One participant on B/F/TAF met criteria for VF at Week 48; baseline and at failure genotypes had no RAMs. In the PI/r group, 3 of 4 participants who met criteria for VF at Week 48 had successful genotyping, one with NRTI and NNRTI RAMs (D67D/G, M184V, K103S, P225H) and two with NNRTI but no NRTI RAMs (K103N; V179V/D).

TABLE 3. Proviral DNA Genotyping Baseline Intermediate or High-Level Resistance by ARV Class

Resistance by ARV Class	n=149
NNRTI	99 (66.4%)
NRTI	79 (53.0%)
PI	13 (8.7%)
INSTI	4 (2.7%)
Overall Class Resistance	
No Resistance Mutations	40 (26.8%)
One-Class Resistance	32 (21.5%)
Two-Class Resistance	68 (45.6%)
Three-Class Resistance	9 (6.0%)

CONCLUSIONS

Switching virally suppressed adults with or without NRTI resistance from a second-line PI/r regimen to B/F/TAF was non-inferior to continuing a PI/r regimen. These results suggest it can be done without baseline or historical drug resistance testing in regions where INSTI resistance is uncommon.

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