Switching from a Second-line Boosted PI Regimen to B/F/TAF: Results of a Randomized Clinical Trial

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BACKGROUND

Patients on second-line ritonavir-boosted protease inhibitor (PI/r)-based regimens in resource-limited settings have high rates of nucleoside reverse transcriptase inhibitor (NRTI) resistance, but this information is unknown in routine clinical care. This study compared continuing PI/r + NRTIs versus bictegravir/tenofovir alafenamide/emtricitabine (B/F/TAF) in persons living with HIV (PWH) on second-line ART with no prior drug resistance testing

METHODS

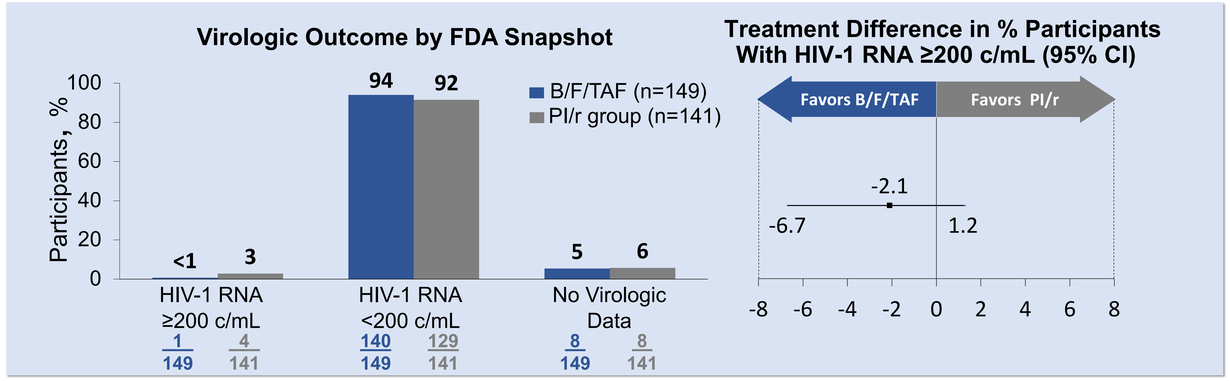
This prospective, open-label trial conducted at GHESKIO in Port-au-Prince, Haiti, randomized adults (≥18 years) with viral suppression on second-line PI/r-based ART to continue their current regimen vs. switch to B/F/TAF.

- **Primary endpoint: Proportion of participants with HIV-1 RNA ≥200 copies/mL at week 48 using the FDA snapshot algorithm.**
- **The difference between groups was assessed with a non-inferiority margin of 4%.**

Enrollment was stopped in December 2023, after 301 participants enrolled (290 with complete data; 11 in follow-up), at the recommendation of the Data Safety Monitoring Board (DSMB), due to limited access to the control regimen in Haiti.

Switching virally suppressed adults on a second-line PI/r regimen to B/F/TAF is non-inferior to continuing PI/r-based ART, even without resistance testing and in a setting of severe civil unrest.

Table 1. Primary End Point – Virologic Outcomes at Week 48



Week 48 Outcome	B/F/TAF (n=149)	Boosted PI (n=141)
Primary end point: HIV-1 RNA ≥200 copies/mL	**1 (0.7%)**	**4 (2.8%)**
HIV-1 RNA ≥200 copies/mL in 48-week window	0	3
Treatment discontinued before week 48 due to lack of efficacy	0	0
Died or LTFU with last available HIV-1 RNA ≥200 copies/mL	1	1
HIV-1 RNA <200 copies/mL in 48-wk window	**140 (94.0%)**	**129 (91.5%)**
No data for final outcome (censored) with last available HIV-1 RNA <200 copies/mL	8 (5.4%)	8 (5.7%)
Completed study without HIV-1 RNA test within the 48-week window	4	2
Died	1	2
LTFU or left the country	3	3
Stopped study medication due to pregnancy	0	1

RESULTS

Between October 2020 and March 2023, 290 participants were randomized and treated (B/F/TAF: 149; bPI: 141). Median age was 50 years (IQR 42, 58) and 165 (57%) were women. At enrollment, 175 (60%) were taking lopinavir/r and 115 (40%) atazanavir/r; 226 (78%) were taking tenofovir disoproxil fumarate, 51 (18%) zidovudine, and 13 (4%) abacavir; all were taking lamivudine or emtricitabine. The median time on PI/r was 3.7 years (IQR 2.2, 5.7) years.

Efficacy at the Week 48 :

In preliminary analysis, at week 48, the proportion with HIV-1 RNA ≥200 copies/mL was 0.7% (1/149) and 2.8% (4/141) in the B/F/TAF and PI/r groups, respectively: difference -2.1 (95% CI: -6.7 to 1.2), meeting non-inferiority for B/F/TAF compared to PI/r (Table 1).

140 (94.0%) and 129 (91.5%), respectively had 48-week HIV-1 RNA <200 copies/mL. Eight in each group were censored – all had HIV-1 RNA <200 copies/mL at latest test. There were no study drug discontinuations due to adverse events in either group.

Safety:

There were no study drug discontinuations due to adverse events in either group.

This study was conducted during both COVID-19 and severe civil unrest and gang-related violence in Haiti. Follow-up was enabled by community health workers and neighborhood drug distribution when travel in Port-au-Prince was not safe or not possible for participants.

CONCLUSIONS

Switching virally suppressed adults on a second-line PI/r regimen to B/F/TAF is non-inferior to continuing PI/r-based ART, despite expected high rates of NRTI resistance and extreme civil unrest. Rates of viral suppression were high in both groups.