Successful Use of B/F/TAF in PWH With nRTI Resistance Including Multiple TAMs and K65R/N Mutations

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BACKGROUND

Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is an efficacious and preferable regimen in many contexts, but experience of its use in people with pre-existing HIV-1 nucleoside reverse transcriptase inhibitor (nRTI) resistance-associated mutations (RAMs) is limited. TAF achieves 4x higher intracellular concentrations of tenofovir compared to tenofovir disproxil fumarate (TDF) and appears to exert higher activity against virus with tenofovir mutations (1,2), and an expanded US-FDA licence for use in people with suppressed viral loads and the M184V/I RAM was granted for B/F/TAF in 2024. Our centre has a significant proportion of people with nRTI RAMs, and B/F/TAF is sometimes recommended off-label in this cohort following MDT discussion. We follow up and review this cohort regularly.

METHODS

We undertook a retrospective analysis of people receiving HIV specialist care at our centre in London, United Kingdom, who had pre-existing nRTI RAMs, no integrase strand transfer inhibitor (INSTI) RAMS, and were prescribed B/F/TAF between 22/Nov/2019 and 27/Jun/2025. Data collected during routine care from electronic patient records and laboratory system including all episodes of viraemia during B/F/TAF therapy were reviewed. Low level viraemia (LLV) was defined as ≥2 sequential measurements of HIV-1 RNA >40 and <1000 copies/mL and virological failure (VF) as HIV-1 RNA >1000 copies/mL not entirely attributable to ART non-adherence.

Table 1. Cohort Characteristics (n=238)

Parameter	n = 238
Age, years (median; IQR)	59 (54 - 63)
Male sex (n, %)	184 (77.3%)
Ethnic origin (n, %)	
White	133 (55.9%)
Black	67 (28.2%)
Asian	9 (3.8%)
Other	29 (12.2%)
CD4⁺ count (median cells/µl; IQR)	
At B/F/TAF initiation	528 (360-716)
Nadir	128 (40-214)
HIV-1 RNA at time of B/F/TAF initiation (n, %)	
<40 copies/mL	207 (87%)
>40 copies/mL	31 (13%)
B/F/TAF treatment duration	
Median days; IQR	829 (394-1163)
>365 days (n, %)	181 (76.1%)

In 238 people with nRTI RAMs including M184V (n=165), K65R/N (n=12), and ≥1TAMs (n=98) B/F/TAF had a low (3.4%) rate of virological failure (VF) over median 2.27 years of treatment. VF did not lead to any major INSTI RAMs.

RESULTS

Baseline characteristics of our cohort including prevalence of nRTI RAMs summarised below (Table 1, Figure 1). End of study (EOS) outcomes during B/F/TAF therapy are presented in Figure 2, broken down by nRTI RAM pattern in Figure 3. Participants received a median of 829 days B/F/TAF exposure, and 203 (85.2%) continued B/F/TAF to the end of the study period. 79.4% of participants either maintained (73.1%) or achieved (6.3%) sustained undetectable HIV-1 RNA following switch to B/F/TAF by EOS. 11/12 participants with K65R/N were undetectable throughout B/F/TAF therapy, 1 had a resolving blip (HIV-1 RNA <200 copies/mL). 8 (3.4%) participants developed confirmed VF or low level viraemia (Table 2). Adherence was a factor in 50% of these cases. No emergent major INSTI RAMs developed after VF.

Figure 1. nRTI RAMs Prevalence (n=238)

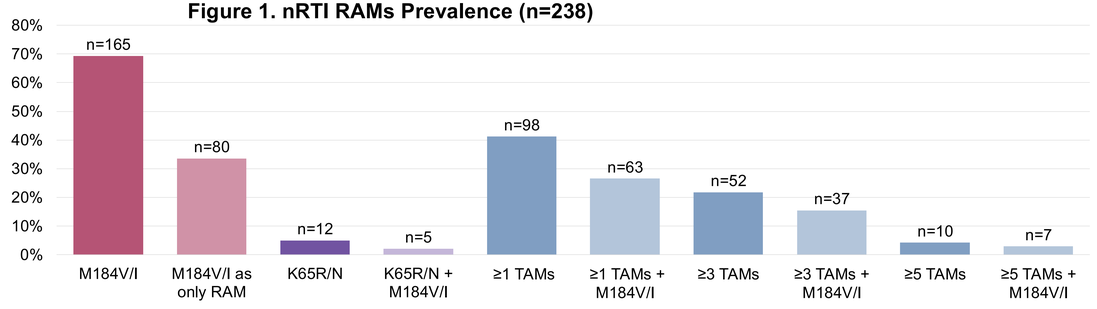


Figure 2. Outcomes on B/F/TAF (n=238)

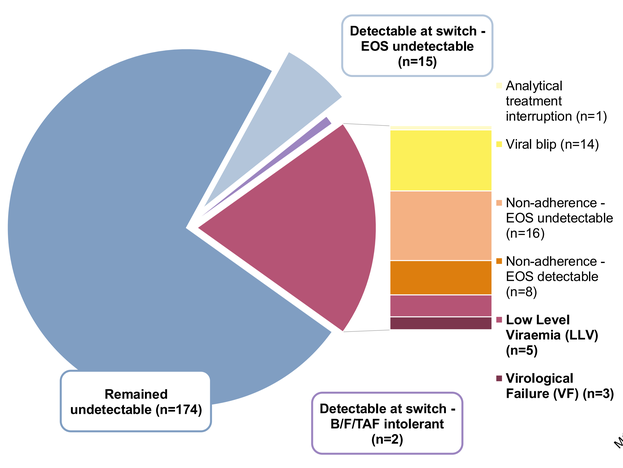


Figure 3. Outcomes for nRTI RAMs

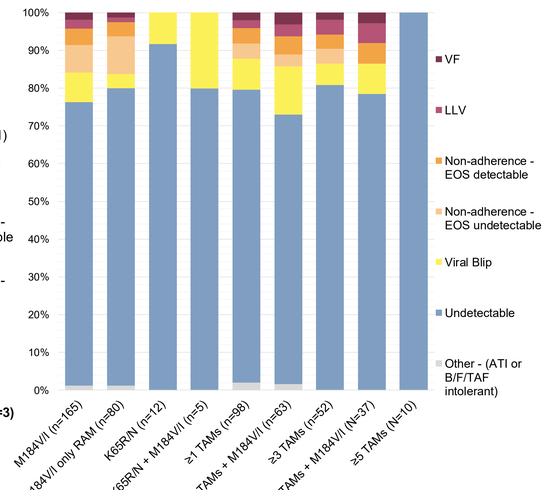


Table 2. Details of People who had VF / LLV on B/F/TAF (n=8)

Demographics	LLV 1	LLV 2	LLV 3	LLV 4	LLV 5	VF 1	VF 2	VF 3
Age, Sex, Ethnic origin	53M, White	55M, Asian	80M, White	42F, Black	41M, White	56M, Black	57F, Asian	52M, White
CD4+ count at switch, cells/µl	1566	191	376	1566	475	679	39	9
HIV-1 RNA at switch, copies/mL	<40	288	<40	50	<40	<40	7943	1023294
B/F/TAF treatment duration, days	917	106	1323	1162	1471	1397	528	389
No. nRTI RAMs	10	1	9	1	1	3	6	5
M184V/I	+	+	+	+	-	+	+	+
K65R/N	-	-	-	-	-	-	-	-
Type 1 TAMs	3*	-	1*	-	-	-	2*	-
Type 2 TAMs	2*	-	3*	-	-	1*	1*	-
Other RAMs	4*	-	3*	-	1*	1*	1*	4*
Emergent RAMs?	No	No	No	No	No	No	No	E157Q, S230R**
B/F/TAF discontinued?	Yes	No	No	No	Yes	Yes	Yes	Yes
New Regimen	B/F/TAF + DOR	-	-	-	B/F/TAF + DOR	B/F/TAF + DOR	DRV/c/TAF/ FTC	DRV/c/TAF/ FTC
Supressed on new regimen?	No*	-	-	-	Yes	Yes	No	Yes
Additional context	Ongoing episodes LLV	LLV on LA-CAB/RPV prior	VL 48 copies/mL at last timepoint	Adherence issues	3 episodes of LLV during study	CD8 encephalitis Adherence issues	Adherence issues	Adherence issues

**LLV1 = M41L, L210W, T215Y, D67N, K219N, E44D, V118I, V75T, L74I; LLV3 = M41L, K70R, T215F, K219E, D67G, V118I/V, G333E; LLV5 = E44D; VF1 = K219E, K70Q; VF2 = L210W, T215Y, D67N, K70K/E, K219N; VF3 = E44D, S68G, K70Q, T215E. **E157Q, S230R are minor INSTI mutations with minimal individual impact on INSTI susceptibility*

CONCLUSIONS

Our data provides further evidence that B/F/TAF is a safe and effective regimen for use in people with pre-existing NRTI resistance including M184V, K65R/N and TAMs. VF and LLV was rare irrespective of the extent of nRTI resistance, and non-adherence was the key driver of viraemia and present in all 3 confirmed VF cases.

ADDITIONAL KEY INFORMATION

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References:

1) Margot N, Ram R, Abram M, Haubrich R, Callebaut C. Antiviral Activity of Tenofovir Alafenamide against HIV-1 with Thymidine Analog-Associated Mutations and M184V. Antimicrob Agents Chemother. 2020 Mar 24;64(4):e02557-19. doi: 10.1128/AAC.02557-19. PMID: 31988104; PMCID: PMC7179327.

2) Cox S, Margot N, Callebaut C. Antiviral activity of tenofovir alafenamide (TAF) against HIV-1 clinical isolates harboring K65R. J Med Virol. 2023 Apr;95(4):e28723. doi: 10.1002/jmv.28723. PMID: 37185867.

PLAIN LANGUAGE SUMMARY

B/F/TAF is an effective and safe regimen for the majority of people with resistance to nRTI drugs. Only a small proportion (<1 in 20) of people with nRTI resistance in our study did not become undetectable whilst taking B/F/TAF as prescribed, and none of the people with detectable virus developed major resistance to integrase inhibitors, the other key drug class B/F/TAF contains.