Virologic Outcomes of B/F/TAF in People with HIV with Resistance to Antiviral Agents Exceeding One Component

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BRACE

Background

Evidence on bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) use in people with HIV (PWH) with pre-existing drug resistance-associated mutations (DRMs) is limited.[1,2]
We evaluated virologic outcomes in PWH, with or without viremia, receiving B/F/TAF in routine care with historical DRMs to at least one component of B/F/TAF.

Methods

Study Population

- BRACE is a German nationwide retrospective cohort study of PWH initiating B/F/TAF with ≥2 major DRMs historically detected by genotypic resistance testing from plasma viral RNA, including ≥1 clinically relevant DRM to BIC, FTC, or TAF.
- Clinically relevant DRMs were defined per Stanford HIVdb algorithm (v9.8; 2025-01-05) as follows:
  - for BIC, either any major INSTI DRM or any mutation with an HIVdb resistance interpretation of at least potential low-level resistance (PLLR)
  - for FTC and TAF, any mutation or combination of mutations conferring ≥PLLR to the respective drug

Outcome measures

- Viral suppression (HIV-1 RNA <50 c/mL), stratified by the genotypic sensitivity score for B/F/TAF (definition see below)
- Confirmed virologic failure (CVF) defined as 2 consecutive HIV-RNA values >200 c/mL, or a single value >200 c/mL followed by treatment discontinuation

Analysis sets

- Overall study population: All participants meeting the study's in/exclusion criteria
- Effectiveness set for year-1 outcomes: Eligible participants with ≥12 months since B/F/TAF initiation

Statistical approaches

- FDA snapshot approach for year-1 outcomes (effectiveness set)
- Last observation carried forward (LOCF) for overall outcomes at last follow-up (FAS)

Genotypic sensitivity score (GSS)

- The GSS for B/F/TAF was used as a measure of the predicted activity of this regimen, with a score of 3 indicating full susceptibility to all three drug components.
- The GSS was based on cumulative historical DRMs, calculated as the sum of the individual drug component scores using the following weighting for the HIVdb interpretation categories:
  - 1: full susceptibility, 0.75: potential low-level resistance, 0.5: low-level resistance, 0.25: intermediate resistance, and 0: high-level resistance
  - '1' was assumed for genotypic susceptibility to BIC if an INSTI resistance test was not available.
  - Resistance interpretation was updated using the recently released Stanford HIVdb algorithm (v10.1, 2026-01-18).

Results

As of 2025-12-22, a total of 156 PWH (3 ART-naive) from 11 centers were identified.

Table 1. Characteristics of the study population

Characteristics at time of B/F/TAF initiation	PWH with viral suppression[a]	PWH with viremia
N[b] (%)	119 (77.3%)	35 (22.7%)
Age [years], median (IQR)	56.0 (48.0, 61.0)	53.0 (42.0, 61.0)
Sex at birth: female/male, n (%)	26 / 93 (22 /78)	10 / 25 (29 / 71)
Time since HIV diagnosis [years], median (IQR)	23.9 (16.2, 28.2)	21.3 (12.6, 27.3)
CD4 nadir [cells/µL][c], median (IQR)	155.5 (56.0, 292.0)	105.5 (34.5, 314.5)
Absolute CD4 count [cells/µL], median (IQR)	684.0 (474.0, 949.0)	363.0 (185.0, 556.0)
HIV-1 RNA level [c/ml], median (IQR)	19.0 (19.0, 49.0)	24,000 (1,100, 73,500)
Duration of viral suppression [months], median (IQR)	74.0 (18.0, 149.0)	N/A
≥3 ART regimens prior to BIC/FTC/TAF	105 (88	25 (78)
Prior exposure to NRTIs, n (%)	117 (98)	31 (97)
Prior exposure to INSTIs, n (%)	85 (71)	16 (50)
Prior exposure to NNRTIs, n (%)	87 (73)	24 (75)
Prior exposure to PIs, n (%)	111 (93)	24 (75)
Prior exposure to EIs, n (%)	14 (12)	4 (12)
Number of previous virologic failures (VFs)[d], median (IQR)	2.0 (1.0, 3.0)	2.0 (1.0, 5.0)

[a] 2 consecutive HIV-1 RNA <50 c/mL prior to B/F/TAF (allowing one blip of 50-200 c/mL) or a single value <50 c/mL if only one measurement was available; [b] HIV-1 RNA prior to B/F/TAF missing in n=2/156 cases; [c] n=28 missing; [d] n=34 missing; IQR, interquartile range; N/A, not applicable

Genotypic sensitivity score for B/F/TAF

The GSS for B/F/TAF was <2.0 in 42% (66/156) of PWH (Figure 1). In 7% (11/156), integrase strand transfer inhibitor (INSTI) DRMs were evident at baseline, with major INSTI DRMs in 6% (10/156), including N155H (5/10), Y143R (3/10), T66I/K variants (2/10), S147G (1/10), and R263K (1/10).

Limitations

- Retrospective, single arm study design without a comparator arm
- Imputing BIC GSS=1 for missing INSTI tests may underestimate the prevalence of INSTI DRMs; single time-point proviral analyses in this study will provide further insights.

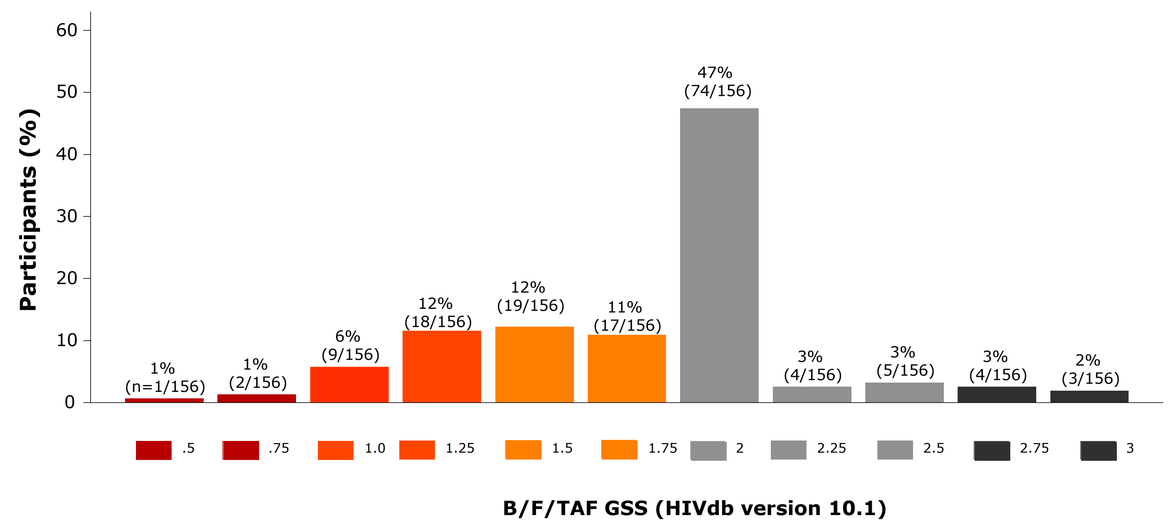

Figure 1. Distribution of GSS for B/F/TAF, including 3 cases with a GSS of 3, with mutational patterns consistent with the thymidine analog mutation (TAM)-2 pathway, involving D67N, K70R, and/or K219Q/E.[3]

Viral outcomes - year 1 (FDA snapshot)

Table 2. Virologic outcomes at year 1, using the effectiveness set

Virologic outcomes	Year 1, FDA snapshot approach	M=E[a]
	N=145	N=134
HIV-1 RNA <50 c/mL, n (%)	114 (78.8)	114 (85.1)
HIV-1 RNA ≥50 c/mL, n (%)	14 (9.6)	14 (10.4)
No data, n (%)	17 (11.6)	6 (4.5)
LOCF HIV-1 RNA **<50 c/mL** & on drug, but **no HIV-1 RNA in window**	11 (7.6)	---
LOCF HIV-1 RNA **<50 c/mL & discontinuation (disc.)** due to safety/tolerability (n=4) or other reasons (n=1)	5 (3.4)	5 (3.7)
LOCF HIV-1 RNA **≥50 c/mL & disc**. due to safety/tolerability	1 (0.7)	1 (0.7)
CVF by year 1	3/145 (2.1)	3/134 (2.2)

[a] M=E, missing equals excluded approach; LOCF, last observation carried forward; CVF, confirmed virologic failure

Viral outcomes – LOCF analysis

The median follow-up on B/F/TAF was 44 months (interquartile range 20–72). Viral suppression rates at last follow-up categorized by GSS are shown in Figure 2 (overall 89.7%, males 88.1%, females 94.7%).

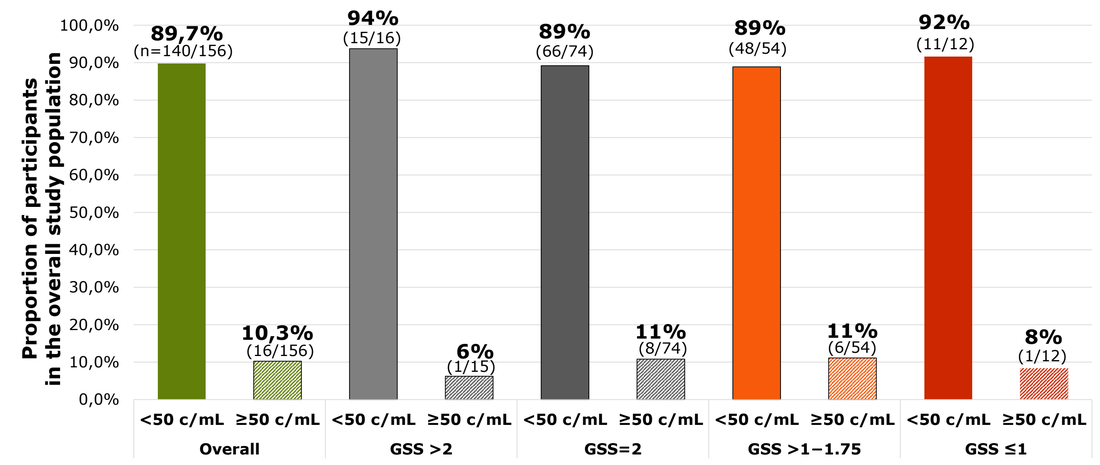

Figure 2. Virologic outcomes at last follow-up (LOCF, last observation carried forward) in the overall study population, stratified by B/F/TAF GSS

Confirmed virologic failures (CVF) until last follow-up

- Overall, we observed 7 CVFs; at B/F/TAF initiation, 5/7 had HIV-1 RNA levels ≥50 cp/mL (range 27,000 – 309,000 c/mL), and 4/5 were assessed as poorly adherent to previous ART by the treating physician (1/5 not assessable).
- In all 7 cases, CVFs were attributed to adherence problems and/or (intermittent) treatment interruptions; 5/7 had viral rebounds >1,000 c/mL, ranging from 29,400 to 332,000 c/mL.
- In 3/7 cases, HIV-1 RNA was re-suppressed to <50 c/mL while remaining on B/F/TAF.
- In 4/7 cases, ART was changed. Reasons for ART change were:
  - Viral rebound to >100.000 c/mL attributed to treatment interruption for tolerability/safety concerns after 41 months of viral suppression (n=1)
  - Delayed recognition of pre-existing INSTI and NRTI resistance (L74I R263R/K and M184V), coupled with insufficient adherence to treatment (n=1)
  - Viral rebound attributed to treatment interruption after >60 months of viral suppression on B/F/TAF (n=1) coupled with pre-existing INSTI and NRTI DRMs (D232D/N, N155H, T97A and D67D/N, M184V). The genotypic resistance pattern upon rebound showed partly reversion to wild type virus.
  - Poor adherence; the genotypic resistance test showed reversion to wild type virus.
- Throughout the observation period, no newly emerging NRTI or INSTI DRMs were observed.

Conclusion

- In this cohort of PWH, including viremic individuals with no apparent adherence issues, viral suppression was generally achieved or maintained despite pre-existing DRMs to one or more B/F/TAF components, regardless of the number of active drugs.
- Confirmed virological failure occurred in 2% within the first year and in 4.5% by last follow-up, largely driven by adherence issues.
- No emergence of new NRTI or INSTI DRMs was observed.

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Notes
[1] FDA. Biktarvy USPI (Rev. 07/2025)
[2] Per EMA Biktary SmPC (Rev. 01/2026), B/F/TAF is indicated for the treatment of HIV-1 infection without known or suspected resistance to INSTI, FTC or TDF/TAF.
[3] https://hivdb.stanford.edu/dr-summary/resistance-notes/NRTI/

Disclosures
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