Comparative Safety of B/F/TAF Versus Other Antiretroviral Therapy Regimens for Treatment-Experienced People with HIV: A Systematic Literature Review and Indirect Comparisons Using Multilevel Network Meta-Regression

Poster SA21

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Conclusions

- Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) demonstrated more favorable estimated glomerular filtration rate (eGFR) outcomes compared to most dolutegravir (DTG)-based regimens
- All-cause discontinuation rates for B/F/TAF were comparable to other antiretroviral therapies (ARTs)
- These findings reinforce renal safety and tolerability when switching to or staying on guideline recommended B/F/TAF in treatment-experienced people with HIV (TE PWH)

Plain Language Summary

- Antiretroviral therapy (ART) has significantly improved the lives of people with HIV
- While integrase inhibitors are effective at controlling the virus, researchers wanted to compare the safety of different treatments in people who had previously used ART
- This study looked at bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) and other ART regimens to assess changes in kidney function and whether patients stopped treatment for any reason, 48 weeks after starting
- Compared with some treatments like dolutegravir/lamivudine (DTG/3TC) or DTG/abacavir/3TC, B/F/TAF was associated with a smaller decline in kidney function
- However, kidney function changes were similar between B/F/TAF and DTG + F/TAF
- People stopped treatment at similar rates across all regimens, with no significant differences
- Overall, the results support that switching to or staying on B/F/TAF does not harm kidney function and is well tolerated by people with HIV

Introduction

- ART has significantly improved HIV management and life expectancy for PWH
- ART selection for TE PWH presents unique clinical challenges due to prior virological failure, drug resistance, and long-term tolerability and safety considerations[1]
- However, since current guideline recommended integrase strand transfer inhibitor (INSTI)-based regimens are effective in maintaining virologic control, there is growing interest in understanding differences in renal and other safety outcomes in TE PWH

Objective

- This study uses multilevel network meta-regression (ML-NMR) to compare renal safety and discontinuation outcomes for B/F/TAF versus other recommended ARTs in TE PWH

Methods

- A systematic literature review was conducted to identify Phase 3/4 randomized controlled trials (RCTs) reporting safety outcomes in TE PWH aged ≥18 years
- MEDLINE, Embase, Cochrane Database of Systematic Reviews (CDSR) and CENTRAL databases were searched on June 14, 2023, and supported by supplementary searches of ClinicalTrials.gov (searched on April 24, 2025), to identify key recent clinical trials in this treatment population
- Indirect comparisons using ML-NMR were deemed feasible and conducted at Week 48 for all-cause discontinuation and change from baseline (CfB) in eGFR
- Analyses were adjusted for age, sex, and race using individual patient data (IPD) from three Phase 3 B/F/TAF trials (GS-US-380-1844, GS-US-380-1878, GS-US-380-4030)[3–4] and aggregate data (AgD) from comparator trials

Results

- Eight studies and eight different ART regimens were included in this ML-NMR analysis (**Table 1**)
- Compared to B/F/TAF, dolutegravir/lamivudine (DTG/3TC) and DTG/abacavir (ABC)/3TC showed significantly greater decline in eGFR from baseline (mean difference [MD; 95% CrI]: −4.40 [−5.30, −3.51] and −3.60 [−5.74, −1.50], respectively). CfB in eGFR with DTG + F/TAF was similar to B/F/TAF (MD [95% CrI]: −1.19 [−3.35, 1.06])
- All-cause discontinuation was comparable across all treatments, with no significant risk difference (RD) for any comparator, including DTG/3TC (RD [95% CrI]: −0.01 [−0.05, 0.10]) or doravirine/islatravir (DOR/ISL) (RD [95% CrI]: −0.01 [−0.04, 0.05]) versus B/F/TAF

B/F/TAF showed significantly smaller decline in eGFR from baseline compared with DTG/3TC and DTG/ABC/3TC. All-cause discontinuation was comparable across all treatments.

Table 1. Summary of Included Studies and Comparators

Included Study	ART	N total	Age at Baseline	Sex	Race (%)					Previous ART: Backbone, %			Previous ART: Third Agent, %		
			Years, Mean (SD)	Male (%)	White	Black	Hispanic	Asian	Other	F/TDF	ABC/3TC	F/TAF	INSTI	PI	NNRTI
BESTT[5]	NNRTI (+ or /) F/TDF	32	50.4 (6.7)	0	-	85.7	-	-	14.3	100	0	0	0	0	100
	DTG/ ABC/3TC	59													
DYAD[6]	B/F/TAF	73	49.7 (-)	83.8	70.3	27.9	-	0.5	1.4	0	0	100	100	0	0
	DTG/3TC	149													
Mills 2024[7]	DOR/ISL	322	48.0 (13.0)	71.6	74.7	17.6	-	4.2	0.5	0	0	100	100	0	0
	B/F/TAF	319													
STRATEGY-NNRTI[8]	EVG/c/F/TDF	290	41.3 (9.6)	92.6	78.3	16.6	10.6	3.0	1.4	100	0	0	0	0	100
	NNRTI (+ or /) F/TDF	143													
STRATEGY-PI[9]	EVG/c/F/TDF	293	41.0 (9.4)	85.7	80.1	14.5	13.6	2.1	1.6	100	0	0	0	100	0
	PI + b + 2 NRTI	140													
GS-US-380-1844[2]	B/F/TAF	282	46.0 (-)	88.6	72.5	21.5	17.4	3.2	2.3	0	100	0	100	0	0
	DTG/ ABC/3TC	281													
GS-US-380-1878[3]	B/F/TAF	290	46.5 (10.5)	82.7	65.5	26.2	18.5	2.8	4.5	84.6	15.4	0	0	100	0
	PI (+ or /) b + 2 NRTI	287													
GS-US-380-4030[4]	B/F/TAF	284	49.5 (11.3)	85.8	70.6	22.8	19.5	1.1	3.9	31.2	0	68.8	100	0	0
	DTG + F/TAF	281													

Footnote: Hyphen (-) indicates that the baseline characteristic was not reported in the publication.
Abbreviations: (+ or /), multi-tablet (+) or single-tablet (/) regimen in combination with; 3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; b (in "PI + b + 2 NRTI"), boosted; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; c (in "EVG/c/F/TDF"), cobicistat; DOR, doravirine; DTG, dolutegravir; EVG, elvitegravir; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; INSTI, integrase strand transfer inhibitor; ISL, islatravir; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; SD, standard deviation.

Figure 1. Network Plot: CfB eGFR at Week 48

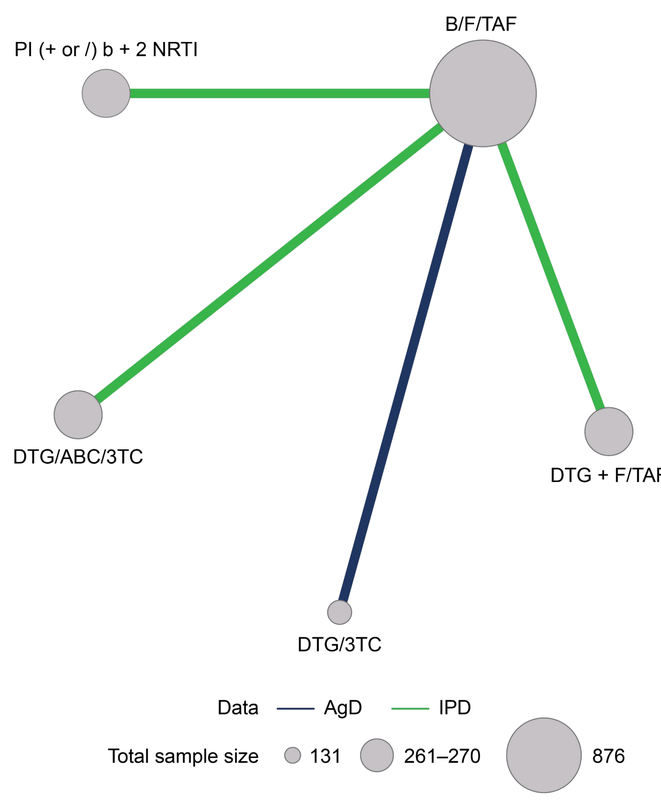
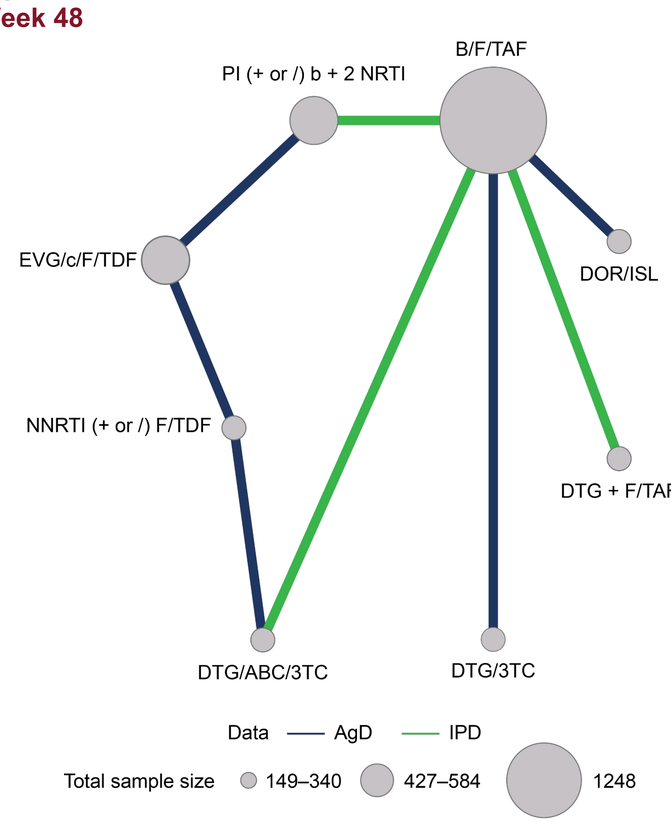


Figure 2. Network Plot: All-Cause Discontinuation at Week 48



Footnote: PI-containing arms in GS-US-380-1878 and STRATEGY-PI were combined in networks in a single node of PI (+ or /) b + 2 NRTI.
Abbreviations: (+ or /), multi-tablet (+) or single-tablet (/) regimen in combination with; 3TC, lamivudine; ABC, abacavir; AgD, aggregate data; ART, antiretroviral therapy; b (in "PI + b + 2 NRTI"), boosted; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; c (in "EVG/c/F/TDF"), cobicistat; CfB, change from baseline; DOR, doravirine; DTG, dolutegravir; eGFR, estimated glomerular filtration rate; EVG, elvitegravir; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; INSTI, integrase strand transfer inhibitor; IPD, individual patient data; ISL, islatravir; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

Figure 3. ML-NMR Results Forest Plot: CfB eGFR at Week 48 (Comparator vs B/F/TAF)

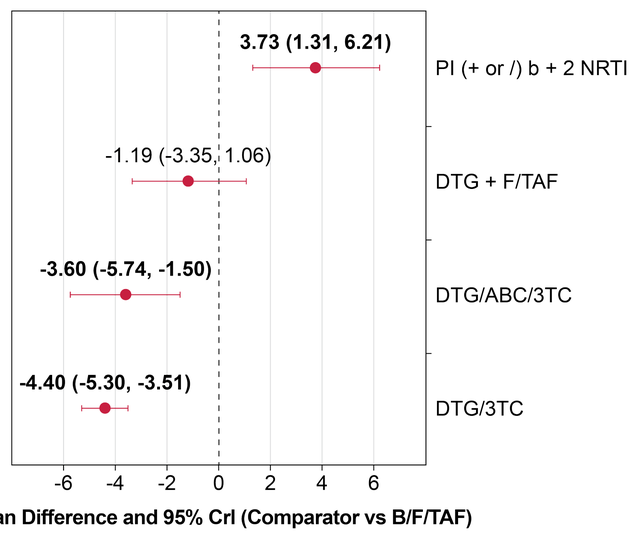
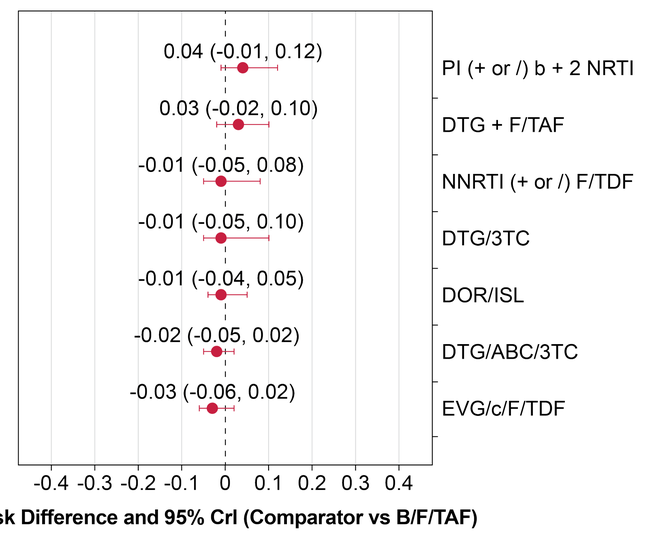


Figure 4. ML-NMR Results Forest Plot: All-Cause Discontinuation at Week 48 (Comparator vs B/F/TAF)



Footnote: Bolded values indicate significant results. PI-ontaining arms in GS-US-380-1878 and STRATEGY-PI were combined in networks in a single node of PI (+ or /) b + 2 NRTI.
Abbreviations: (+ or /), multi-tablet (+) or single-tablet (/) regimen in combination with; 3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; b (in "PI + b + 2 NRTI"), boosted; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; c (in "EVG/c/F/TDF"), cobicistat; CfB, change from baseline; CrI, credible interval; DOR, doravirine; DTG, dolutegravir; eGFR, estimated glomerular filtration rate; EVG, elvitegravir; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; INSTI, integrase strand transfer inhibitor; ISL, islatravir; ML-NMR, multilevel network meta-regression; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

Abbreviations: (+ or /), multi-tablet (+) or single-tablet (/) regimen in combination with; 3TC, lamivudine; ABC, abacavir; AgD, aggregate data; ART, antiretroviral therapy; b, boosted (in "PI + b + 2 NRTI"); B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; c (in "EVG/c/F/TDF"), cobicistat; CENTRAL, Cochrane Controlled Register of Trials; CDSR, Cochrane Database of Systematic Reviews; CfB, change from baseline; CrI, credible interval; DOR, doravirine; DTG, dolutegravir; eGFR, estimated glomerular filtration rate; EVG, elvitegravir; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; INSTI, integrase strand transfer inhibitor; IPD, individual patient data; ISL, islatravir; MD, mean difference; ML-NMR, multilevel network meta-regression; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PWH, people with HIV; RCT, randomised clinical trial; RD, risk difference; SD, standard deviation; TE, treatment-experienced.

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