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Efficacy of Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) Versus Dolutegravir (DTG)-Based 3-Drug Regimens in Adults With HIV Who Have Suboptimal Antiretroviral Adherence

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Key Findings

- Most participants in these double-blind, placebo-controlled trials receiving either B/F/TAF or DTG + 2 NRTIs demonstrated intermediate or high adherence by pill count (≥ 85%) to study drugs at Weeks 48, 96 and 144
- Participants with low adherence (< 85%) were younger, more likely to be Black and more likely to be treatment naïve (TN) than participants with high and intermediate adherence
- In the B/F/TAF group, virologic suppression was similar in participants with high and intermediate adherence compared with those with low adherence
- In the DTG + 2 NRTI group, virologic suppression was significantly lower in those with low adherence compared with those with high and intermediate adherence at Weeks 48, 96 and 144
  - Viremia at last visit was observed at similar frequencies for each of the DTG + 2 NRTI regimens, suggesting that this effect was not driven by one regimen
- Virologic suppression among participants with low adherence was significantly higher with B/F/TAF than DTG + 2 NRTIs at Week 144
- There were two cases of treatment-emergent M184V resistance in the DTG + 2 NRTI group
- There was no treatment-emergent resistance to B/F/TAF

Conclusion

- These data suggest that B/F/TAF is more effective than DTG + 2 NRTIs in achieving and maintaining virologic suppression in participants with suboptimal (< 85%) adherence to study drugs

Introduction

- Adherence to antiretroviral therapy is important for HIV viral suppression[1,2]
  - Durable viral suppression prevents emergence of drug resistance, improves HIV morbidity and mortality outcomes, and prevents transmission of HIV to others[1–3]
- The single tablet regimen B/F/TAF is a DHHS, IAS-USA and EACS guideline-recommended regimen for adults, adolescents and children weighing ≥ 14 kg,[4–6] with demonstrated efficacy and tolerability and a high barrier to resistance
- Studies 1489, 1490, 4458, 1844 and 4030 were double-blind, placebo-controlled trials evaluating B/F/TAF versus DTG + 2 NRTIs in participants with HIV who were either TN or virologically suppressed (VS)[9–14]
  - During the blinded phase of each trial, all participants received multiple daily tablets (active agent and placebo), allowing for unbiased comparison of adherence between treatment groups

Objective

- To evaluate adherence and determine the effect of adherence on virologic outcomes for participants receiving B/F/TAF versus DTG + 2 NRTIs

Methods

Studies Included and Analysis Populations

	Study 1489[9,11]	Study 1490[10,11]	Study 4458[12]	Study 1844[13]	Study 4030[14]	Total
Population	TN	TN	TN HIV/HBV	VS	VS	
Comparator regimen	DTG/ABC/3TC	DTG + F/TAF	DTG + F/TDF	DTG/ABC/3TC	DTG + F/TAF	
Analysis population,* n B/F/TAF DTG + 2 NRTIs	626 312 314	634 311 323	240 119 121	562 281 281	560 283 277	2,622 1,306 1,316
Analysis timepoints	Weeks 48, 96, 144	Weeks 48, 96, 144	Weeks 48, 96	Week 48	Week 48	

*Only participants with ≥ 1 returned pill bottle and ≥ 1 postbaseline HIV-1 RNA measurement were included.

- We performed a retrospective analysis of treatment adherence in clinical studies and its effect on virologic outcomes
- Adherence through Week 48, 96 or 144 was calculated as:

$$\text{Adherence (\%)} = 100 \times \frac{\text{Total no. of pills taken}*}{\text{Total no. of pills prescribed}}$$

$$= 100 \times \frac{\sum \text{No. of pills taken}* \text{ at each dispensing period}}{\sum \text{No. of pills prescribed at each dispensing period}}$$

*Imputed from unreturned pills.

  - Assessment was limited to returned pill bottles
  - Adherence was categorized as high (≥ 95%), intermediate (≥ 85%–< 95%) or low (< 85%)
- Baseline demographics and clinical characteristics were summarized according to treatment group and adherence category for both B/F/TAF and DTG + 2 NRTIs

Methods (Continued)

- Virologic outcomes were based on last available on-treatment HIV-1 RNA value through Weeks 48, 96 and 144 using LOCF imputation: < 50 c/mL (suppression) or ≥ 50 c/mL (viremia)
- Postbaseline resistance testing was performed for participants with confirmed virologic failure (HIV-1 RNA ≥ 50 c/mL at two consecutive visits) and HIV-1 RNA ≥ 200 c/mL at the confirmation visit, or with HIV-1 RNA ≥ 200 c/mL at Week 48 or last visit, with no resuppression of HIV-1 RNA to < 50 c/mL while on study drug

Results

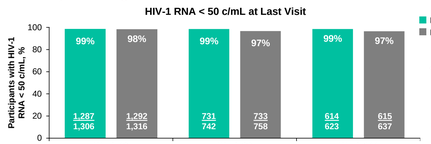
Demographics and Baseline Characteristics

Characteristic	B/F/TAF (n = 1,306)	DTG + 2 NRTIs (n = 1,316)
Age, years, median (Q1, Q3)	40 (29, 51)	39 (29, 50)
Race, n (%)* Asian / Black / White / Other	131 (10) / 333 (25) / 773 (59) / 65 (5)	138 (10) / 339 (26) / 778 (59) / 55 (4)
Ethnicity, n (%)* Hispanic or Latinx	268 (21)	255 (19)
TN, n (%)	742 (57)	758 (58)
CD4 count, cells/μL, median (Q1, Q3)	513 (344, 729)	505 (335, 701)

*Race and ethnicity data were missing for four participants in the B/F/TAF group and six participants in the DTG + 2 NRTI group.

- Baseline characteristics were similar between treatment groups

Summary of Virologic Outcomes



- Overall, virologic suppression was high for both treatment groups through all analysis timepoints

Week 48: Studies 1489, 1490, 4458, 1844 and 4030; Week 96: Studies 1489, 1490 and 4458; Week 144: Studies 1489 and 1490.

HIV-1 RNA ≥ 50 c/mL at Last Visit

% (n/N)	Week 48 Studies 1489, 1490, 4458, 1844, 4030	Week 96 Studies 1489, 1490, 4458	Week 144 Studies 1489, 1490
B/F/TAF	1.5 (19/1,306)	1.5 (11/742)	1.4 (9/623)
DTG + 2 NRTIs	1.8 (24/1,316)	3.3 (25/758)	3.5 (22/637)
DTG/ABC/3TC	1.8 (11/595)	2.9 (9/314)	3.8 (12/314)
DTG + F/TAF	1.2 (7/600)	2.8 (9/323)	3.1 (10/323)
DTG + F/TDF	5.0 (6/121)	5.8 (7/121)	–

- HIV-1 RNA ≥ 50 c/mL at last visit was observed at similar frequencies for each of the DTG + 2 NRTI regimens, suggesting that viremia was not driven by one regimen

Demographics and Baseline Characteristics By Adherence Category Through Week 48

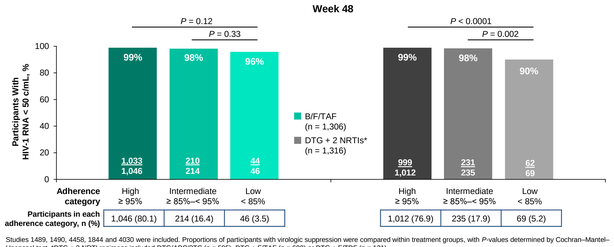
Characteristic	Adherence category through Week 48 High ≥ 95% (n = 2,058)	Intermediate ≥ 85%–< 95% (n = 449)	Low < 85% (n = 115)
Age, years, median (Q1, Q3)	40 (30, 51)	36 (26, 49)	34 (25, 47)
Race, n (%)* Asian / Black / White / Other	243 (12) / 449 (22) / 1,266 (62) / 92 (4)	19 (4) / 164 (37) / 244 (54) / 20 (4)	7 (6) / 59 (51) / 41 (36) / 8 (7)
Ethnicity, n (%)* Hispanic or Latinx	408 (20)	94 (21)	21 (18)
TN, n (%)	1,166 (57)	255 (57)	79 (69)
CD4 count, cells/μL, median (Q1, Q3)	506 (332, 711)	540 (369, 718)	474 (296, 725)

*Race and ethnicity data were missing for four participants in the B/F/TAF group and six participants in the DTG + 2 NRTI group.

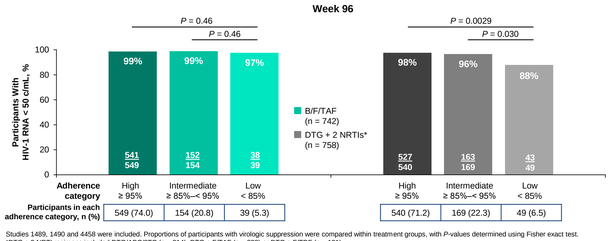
- Those with low adherence were younger, more likely to be Black and more likely to be TN at entry compared with those with high and intermediate adherence

Results (Continued)

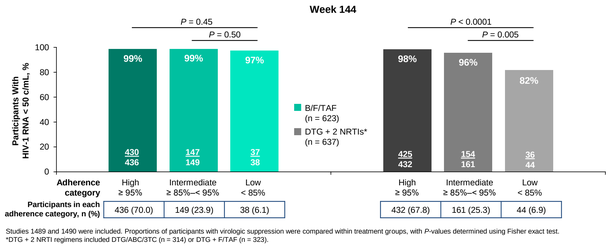
Virologic Suppression by Adherence



Studies 1489, 1490, 4458, 1844 and 4030 were included. Proportions of participants with virologic suppression were compared within treatment groups, with *P*-values determined by Cochran–Mantel–Haenszel test. *DTG + 2 NRTI regimens included DTG/ABC/3TC (n = 595), DTG + F/TAF (n = 600) or DTG + F/TDF (n = 121).



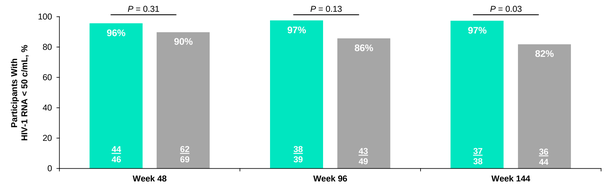
Studies 1489, 1490 and 4458 were included. Proportions of participants with virologic suppression were compared within treatment groups, with *P*-values determined using Fisher exact test.
*DTG + 2 NRTI regimens included DTG/ABC/3TC (n = 314), DTG + F/TAF (n = 323) or DTG + F/TDF (n = 121).



Studies 1489 and 1490 were included. Proportions of participants with virologic suppression were compared within treatment groups, with *P*-values determined using Fisher exact test.
*DTG + 2 NRTI regimens included DTG/ABC/3TC (n = 314) or DTG + F/TAF (n = 323).

High levels of virologic suppression were observed regardless of adherence category for participants receiving B/F/TAF; however, virologic suppression was lower in participants with < 85% adherence compared with those with intermediate or high adherence (≥ 85%) receiving DTG + 2 NRTIs

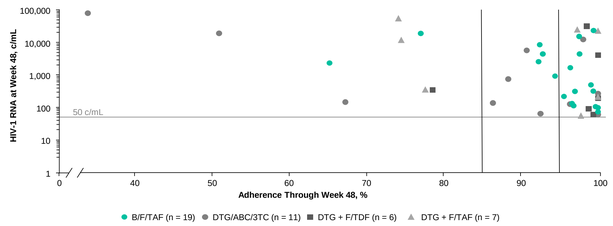
Virologic Suppression in Participants With Low Adherence (< 85%)



Week 48: Studies 1489, 1490, 4458, 1844 and 4030; Week 96: Studies 1489, 1490 and 4458; Week 144: Studies 1489 and 1490.
Proportions of participants with virologic suppression were compared between treatment groups, with *P*-values determined using Fisher exact test.

At Week 144, virologic suppression was significantly higher among participants with low adherence receiving B/F/TAF compared with DTG + 2 NRTIs

Adherence and HIV-1 RNA Level in Participants With Viremia at Week 48 by LOCF Analysis



Among participants with Week 48 viremia, the range of HIV-1 RNA levels and the distribution of DTG + 2 NRTI regimens were broadly similar between adherence categories

Postbaseline Resistance Analysis

Participant number	Study	Regimen	Adherence through Week 144	Emergent resistance substitution
1	1489	DTG/ABC/3TC	92.9%	M184V
2	1489	DTG/ABC/3TC	86.4%	M184V

- Two participants on DTG/ABC/3TC had HIV-1 RNA ≥ 200 c/mL at their last visit during the blinded phase and were found to have emergent M184V; both resuppressed on open-label B/F/TAF
- No participants in the B/F/TAF group had treatment-emergent resistance

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Abbreviations: 3TC, lamivudine; ABC, abacavir; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; c, copies; CD, cluster of differentiation; DHHS, Department of Health and Human Services; DTG, dolutegravir; EACS, European AIDS Clinical Society; F, emtricitabine; HBV, hepatitis B virus; IAS-USA, International Antiviral Society–USA; LOCF, last observation carried forward; NRTI; nucleos(t)ide reverse transcriptase inhibitor; Q, quartile; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TN, treatment naïve; VS, virologically suppressed.