

Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) in Treatment-Naïve People With Both HIV-1 and Hepatitis B: 3-Year Outcomes From ALLIANCE

Poster 373

ALLIANCE

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Conclusions

- Through 3 years of follow-up, B/F/TAF maintained high rates of HIV-1 and HBV virologic suppression, with favorable HBV treatment outcomes and HBeAg and HBsAg loss/seroconversion continuing in Year 3
- B/F/TAF was well tolerated, with a single study drug discontinuation due to TEAEs
 - Safety findings through 3 years were consistent with the established profile of B/F/TAF
 - Most TEAEs were mild to moderate
- These results further support the longer-term use of B/F/TAF in people with both HIV-1 and HBV

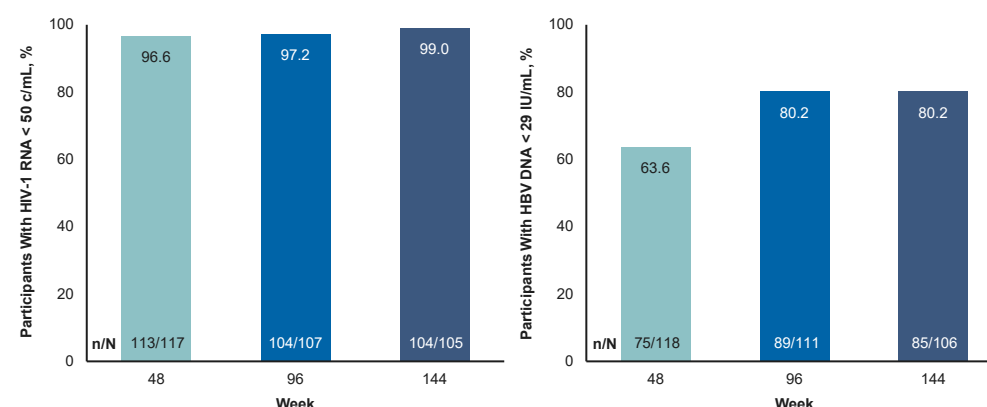
Plain Language Summary

- The ALLIANCE study looked at how well two treatments called B/F/TAF and DTG + F/TDF work to treat adults who had both human immunodeficiency virus type 1 (HIV-1) and hepatitis B virus (HBV) infection
- The study compared how effective B/F/TAF and DTG + F/TDF were at lowering levels of the two viruses (HIV-1 and HBV) in the blood
 - After 96 weeks, both treatments lowered the levels of HIV-1 and HBV in the blood. These results were published in 2023 in a medical journal called *The Lancet HIV*¹
- Two proteins called HBeAg and HBsAg are signs of HBV infection. A goal of treatment is to remove these proteins from the blood
 - The published study¹ showed that fewer people taking B/F/TAF than DTG + F/TDF had these proteins in the blood after 96 weeks of treatment
- In our study, researchers wanted to see how effective and safe B/F/TAF is when taken for 3 years
- After 3 years of treatment, B/F/TAF was very effective at keeping HIV-1 and HBV at very low levels in the blood
 - During that time, the number of people with HBeAg and HBsAg proteins in the blood also continued to go down
- Side effects were rare
- This study shows that B/F/TAF is an effective long-term treatment for people with both HIV-1 and HBV infection

- In total, 109 participants received B/F/TAF for at least 144 weeks^a
- Median (quartile [Q1, Q3]) exposure to B/F/TAF was 186 (160, 222) weeks
- 86% (95/111) participants who completed blinded phase entered the OLE phase and were treated; 95% (90/95) of whom completed the OLE phase
- 12% (15/121) participants discontinued the study drug prematurely^b

^a14 of 109 participants did not opt into the OLE phase
^bPremature discontinuations in the randomized phase (n = 10; due to lost to follow-up [n = 3], death and investigator discretion [n = 2 each], and treatment-emergent adverse event, noncompliance with study drug, and participant decision [n = 1 each]); and in the OLE phase (n = 5; due to lost to follow-up [n = 3], death and noncompliance with study drug [n = 1 each]).

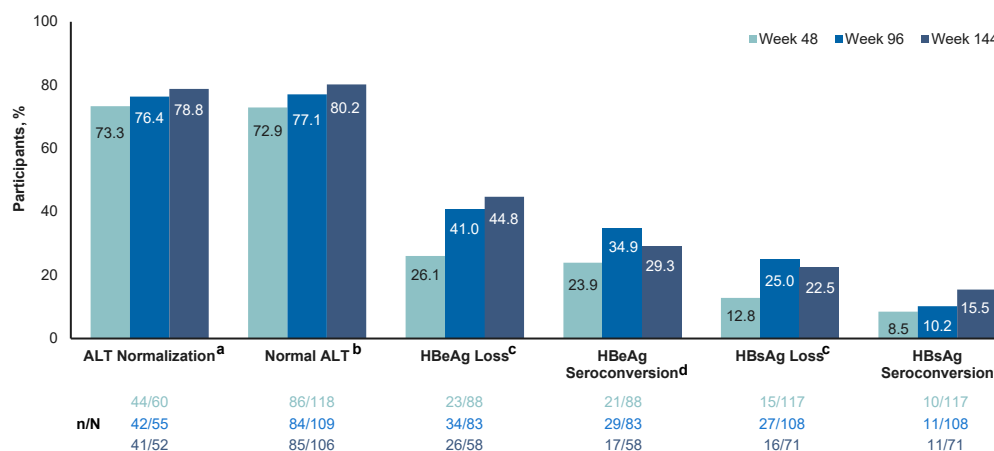
HIV-1 and HBV Suppression Through Week 144 (M = E)



Outcomes are from a M = E analysis in the all B/F/TAF full analysis set (N = 119), which included all data collected up to 1 day after permanent discontinuation of B/F/TAF. The denominator is the number of participants with non-missing data for the endpoint at each visit.
B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; c, copies; HBV, hepatitis B virus; IU/mL, international units per milliliter; M = E, missing = excluded.

- B/F/TAF achieved high rates of HIV-1 RNA and HBV DNA suppression, which were maintained through Week 144

HBV Outcomes Through Week 144 (M = E)



All outcomes are from a M = E analysis; all except HBeAg and HBsAg loss/seroconversion were assessed in the all B/F/TAF full analysis set (N = 119), which included all randomized participants who received ≥ 1 dose of study drug and had ≥ 1 post-baseline HIV-1 RNA or HBV DNA result while on study drug. The all B/F/TAF serologically evaluable full analysis set, defined as all participants in the all B/F/TAF full analysis set who were HBeAg positive and HBeAb negative or missing at baseline, was used for assessment of HBeAg and HBsAg loss/seroconversion (N = 119 and N = 90). ALT normalization was assessed in the all B/F/TAF full analysis set with baseline ALT > ULN. The denominator is the number of participants with non-missing data for the endpoint at the Week 144 visit.
^aReduction in ALT to < ULN for participants with ALT > ULN at baseline based on AASLD 2018 criteria, where ULN is 25 U/L for females and 35 U/L for males.
^bProportion of participants with normal ALT (by AASLD 2018 criteria).
^cDefined as loss of serum HBeAg/HBsAg and serum HBeAb/HBsAb change from negative or missing at baseline to positive at a post-baseline visit.
^dALT, alanine aminotransferase; AASLD, American Association for the Study of Liver Diseases; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; HBeAg, hepatitis B envelope antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; M = E, missing = excluded; ULN, upper limit of normal.

- Alanine aminotransferase (ALT) normalization was maintained, and hepatitis B envelope antigen (HBeAg) and hepatitis B surface antigen (HBsAg) loss/seroconversion continued through Week 144, indicating sustained anti-HBV activity of B/F/TAF

Safety Through End of Study

| n (%) | B/F/TAF (N = 121) |
|---|-------------------|
| Any TEAE | 117 (97) |
| Study drug-related TEAEs | 39 (32) |
| Any Grade 3 or 4 TEAEs | 26 (21) |
| Study drug-related Grade 3 or 4 TEAEs ^a | 8 (7) |
| Any serious TEAEs | 20 (17) |
| Study drug-related serious TEAEs ^b | 1 (< 1) |
| Study drug discontinuation due to TEAE ^c | 1 (< 1) |
| Death | 3 (2) |

Safety outcomes were assessed in the all B/F/TAF safety analysis set (N = 121), which included all randomly assigned participants who received ≥ 1 dose of study drug.
^aAll events were Grade 3: abnormal weight gain (n = 2), ALT increased, cryptococcal meningitis, hypomagnesemia, major depression, serum creatinine increased, serum triglycerides increased, and weight increased (n = 1 each); hypomagnesemia and serum triglycerides increased in the same participant.
^bCryptococcal meningitis. ^cDue to hepatocellular carcinoma.
ALT, alanine aminotransferase; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; TEAE, treatment-emergent adverse event.

- B/F/TAF was well tolerated, as demonstrated by the low rate of study drug discontinuation due to treatment-emergent adverse events (TEAEs; < 1%)
- The most commonly reported study drug-related TEAEs were weight increased (7%), abnormal weight gain, ALT increased, dyslipidemia, and headache (3% each)

Treatment-Emergent Laboratory Abnormalities

| n (%) | B/F/TAF (N = 120) |
|--|-------------------|
| Any Grade 3 or 4 abnormalities occurring in ≥ 3% of participants | 54 (45) |
| Increased ALT (> 5 ULN) | 27 (23) |
| ALT elevation ^a | 9 (7) |
| Confirmed ALT elevation (ALT flare) ^b | 7 (6) |
| Increased AST (> 5 ULN) | 16 (13) |
| Increased LDL, fasting | 11 (9) |
| Increased amylase | 9 (8) |
| Hypercholesterolemia, fasting | 5 (4) |
| Glycosuria | 4 (3) |
| GGT increased | 3 (3) |
| Hematuria, quantitative | 3 (3) |

Treatment-emergent laboratory abnormalities were assessed in the all B/F/TAF safety analysis set (N = 121) with ≥ 1 post-baseline laboratory value (n = 120); hypercholesterolemia and increased LDL, n = 119.
^aTreatment-emergent ALT elevation was defined as ALT elevation at any post-baseline timepoint, up to 1 day after discontinuation of B/F/TAF; all nine participants were HCV RNA positive.
^bConfirmed treatment-emergent ALT elevation (ALT flare) was defined as treatment-emergent ALT elevations at ≥ 2 consecutive post-baseline visits. The first occurrence of ≥ 2 consecutive ALT elevations was identified as the ALT flare. In six participants the ALT flare occurred within the first 3 months. None were drug related or serious and all resolved within 3 months, except for one participant who had a flare for 116 days. ALT, alanine aminotransferase; AST, aspartate aminotransferase; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; GGT, gamma-glutamyl transferase; LDL, low-density lipoprotein; ULN, upper limit of normal.

Disclosures: AA reports research/grant support to institute from Gilead Sciences, Inc., GSK/VIV Healthcare, MSD, and Roche; travel support from Gilead Sciences, Inc.; and membership with the Committee of The AIDS Society Strategic and Technical Advisory Group on HIV, Hepatitis and STI for WHO/SEARO, and the Thailand National Committee on ART, Hepatitis and TB/TPT. HL, CL, SK, M-PL, and KS have no conflicts of interest to report. C-CH reports support for the present study, consulting fees, and speaker honoraria from Gilead Sciences, Inc. SM, HW, and JH are employees of, and own stocks/shares in, Gilead Sciences, Inc. TL reports support for the present study from Gilead Sciences, Inc.; speaker honoraria from Gilead Sciences, Inc.; GSK Pharmaceuticals, and PerkinElmer; travel support from Gilead Sciences, Inc.; GSK Pharmaceuticals, and Sansure Biotech; and is the Chair of the Chinese Society of Infectious Diseases.
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Introduction

- Globally, an estimated 2.7 million people are living with both HIV-1 and hepatitis B virus (HBV)²
- Tenofovir alafenamide (TAF)- or tenofovir disoproxil fumarate (TDF)-based antiretroviral therapy are recommended as an initial regimen for most adults and adolescents with HIV-1 and HBV³⁻⁵
- The ALLIANCE study showed that bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) was noninferior to dolutegravir (DTG) + emtricitabine/tenofovir disoproxil fumarate (F/TDF) at achieving HIV-1 RNA suppression, and superior at achieving HBV DNA suppression at Week 48 in treatment-naïve adults with both HIV-1 and HBV, with high rates of HIV-1 and HBV suppression observed at Week 96¹

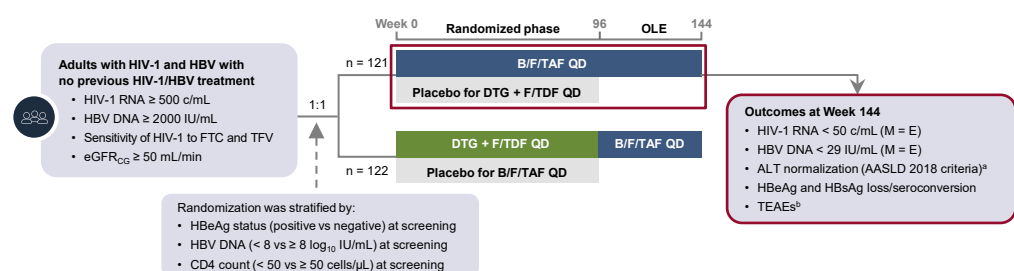
Objective

- To evaluate the long-term efficacy and safety of B/F/TAF in adults with HIV-1 and HBV through 3 years (144 weeks) of treatment

Methods

Study Design

- ALLIANCE (NCT03547908) was a randomized, double-blind, active-controlled Phase 3 clinical study¹
- This analysis reports data from participants who received B/F/TAF in the 96-week randomized phase, plus 48 weeks of B/F/TAF in an optional open-label extension (OLE)



^aChange in ALT concentration from > ULN (female participants: 25 U/mL; male participants: 35 U/mL) at baseline to ≤ ULN at Week 144. ^bSafety was assessed through the end of study.
AASLD, American Association for the Study of Liver Diseases; ALT, alanine aminotransferase; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; c, copies; CD4, cluster of differentiation 4; DTG, dolutegravir; eGFR_{CR}, estimated glomerular filtration rate by Cockcroft-Gault equation; F/TDF, emtricitabine/tenofovir disoproxil fumarate; FTC, emtricitabine; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; M = E, missing = excluded; OLE, open-label extension; QD, once daily; TEAE, treatment-emergent adverse event; TDF, tenofovir; ULN, upper limit of normal.

Results

Baseline Demographics and Disease Characteristics

| | B/F/TAF (N = 121) | |
|--|--------------------|---------|
| Age, years, median (Q1, Q3) | 31 (27, 39) | |
| Male sex at birth, n (%) | 112 (93) | |
| Race, n (%) | 108 (89) | |
| Asian | | |
| HIV disease status: asymptomatic, n (%) | 83 (69) | |
| HIV-1 RNA, log ₁₀ c/mL, median (Q1, Q3) | 4.66 (4.22, 5.12) | |
| CD4 count, cells/μL, median (Q1, Q3) | 245 (127, 383) | |
| HBV genotype | A | 7 (6) |
| | B | 21 (19) |
| | C | 63 (56) |
| | D | 15 (13) |
| | Other ^a | 6 (5) |
| HBV DNA, log ₁₀ IU/mL, median (Q1, Q3) | 7.96 (6.52, 8.38) | |
| HBeAg positive, n (%) | 92 (76) | |
| ALT, U/L, median (Q1, Q3) | 34 (23, 60) | |
| ALT > ULN (AASLD 2018 criteria), n (%) | 60 (50) | |

^aOther consists of HBV genotype F and mixed. Percentage based on participants with available HBV genotype (missing genotype: n = 9 for B/F/TAF).
AASLD 2018, American Association for the Study of Liver Diseases; ALT, alanine aminotransferase; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; c, copies; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; Q, quartile; ULN, upper limit of normal.

Acknowledgments: We thank all study participants, investigators, and staff. We also thank Hongzhou Lu for his contributions to the abstract development. This study was sponsored by Gilead Sciences, Inc. Medical writing support was provided by Joanna Nikitorowicz-Buniak, PhD (Aspire Scientific Ltd, UK), and was funded by Gilead Sciences, Inc.