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

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 study[1] 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

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 HBV[3-5]
- 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 96[1]

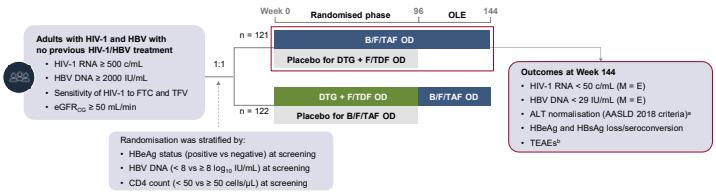
Objective

- 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 randomised, double-blind, active-controlled Phase 3 clinical study[1]
- This analysis reports data from participants who received B/F/TAF in the 96-week randomised phase, plus 48 weeks of B/F/TAF in an optional open-label extension (OLE)



[a]Change in ALT concentration from > ULN (female participants: 25 U/mL; male participants: 35 U/mL)[5] at baseline to ≤ ULN at Week 144. [b]Safety 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; $eGFR_{CG}$, 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; TFV, tenofovir; ULN, upper limit of normal.

Results

Baseline Demographics and Disease Characteristics

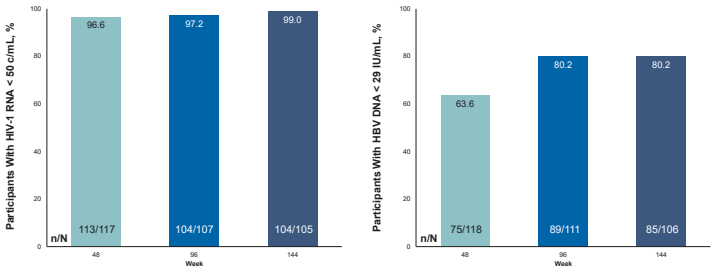
		B/F/TAF (N = 121)
Age, years, median (Q1, Q3)		31 (27, 39)
Male sex at birth, n (%)		112 (93)
Race, n (%)	Asian	108 (89)
HIV disease status: asymptomatic, n (%)		83 (69)
HIV-1 RNA, log_{10} c/mL, median, (Q1, Q3)		4.66 (4.22, 5.12)
CD4 count, cells/μL, median (Q1, Q3)		245 (127, 383)
HBV genotype	A	7 (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)

[a]'Other' 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.

- In total, 109 participants received B/F/TAF for at least 144 weeks[a]
- Median (quartile [Q]1, 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]

[a]14 of 109 participants did not opt into the OLE phase
[b]Premature 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]).

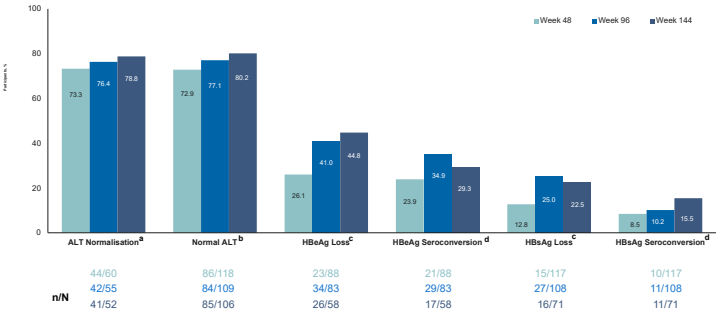
HIV-1 and HBV Suppression Through Week 144 (M = E)



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 HBe/sAb negative or missing at baseline, was used for assessment of HBsAg and HBeAg 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.
[a]Reduction 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.
[b]Proportion of participants with normal ALT (by AASLD 2018 criteria).
[c]Defined as loss of serum HBeAg/HBsAg and with baseline HBeAb/HBsAb negative/missing.
[d]Defined as loss of serum HBeAg/HBsAg and serum HBeAb/HBsAb change from negative or missing at baseline to positive at a post-baseline visit.
ALT, 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.
[a]All events were Grade 3: abnormal weight gain (n = 2), ALT increased, cryptococcal meningitis, hypomagnesaemia, major depression, serum creatinine increased, serum triglycerides increased, and weight increased (n = 1 each; hypomagnesaemia and serum triglycerides increased in the same participant).
[b]Cryptococcal meningitis. [c]Due 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.
[a]Treatment-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.
[b]Confirmed 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.

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