Note to all authors: This is an
8-minute oral presentation (plus Q&A)

Week-96 results of ALLIANCE, a Phase 3, randomized, double-blind study comparing bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) versus dolutegravir + emtricitabine/tenofovir disoproxil fumarate (DTG+F/TDF) in treatment-naïve people with both HIV-1 and hepatitis B

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IAS 2023
23–26 July
Brisbane, Australia

Introduction

- Approximately 2.7 million individuals globally are living with both HIV-1 and HBV, with rates of coinfection reaching 20% in some areas[1,2]
- International guidelines recommend a TDF- or TAF-containing antiretroviral regimen for most adults with HIV-1/HBV coinfection,[3-6] but no randomized studies have compared these approaches in this population
- ALLIANCE (NCT03547908) is an ongoing randomized, double-blind, multicenter, Phase 3 study of B/F/TAF, a single-tablet regimen recommended for treatment of HIV-1,[4-6] as initial treatment for adults with HIV-1/HBV coinfection[7]
- In the primary analysis at Week 48, B/F/TAF demonstrated[7]
  - Noninferiority to DTG + F/TDF (95% vs. 91%) in achieving HIV-1 RNA < 50 c/mL
  - Superiority to DTG + F/TDF (63% vs. 43%) in achieving HBV DNA < 29 IU/mL

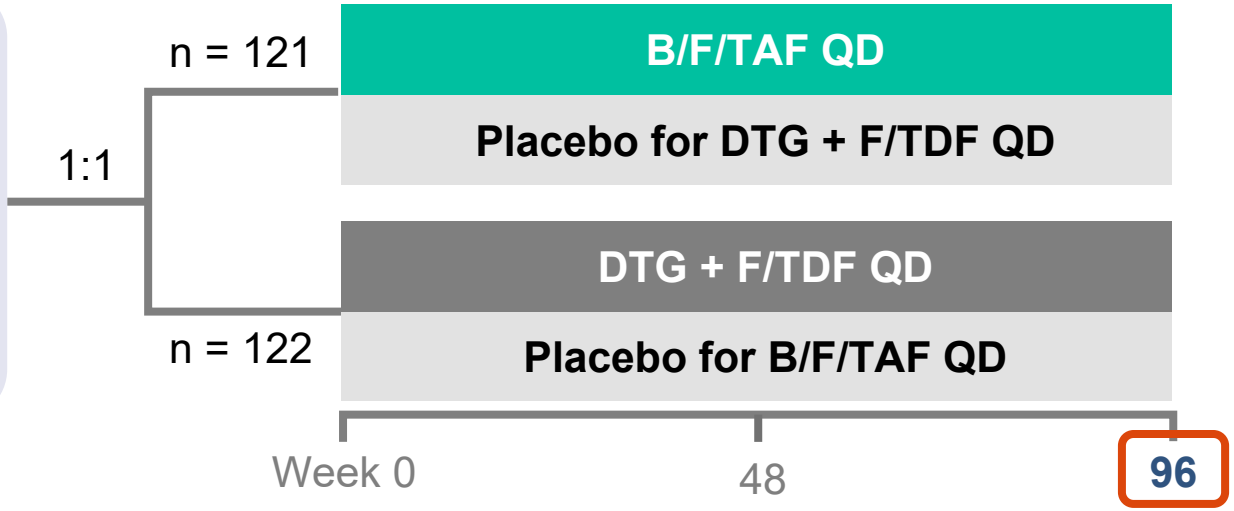
Authors: As this is a busy slide and we are citing AIDS oral here, we did not include in the last bullet that the primary data was presented at AIDS. Let us know if you would still prefer to add it.

1. Platt L, French CE, McGowan CR, et al. J Viral Hepat 2020;27:294-315 ; 2. Thio CL. Hepatology 2009;49(5 Suppl.):S138-S145; 3. WHO. https://www.who.int/publications/i/item/9789240031593 (accessed May 20, 2023); 4. EACS. https://www.eacsociety.org/media/guidelines-11.1_final_09-10.pdf (accessed May 20, 2023); 5. DHHS. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf (accessed May 20, 2023); 6. Gandhi et al. JAMA. 2023;329(1):63-84; 7. Avihingsanon A, et al. AIDS 2022, Oral OALBX0105.
B/F/TAF, bictegravir, emtricitabine and tenofovir alafenamide; c, copies; DTG, dolutegravir; HBV, hepatitis B virus; F/TDF, emtricitabine and tenofovir disoproxil fumarate; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate

Study Design

Adults with HIV-1/HBV coinfection with no previous treatment of HIV-1 or HBV

- HIV-1 RNA ≥ 500 c/mL
- HBV DNA ≥ 2,000 IU/mL
- Sensitivity of HIV-1 to FTC and TFV
- $eGFR_{CG}$ ≥ 50 mL/min



Secondary endpoints at W96

- HIV-1 suppression (HIV-1 RNA <50 copies/mL)
- HBV suppression (HBV DNA <29 IU/mL)
- Change in CD4 cell count/percentage
- ALT normalization
- HBsAg loss

Additional endpoints at W96

- HBeAg loss
- HBeAg seroconversion
- HBsAg seroconversion

For baseline and disease characteristics, please see the supplementary material available via the QR code

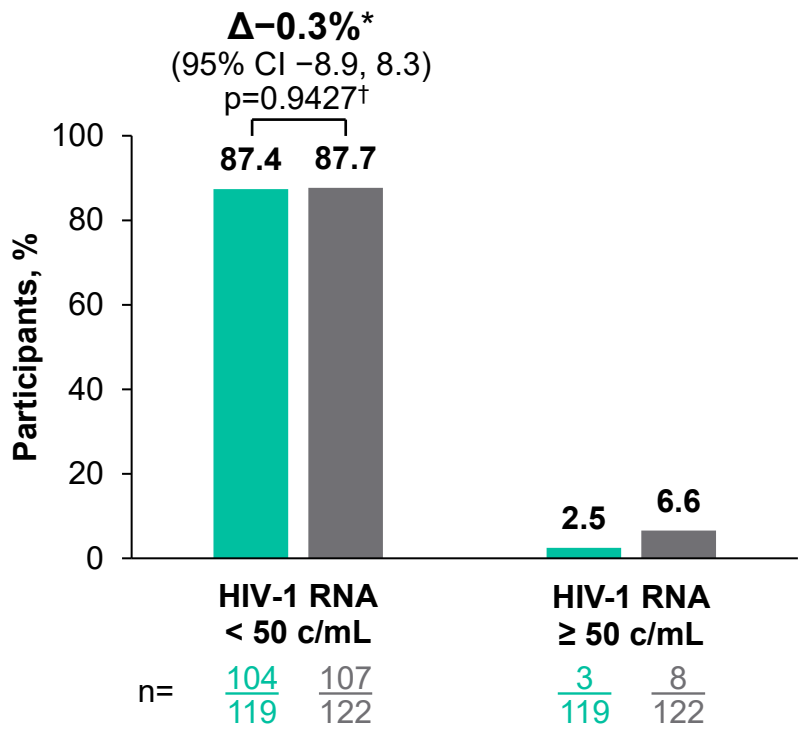
Material for the QR code is currently in the back up section of this deck

NCT03547908

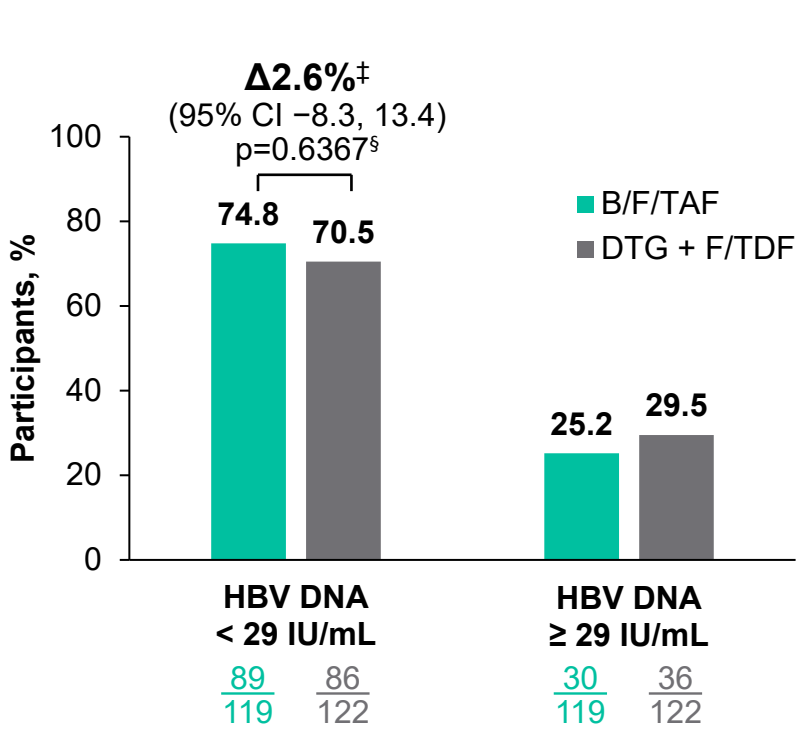
ALT, alanine aminotransferase; B/F/TAF, bictegravir, emtricitabine and tenofovir alafenamide; DTG, dolutegravir; $eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft–Gault equation; F/TDF, emtricitabine a fumarate; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; QD, once daily.

Virologic Outcomes at Week 96 (Full analysis set)

HIV-1 RNA < 50 c/mL (FDA Snapshot algorithm)



HBV DNA < 29 IU/mL (M=F analysis)



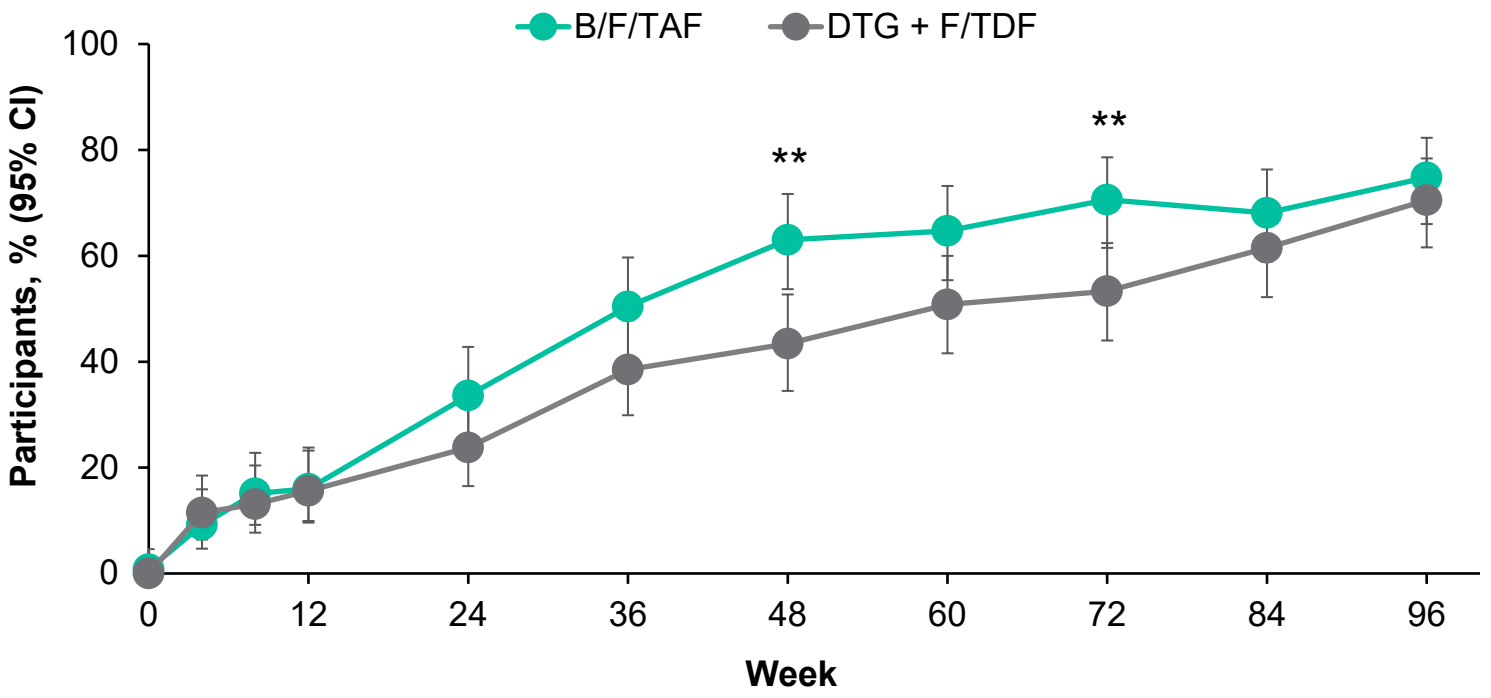
Mean change from baseline in CD4 cells with B/F/TAF vs. DTG + F/TDF

- +261 cells/μL vs. +229 cells/μL

Rates of HIV-1 RNA and HBV DNA suppression were high with both B/F/TAF and DTG + F/TDF. Viral suppression rates, CD4 cell counts and CD4 percentages were similar between groups

*Based on Mantel-Haenszel (MH) proportions adjusted by baseline HIV-1 RNA stratum (<100,000 vs. ≥100,000 c/mL). †CMH test stratified by baseline HIV-1 RNA stratum. ‡Based on MH proportions adjusted by baseline HBeAg status (positive vs. negative) and HBV DNA category (< 8 vs ≥ 8 log10 IU/mL). §CMH test stratified by baseline HBeAg status and baseline HBV DNA category. B/F/TAF, bictegravir; emtricitabine and tenofovir alafenamide; c, copies; CMH, Cochran–Mantel–Haenszel; DTG + F/TDF, dolutegravir, plus emtricitabine and tenofovir disoproxil fumarate; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; M=F, missing=failure.

Proportion of Participants with HBV DNA < 29 IU/mL by Visit (M=F)



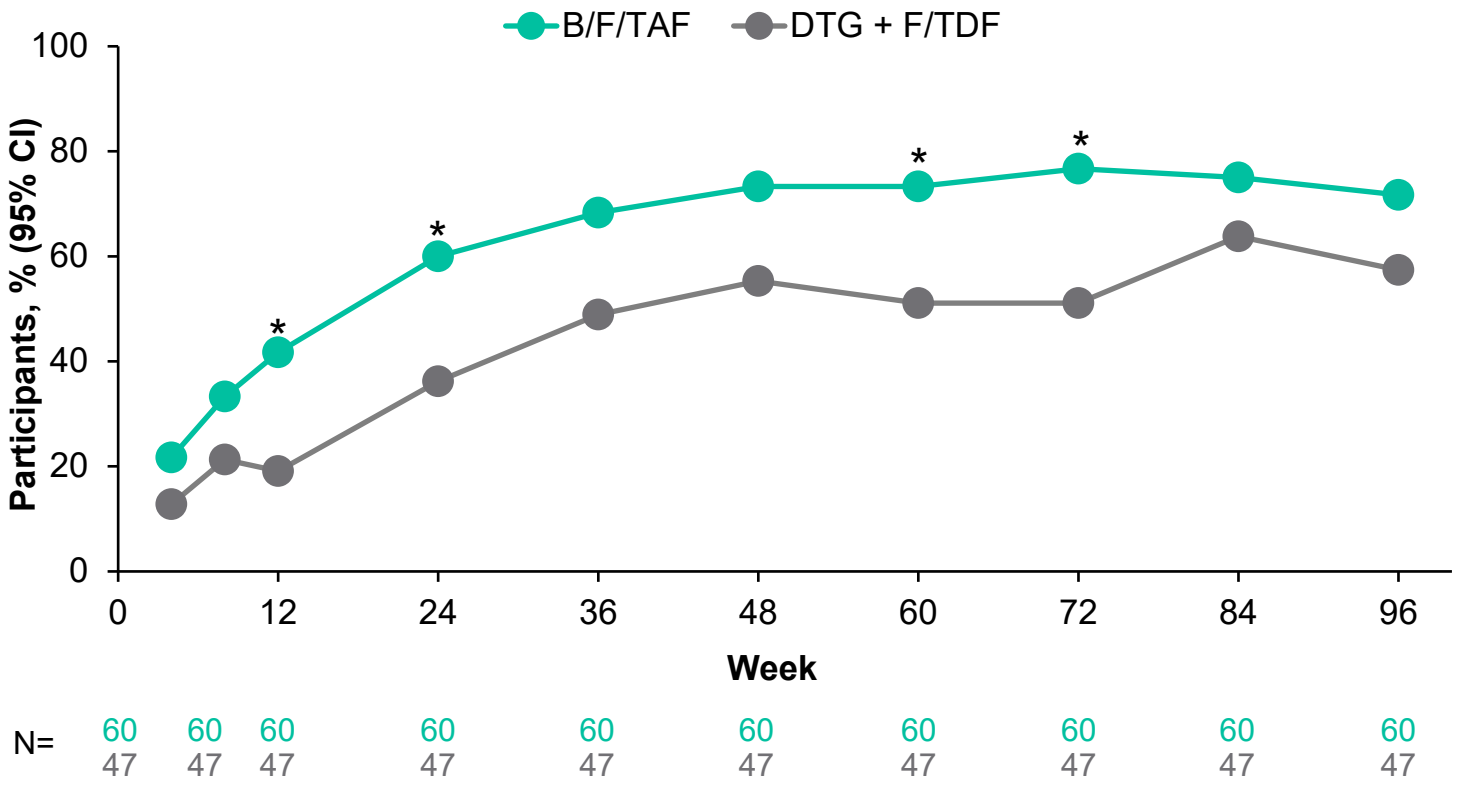
For further information on change in HBV DNA by visit, please see the supplementary material available via the QR code

Material for the QR code is currently in the back up section of this deck

Rates of HBV DNA suppression were significantly higher with B/F/TAF versus DTG +F/TDF at Weeks 48 and 72, but were similar thereafter

Error bars show 95% CI, calculated using the Clopper-Pearson exact method. **p<0.01 calculated using the CMH test stratified by baseline HBeAg stratum and HBV DNA stratum.
B/F/TAF, bictegravir; emtricitabine and tenofovir alafenamide; CI, confidence interval; CMH, Cochran–Mantel–Haenszel; DTG + F/TDF, dolutegravir, plus emtricitabine and tenofovir disoproxil fumarate; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; M=F, missing=failure.

ALT Normalization by Visit Through Week 96 (AASLD criteria; full analysis set)



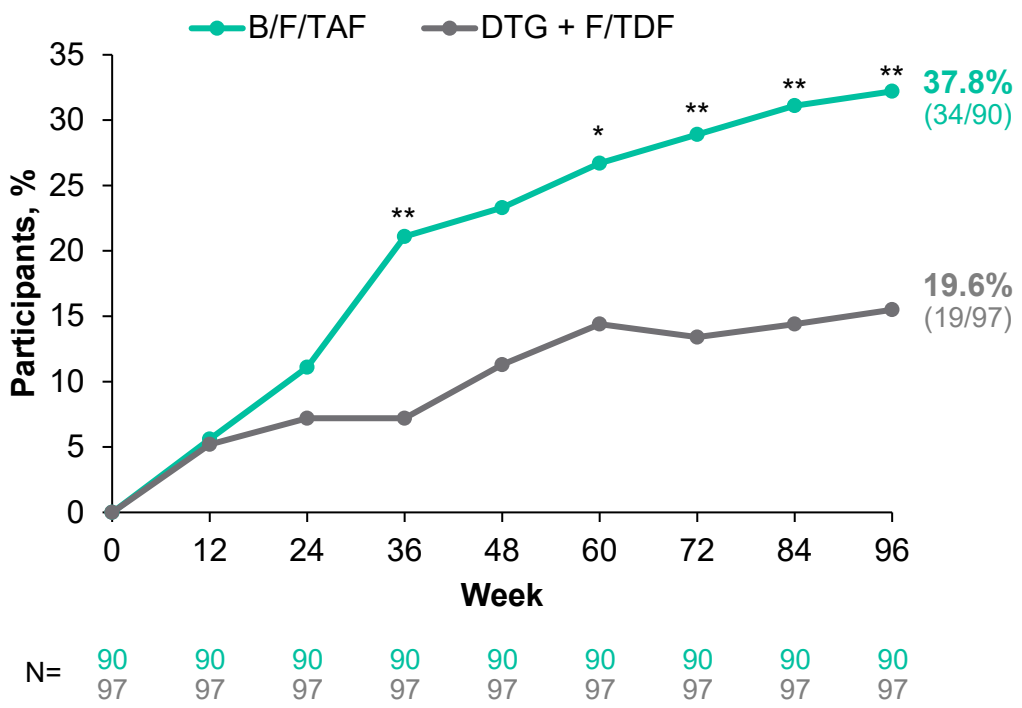
ALT normalization was greater with B/F/TAF versus DTG + F/TDF over 96 weeks

AASLD criteria: ULN of 25 U/L for females and 35 U/L for males[1]. *p<0.05, CMH tests stratified by baseline HBeAg status (positive vs. negative) and baseline HBV DNA (< 8 vs. ≥ 8 log10 IU/mL).
ALT, alanine aminotransferase; AASLD, American Association for the Study of Liver Diseases; B/F/TAF, bictegravir; emtricitabine and tenofovir alafenamide; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; DTG + F/TAF, dolutegravir, plus emtricitabine and tenofovir disoproxil fumarate; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; ULN, upper limit of normal.

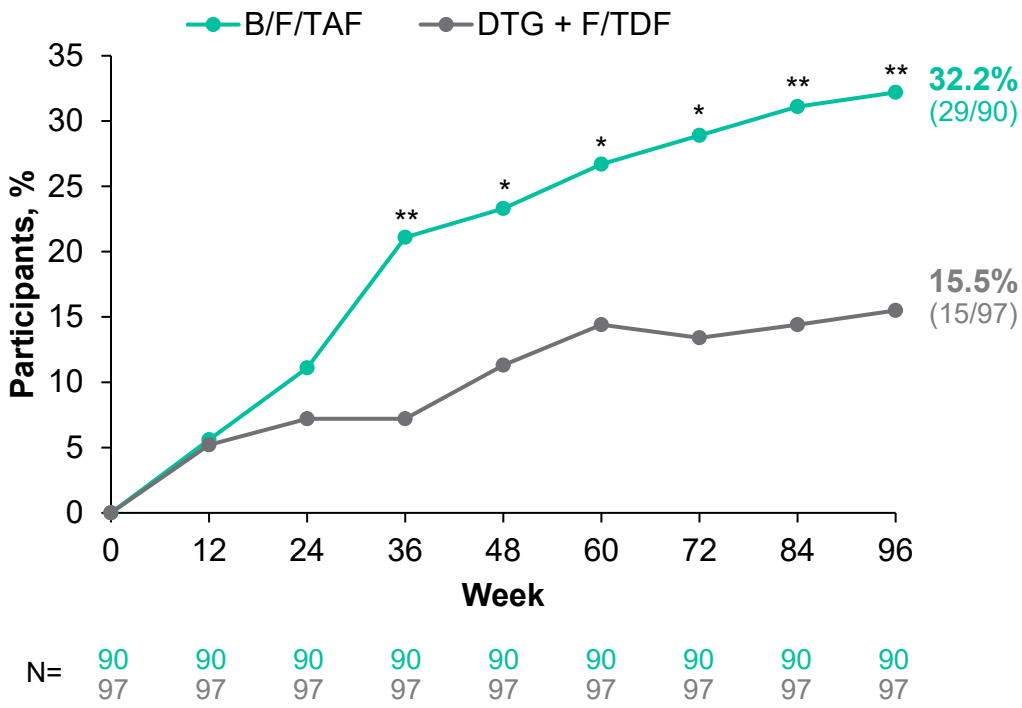
1. Terrault NA, et al. Hepatology 2018;67:1560-99

HBeAg Loss and Seroconversion by Visit Through Week 96

HBeAg loss



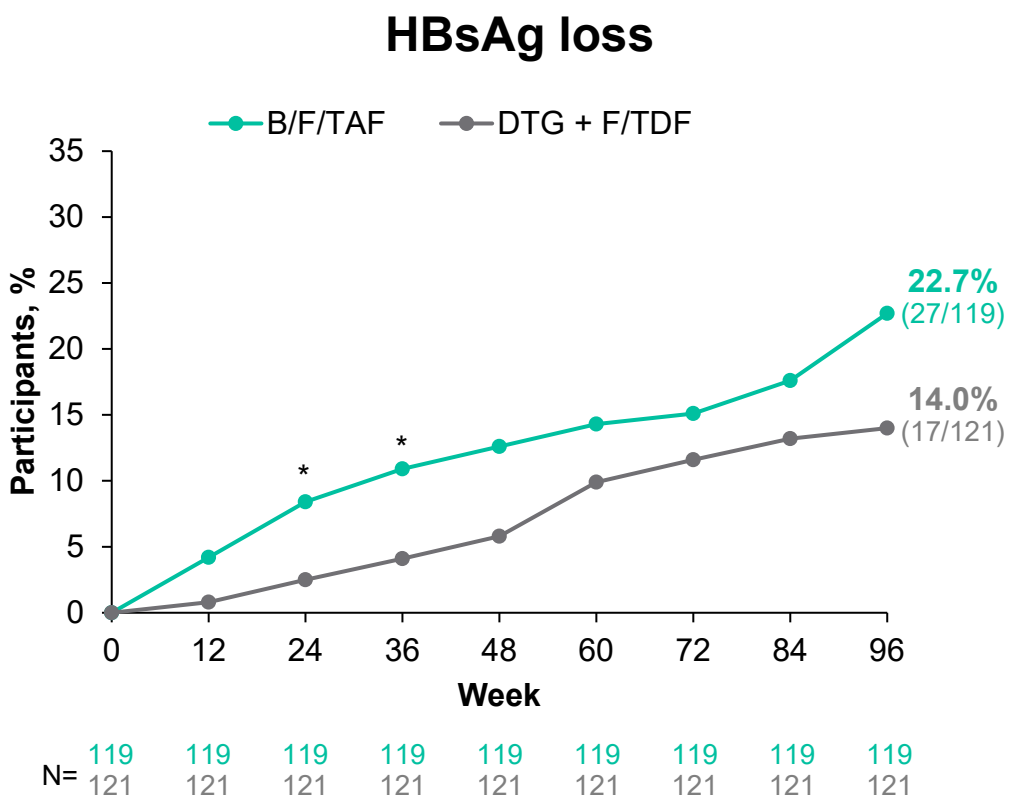
HBeAg seroconversion

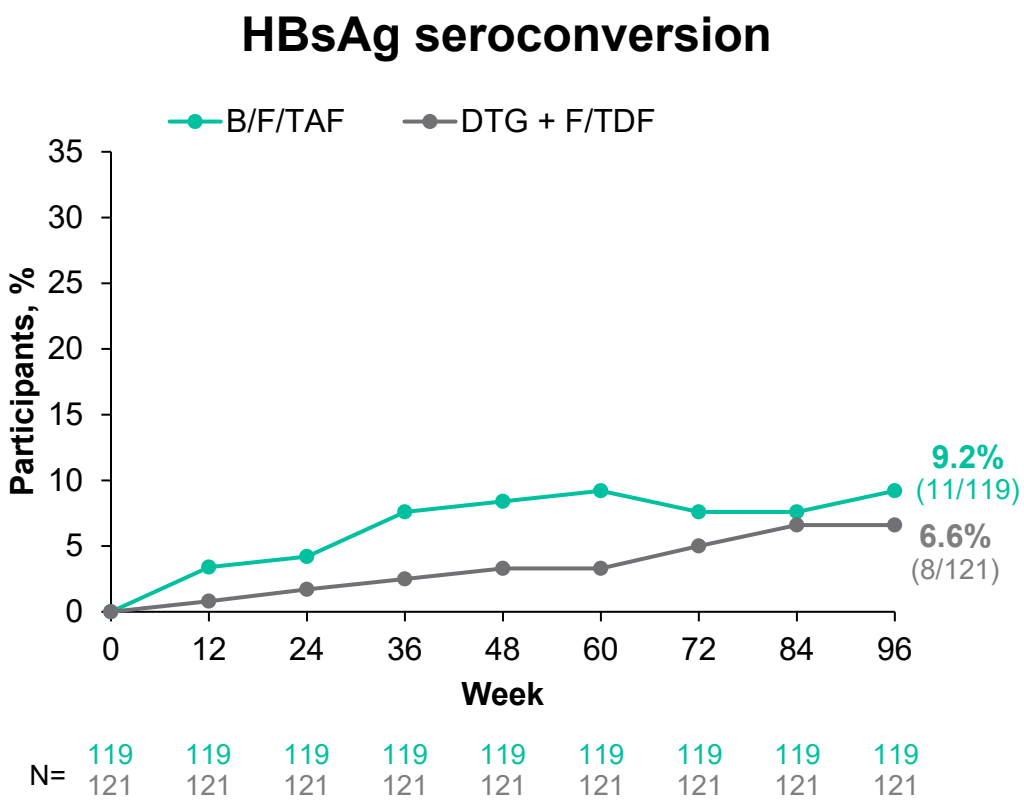


Rates of HBeAg loss and seroconversion were significantly higher with B/F/TAF versus DTG + F/TDF

HBsAg loss and seroconversion in serologically evaluable full analysis set.. *p<0.05, **p<0.01, CMH tests for HBeAg loss and seroconversion stratified by baseline HBV DNA (< 8 vs. ≥ 8 log10 IU/mL).
B/F/TAF, bictegravir; emtricitabine and tenofovir alafenamide; CMH, CMH, Cochran–Mantel–Haenszel; DTG + F/TAF, dolutegravir, plus emtricitabine and tenofovir disoproxil fumarate; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus.

HBsAg Loss and Seroconversion by Visit Through Week 96 (M=F)





Rates of HBsAg loss and seroconversion were numerically higher with B/F/TAF versus DTG + F/TDF at all timepoints

HBsAg loss and seroconversion in serologically evaluable full analysis set. *p<0.05, CMH tests for HBsAg loss and seroconversion stratified by baseline HBeAg status (positive vs. negative) and baseline HBV DNA (< 8 vs ≥ 8 log10 IU/mL).

B/F/TAF, bictegravir; emtricitabine and tenofovir alafenamide; CMH, Cochran–Mantel–Haenszel; DTG + F/TAF, dolutegravir, plus emtricitabine and tenofovir disoproxil fumarate; HBsAg, hepatitis B surface antigen; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; M=F, missing = failure;

Safety of B/F/TAF versus DTG + F/TDF Through Week 96 (Safety analysis set)

AEs and laboratory abnormalities, n (%)	B/F/TAF (n=121)	DTG + F/TDF (n=122)
Any AE	116 (95.9)	117 (95.9)
Any Grade 3 or 4 AE	22 (18.2)	21 (17.2)
Serious AE	17 (14.0)	16 (13.1)
AE leading to treatment discontinuation	1 (0.8)*	0
Any study drug-related AE	35 (28.9)	34 (27.9)
Study drug-related AEs in ≥ 5% of participants in either treatment group		
Weight increased†	7 (5.8)	9 (7.4)
ALT increased	2 (1.7)	8 (6.6)
Study drug-related serious AE	1 (0.8)‡	0
Death§	1 (0.8)	1 (0.8)
Any Grade 3 or 4 laboratory abnormalities	45 (37.5)	39 (32.2)
Grade 3 or 4 laboratory abnormalities occurring in ≥ 10% in either group		
ALT increased (> 5 × ULN)	26 (21.7)	16 (13.2)
AST increased (> 5 × ULN)	16 (13.3)	14 (11.6)

For further information on adverse events and laboratory results, please see the supplementary material available via the QR code

Material for the QR code is currently in the back up section of this deck

Incidence of adverse events and laboratory abnormalities was similar between treatment groups

Multiple AEs were counted only once per participant for the highest severity grade for each preferred term. *Hepatocellular carcinoma on Day 1115 (subsequently died in hospice); †AEs of weight increased or abnormal weight gain; ‡Cryptococcal meningitis attributed to immune reconstitution inflammatory syndrome on Day 32 (resolved on Day 40). §Both deaths, occurring on Days 28 (B/F/TAF group) and 38 (DTG + F/TDF group), were due to unknown causes. A third participant, in the B/F/TAF group, discontinued study treatment after Week 48, on Day 1115, after developing hepatocellular carcinoma; this participant subsequently died in hospice.
AE, adverse events, ALT, alanine transaminase; AST, aspartate aminotransferase; B/F/TAF, bictegravir; emtricitabine and tenofovir alafenamide; DTG + F/TAF, dolutegravir, plus emtricitabine and tenofovir disoproxil fumarate; ULN, upper limit of normal.

Conclusions

- Treatment with B/F/TAF and DTG + F/TDF resulted in high rates of HIV-1 and HBV viral suppression sustained over 96 weeks in adults with both HIV-1 and HBV
- Markers of anti-HBV activity (ALT normalization, HBeAg/HBsAg loss and seroconversion) showed greater improvement with B/F/TAF than with DTG + F/TDF
- Rates of HBsAg loss (functional cure) were high in both groups, particularly in individuals received B/F/TAF

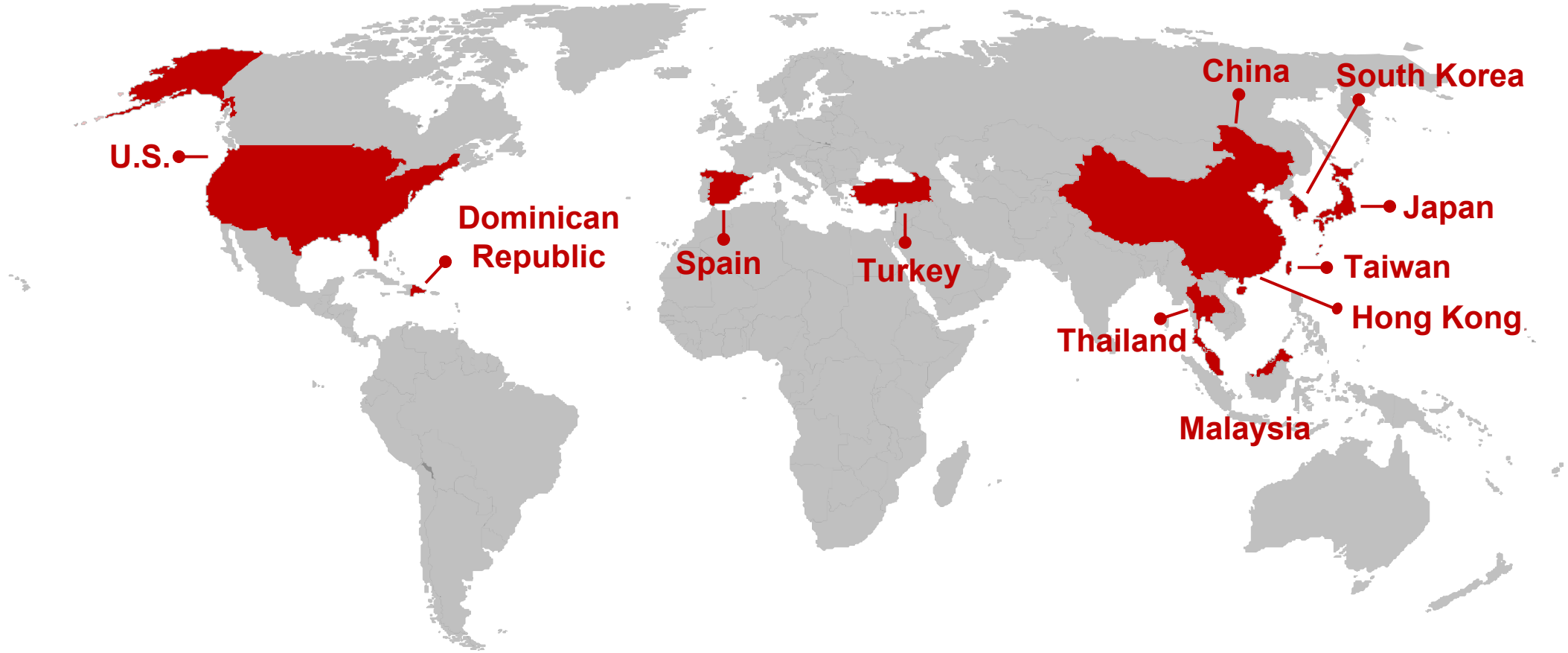
These data, combined with the lower impact of TAF versus TDF on bone and renal health,[8,9] show potential clinical benefits of the single-tablet regimen B/F/TAF for people with both HIV-1 and HBV

B/F/TAF, bictegravir; emtricitabine and tenofovir alafenamide; DTG + F/TAF, dolutegravir, plus emtricitabine and tenofovir disoproxil fumarate; HBeAg, hepatitis B surface antigen; HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen; TAF, tenofovir disoproxil fumarate; TDF, tenofovir disoproxil fumarate.

1. Buti M, et al. Lancet Gastroenterol Hepatol 2016;1:196-206; 2. Chan HLY, et al. Lancet Gastroenterol Hepatol 2016;1:185-95.

Acknowledgments

Thank you to the investigators, study staff and all participants



This study was funded by Gilead (NCT03547908). Medical writing support was provided by Joanna Nikitorowicz-Buniak, PhD, of Aspire Scientific Ltd and funded by Gilead.

Author Disclosures

Note to all authors: TBC
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- Anchalee Avihingsanon has received research/grant support and honoraria from Gilead Sciences, speaker honoraria from ViiV Healthcare and GSK, and research/grant support, speaker honoraria, and consulting fees from Viatris. The potential effects of relevant financial relationships with ineligible companies have been mitigated.
- Hongzhou Lu TBC
- Chee Loon Leong TBC
- Chien-Ching Hung has received support for the present study, research grants, and speaker honoraria from Gilead Sciences. The potential effects of relevant financial relationship with ineligible company have been mitigated.
- Ellen Koenig has no relevant financial relationships with ineligible companies to disclose.
- Sasisopin Kiertiburanakul TBC
- Man-Po Lee TBC
- Khuanchai Supparatpinyo TBC
- Fujie Zhang TBC
- Taisheng Li has received support for the present study from Gilead Sciences; speaker honoraria from Perkin Elmer, Gilead Sciences, and GSK Pharmaceuticals; support for travel from Gilead Sciences, GSK Pharmaceuticals, and Sansure Biotech; and is Chairman of the Chinese Society of Infectious Diseases. The potential effects of relevant financial relationships with ineligible companies have been mitigated.
- Sophia Rahman, Michelle L. D'Antoni, Hongyuan Wang, Jason T. Hindman, Hal Martin, and Jared M. Baeten are employees of Gilead and hold stocks/shares in Gilead. The potential effects of relevant financial relationships with ineligible company have been mitigated.

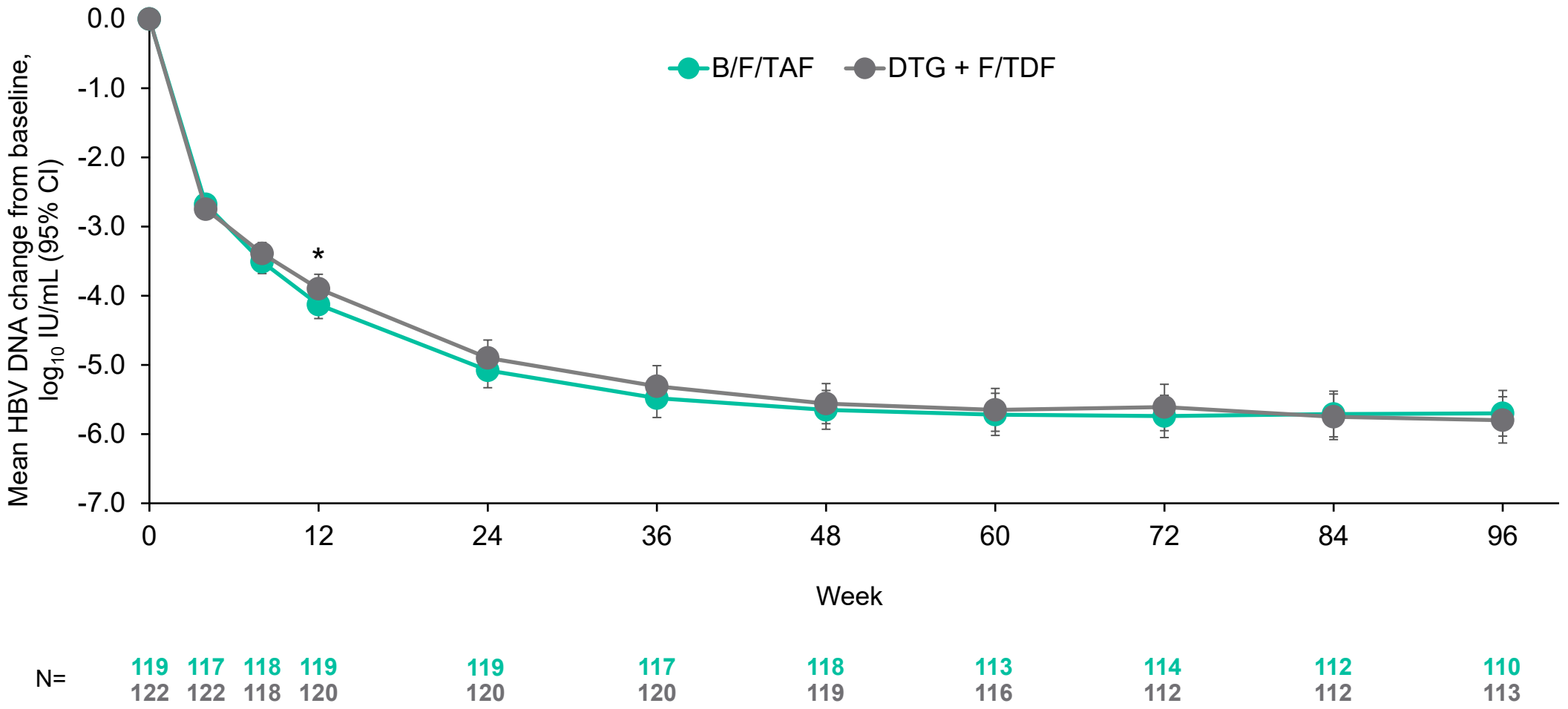
Baseline Demographic and Disease Characteristics

	B/F/TAF (n=121)	DTG + F/TDF (n=122)	Total (N=243)
Age, median (IQR), years	31 (27, 39)	32 (25, 38)	32 (26, 38)
Sex at birth, n (%)			
Male	112 (92.6)	120 (98.4)	232 (95.5)
Female	9 (7.4)	2 (1.6)	11 (4.5)
Race, n (%)			
Asian	108 (89.3)	106 (86.9)	214 (88.1)
White	10 (8.3)	9 (7.4)	19 (7.8)
Black	2 (1.7)	6 (4.9)	8 (3.3)
Other	1 (0.8)	1 (0.8)	2 (0.8)
Hispanic or Latino ethnicity, n (%)	7 (5.8)	10 (8.2)	17 (7.0)
BMI, median (IQR), kg/m^2	22.2 (19.9, 24.7)	21.7 (19.3, 23.7)	21.9 (19.3, 24.2)
Weight, median (IQR), kg	63.7 (57.0, 73.9)	63.8 (56.6, 71.0)	63.7 (56.7, 72.0)
ALT, median (IQR), U/L	34 (23, 60)	27 (19, 51)	31 (20, 58)
> ULN, n (%)*	60 (49.6)	47 (38.5)	107 (44.0)
HIV-1 RNA, median (IQR) log_{10}, copies/mL	4.66 (4.22, 5.12)	4.69 (4.26, 5.04)	4.67 (4.24, 5.08)
CD4 cell count, median (IQR), cells/μL	245 (127, 383)	236 (121, 380)	243 (122, 383)
HBV DNA, median (IQR) log_{10}, IU/mL	7.96 (6.52, 8.38)	8.08 (6.59, 8.50)	8.07 (6.52, 8.44)
HBsAg positive, n (%)	121 (100.0)	121 (99.2)	242 (99.6)
HBeAg positive, n (%)	92 (76.0)	97 (79.5)	189 (77.8)
HBV genotype, n (%)‡			
A	7 (6.3)	19 (17.4)	26 (11.8)
B	21 (18.8)	24 (22.0)	45 (20.4)
C	63 (56.3)	50 (45.9)	113 (51.1)
D	15 (13.4)	14 (12.8)	29 (13.1)
F	3 (2.7)	1 (0.9)	4 (1.8)
Mixed	3 (2.7)	1 (0.9)	4 (1.8)
Missing	9	13	22

*Based on the 2018 AASLD criteria: ULN is 25 U/L for females and 35 U/L for males; ‡Percentage based on individuals with non-missing HBV genotype.

AASLD, American Association for the Study of Liver Diseases; ALT, alanine aminotransferase. B/F/TAF, bictegravir; emtricitabine and tenofovir alafenamide; BMI, body mass index; DTG + F/TAF, dolutegravir, plus emtricitabine and tenofovir disoproxil fumarate; $eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault formula; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B; IQR, interquartile range; ULN=upper limit of normal.

Change in HBV DNA From Baseline by Visit



*p<0.05 using ANOVA model adjusted by baseline HBeAg stratum and HBV DNA stratum.
B/F/TAF, bictegravir; emtricitabine and tenofovir alafenamide; CI, confidence intervals; DTG + F/TAF, dolutegravir, plus emtricitabine and tenofovir disoproxil fumarate; HBeAg, hepatitis B e antigen; HBV, hepatitis B.

Adverse Events Through Week 96

AE, n (%)	B/F/TAF (n = 121)	DTG + F/TDF (n = 122)
AEs in ≥ 10% in either treatment group		
COVID-19	46 (38.0)	44 (36.1)
Upper respiratory tract infection	24 (19.8)	18 (14.8)
Pyrexia	15 (12.4)	16 (13.1)
Nasopharyngitis	15 (12.4)	8 (6.6)
ALT increased	10 (8.3)	15 (12.3)
Diarrhoea	13 (10.7)	11 (9.0)
Study drug-related AEs in ≥ 2% in either treatment group*		
Weight increased†	7 (5.8)	9 (7.4)
ALT increased	2 (1.7)	8 (6.6)
Nausea	1 (0.8)	5 (4.1)
Headache	4 (3.3)	2 (1.6)
AST increased	3 (2.5)	3 (2.5)
Dizziness	2 (1.7)	3 (2.5)
Protein urine present	3 (2.5)	1 (0.8)
Dyslipidaemia	3 (2.5)	1 (0.8)

Multiple AEs were counted only once per participant for the highest severity grade for each preferred term. *AST increased, protein urine present, dyslipidaemia and leukopenia occurred in 2 and 2, 1 and 0, 1 and 1, and 1 and 0 participants in the B/F/TAF and DTG + F/TDF groups, respectively, at Week 48, corresponding to < 2% of either treatment group; †AEs of weight increased or abnormal weight gain.
AE, adverse event; ALT, alanine transaminase; AST, aspartate aminotransferase; B/F/TAF, bictegravir; emtricitabine and tenofovir alafenamide; DTG + F/TAF, dolutegravir, plus emtricitabine and tenofovir disoproxil fumarate.

Other Laboratory Results at Week 96

	B/F/TAF (n=121)	DTG + F/TDF (n=122)
Median (IQR) change in $eGFR_{CG}$ from baseline, mL/min	−9.9 (−21.6, −0.6)	−12.0 (−17.4, −5.3)
Median (IQR) change in fasting cholesterol from baseline, mg/dL	16 (−9, 35)	−15 (−34, 6)
Median (IQR) change in fasting LDL from baseline, mg/dL	3 (−13, 26)	−33 (−79, −14)

B/F/TAF, bictegravir; emtricitabine and tenofovir alafenamide; DTG + F/TAF, dolutegravir, plus emtricitabine and tenofovir disoproxil fumarate; $eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault formula; IQR, interquartile range; LDL, low-density lipoprotein.