Week-96 Results of ALLIANCE, a Phase 3, Randomized, Double-Blind Study Comparing B/F/TAF Versus DTG + F/TDF in Treatment-Naïve People With Both HIV-1 and Hepatitis B

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Anchalee Avihingsanon,[1] Hongzhou Lu,[2] Chee Loon Leong,[3] Chien-Ching Hung,[4] Ellen Koenig,[5] Sasisopin Kiertiburanakul,[6] Man-Po Lee,[7] Khuanchai Supparatpinyo,[8] Fujie Zhang,[9] Sophia Rahman,[10] Michelle L. D'Antoni,[10] Hongyuan Wang,[10] Jason T. Hindman,[10] Hal Martin,[10] Jared M. Baeten,[10] Taisheng Li[11]

[1]HIV-NAT, Thai Red Cross AIDS Research Centre and Centre of Excellence in Tuberculosis, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand; [2]Shanghai Public Health Clinical Center, Shanghai, China; [3]Department of Medicine, Kuala Lumpur General Hospital, Kuala Lumpur, Malaysia; [4]National Taiwan University Hospital Yunlin, Yunlin, Taiwan; [5]Instituto Dominicano de Estudio Virologicos – IDEV, Santo Domingo, Dominican Republic; [6]Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; [7]Queen Elizabeth Hospital, Kowloon, Hong Kong; [8]Chiang Mai University, Chiang Mai, Thailand; [9]Beijing Ditan Hospital, Capital Medical University, Beijing, China; [10]Gilead Sciences, Inc., Foster City, California, U.S.A.; [11]Peking Union Medical College Hospital, Beijing, China

Key Findings

- Treatment with B/F/TAF and DTG + F/TDF achieved high rates of HIV-1 and HBV viral suppression, which were maintained over 96 weeks in adults who had both HIV-1 and HBV, and who were initiating antiviral therapy
- Rates of HBeAg loss and seroconversion were significantly higher with B/F/TAF than with DTG + F/TDF through Week 96
- Other markers of anti-HBV activity (ALT normalization, HBsAg loss and seroconversion) also trended toward improvement with B/F/TAF versus DTG + F/TDF through Week 96
- Rates of HBsAg loss (functional cure) were high through 96 weeks in both groups, particularly in individuals who were receiving B/F/TAF

Conclusion

- These data, combined with the lower impact of TAF versus TDF on bone and renal health,[1,2] show clinical benefits of the single-tablet regimen B/F/TAF for adults with both HIV-1 and HBV initiating antiviral therapy

Introduction

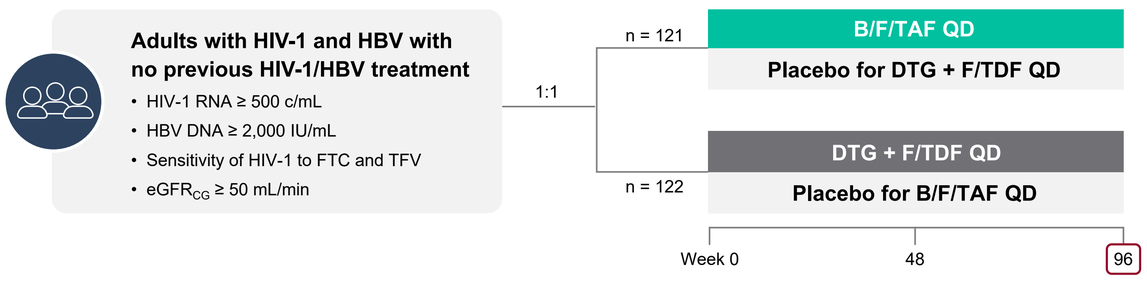
- Globally, approximately 2.7 million individuals are living with both HIV-1 and HBV, with rates of coinfection reaching 20% in some areas[3,4]
- International guidelines recommend a TDF- or TAF-containing antiretroviral regimen for most adults with HIV-1/HBV coinfection,[5–8] but no randomized studies 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 the treatment of HIV-1,[6–8] as initial treatment for adults with HIV-1/HBV coinfection[9]
- In the primary analysis at Week 48 (AIDS 2022),[9] B/F/TAF demonstrated:
  - 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

Objective

- To investigate the efficacy and safety of B/F/TAF in HIV-1/HBV coinfection over 96 weeks in a prespecified secondary analysis

Methods

Study Design



- Secondary endpoints at Week 96 were HIV-1 suppression (HIV-1 RNA < 50 c/mL), HBV suppression (HBV DNA < 29 IU/mL), change in CD4 cell count/percentage, ALT normalization and HBsAg loss
- Additional endpoints at Week 96 were HBeAg loss, HBeAg seroconversion and HBsAg seroconversion

Results

Key Baseline Demographic and Disease Characteristics

Characteristic	B/F/TAF n = 121	DTG + F/TDF n = 122
Age, years, median (IQR)	31 (27, 39)	32 (25, 38)
Male at birth, n (%)	112 (93)	120 (98)
HIV-1 RNA, log_{10} c/mL, median (IQR)	4.66 (4.22, 5.12)	4.69 (4.26, 5.04)
CD4 cell count, cells/μL, median (IQR)	245 (127, 383)	236 (121, 380)
HBV DNA, log_{10} IU/mL, median (IQR)	7.96 (6.52, 8.38)	8.08 (6.59, 8.50)
HBeAg positive, n (%)	92 (76)	97 (80)
ALT > ULN, n (%)	60 (50)	47 (39)

References: **1.** Buti M, et al. Lancet Gastroenterol Hepatol 2016;1:196-206. **2.** Chan HLY, et al. Lancet Gastroenterol Hepatol 2016;1:185-195. **3.** Platt L, et al. J Viral Hepat 2020;27:294-315. **4.** Thio CL. Hepatology 2009;49(5 Suppl.):S138-S145. **5.** WHO. https://www.who.int/publications/i/item/9789240031593 (accessed May 20, 2023); **6.** EACS. https://www.eacsociety.org/media/guidelines-11.1_final_09-10.pdf (accessed May 20, 2023). **7.** DHHS. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf (accessed May 20, 2023). **8.** Gandhi RT, et al. JAMA 2023;329:63-84. **9.** Avihingsanon A, et al. AIDS 2022, Oral OALBX0105. **10.** Terrault NA, et al. Hepatology 2018;67:1560-1599.

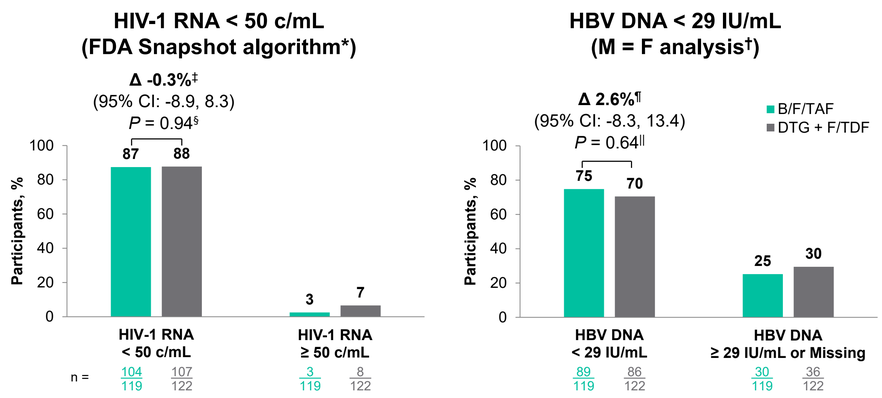
Acknowledgments: This study (NCT03547908) was sponsored by Gilead Sciences. We thank all study participants, investigators and staff. Medical writing support was provided by Joanna Nikitorowicz-Buniak, PhD (Aspire Scientific Ltd, U.K.), and was funded by Gilead.

Disclosures: **AA:** research/grant support and honoraria from Gilead Sciences; speaker honoraria from ViiV Healthcare and GSK; research/grant support, speaker honoraria and consulting fees from Viatris. **C-CH:** support for the present study, research grants and speaker honoraria from Gilead Sciences. **SR**, **MLDA**, **HW**, **JTH** and **HM:** employees and stockholders of Gilead Sciences. **JMB:** employee and stockholder of Gilead Sciences; grants from the National Institutes of Health outside of the present work. **TL:** 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; Chair of the Chinese Society of Infectious Diseases. The potential effects of relevant financial relationships with ineligible companies have been mitigated. **HL**, **CLL**, **EK**, **SK**, **M-PL**, **KS** and **FZ** have no relevant financial relationships with ineligible companies to disclose.

Abbreviations: AASLD, American Association for the Study of Liver Diseases; AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; c, copies; CD, cluster of differentiation; CI, confidence interval; CMH, Cochran–Mantel–Haenszel; DTG, dolutegravir; $eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft–Gault equation; FTC, emtricitabine; F/TDF, emtricitabine/tenofovir disoproxil fumarate; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IQR, interquartile range; M = F, missing = failure; MH, Mantel–Haenszel; QD, once daily; SD, standard deviation; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TFV, tenofovir; ULN, upper limit of normal.

Results (continued)

Virologic Outcomes at Week 96

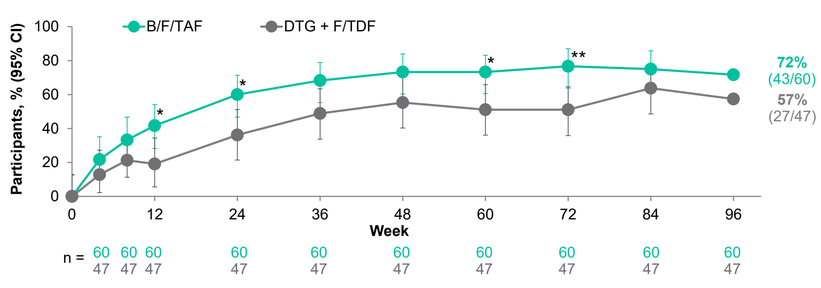


Mean (SD) change from baseline in CD4 cells
- B/F/TAF: +261 (162) cells/μL
- DTG + F/TDF: +229 (174) cells/μL

All *P*-values are nominal. *No data for 12 (10%) and 7 (6%) participants in the B/F/TAF and DTG + F/TDF groups, respectively. †No data for 9 (8%) and 9 (7%) participants in the B/F/TAF and DTG + F/TDF groups, respectively. ‡Based on 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 log_{10} IU/mL). ||CMH test stratified by baseline HBeAg status and baseline HBV DNA category.

Rates of HIV-1 RNA and HBV DNA suppression were high with both B/F/TAF and DTG + F/TDF

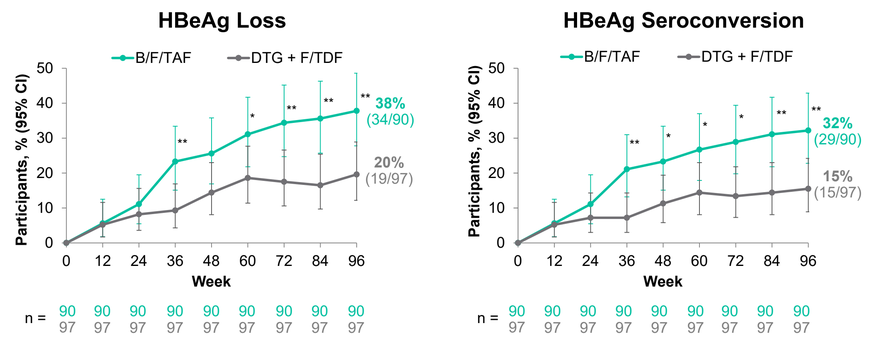
ALT Normalization by Visit (AASLD criteria)



Rates of ALT normalization were numerically or statistically significantly higher with B/F/TAF versus DTG + F/TDF over 96 weeks

M = F analysis, full analysis set. AASLD criteria: ULN of 25 U/L for females and 35 U/L for males.[10] *P < 0.05, **P < 0.01; CMH tests stratified by baseline HBeAg status (positive vs. negative) and baseline HBV DNA (< 8 vs. ≥ 8 log_{10} IU/mL).

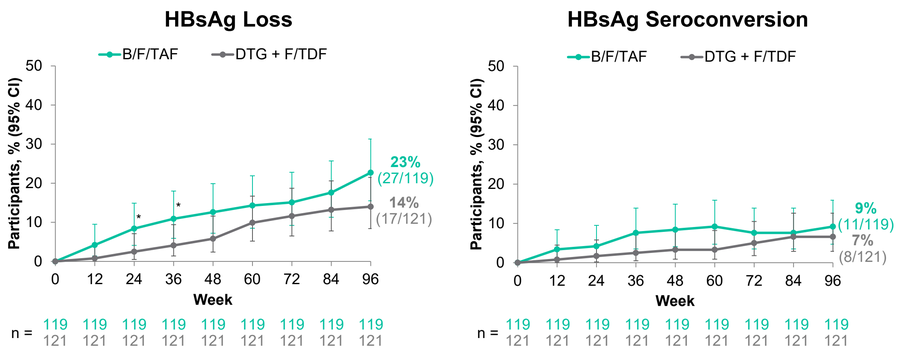
HBeAg Loss and Seroconversion by Visit



Rates of HBeAg loss and seroconversion were significantly higher with B/F/TAF versus DTG + F/TDF at 96 weeks, and remained higher throughout

M = F analysis in serologically evaluable full analysis set; two participants in the B/F/TAF group were HBeAg positive at baseline but did not meet the criteria for inclusion in the full analysis set (received ≥ 1 dose of study drug and had ≥ 1 post-baseline HIV-1 RNA or HBV DNA result while on study drug). *P < 0.05, **P < 0.01; CMH tests for HBeAg loss and seroconversion stratified by baseline HBV DNA (< 8 vs. ≥ 8 log_{10} IU/mL).

HBsAg Loss and Seroconversion by Visit



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

M = F analysis 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 log_{10} IU/mL).

Safety of B/F/TAF Versus DTG + F/TDF

AEs and laboratory abnormalities, n (%)		B/F/TAF n = 121	DTG + F/TDF n = 122
Any AE		116 (96)	117 (96)
Any Grade 3 or 4 AE		22 (18)	21 (17)
Serious AE		17 (14)	16 (13)
AE leading to treatment discontinuation		1 (1)*	0
Any study drug–related AE		35 (29)	34 (28)
Study drug–related AEs in ≥ 5% of participants in either treatment group	Weight increased† ALT increased	10 (8) 2 (2)	12 (10) 8 (7)
Study drug–related serious AE		1 (1)‡	0
Death§		2 (2)	1 (1)
Any laboratory abnormalities		114 (95)	114 (94)
Any Grade 3 or 4 laboratory abnormalities		45 (38)	39 (32)
Grade 3 or 4 laboratory abnormalities occurring in ≥ 10% in either group	ALT increased (> 5 × ULN) AST increased (> 5 × ULN)	26 (22) 16 (13)	16 (13) 14 (12)

Safety analysis set reported through Week 96 data cut; multiple AEs were counted only once per participant for the highest severity grade for each Preferred Term. *After Week 48, on Day 1,115, after developing hepatocellular carcinoma (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). §Two participants in the B/F/TAF group died (one due to ischemic heart disease and one due to unknown causes) and one participant in DTG + F/TDF group due to unknown causes.

Incidences of AEs and laboratory abnormalities were similar between treatment groups

IAS 2023, the 12th IAS Conference on HIV Science; July 23–26, 2023; Brisbane, Australia