Efficacy, Safety, and Tolerability Bictegravir/Emtricitabine/Tenofovir Alafenamide in Adults HIV-HBV Coinfection **(BEST-HBV Study)** Interim Week 24 Results

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Introduction

Coinfection with HIV and hepatitis B (HBV) has been associated with higher risk of morbidity and mortality, especially acceleration of liver disease. HBV-active antiretroviral (ARV) regimens have significantly improved the outcome of people with HIV-HBV coinfection. Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) has been shown to be highly effective in the treatment of HIV infection based on treatment naïve and switch trials. [1,2] Although it is an HBV-active regimen, there was few data[3,4] on the use of B/F/TAF for people with HIV-HBV coinfection. We hypothesize that B/F/TAF is both safe and efficacious in the treatment of coinfected adults.

Objectives

Primary objective is to evaluate the efficacy of fixed dose combination (FDC) B/F/TAF in HIV-HBV coinfected adults.

Primary Endpoints

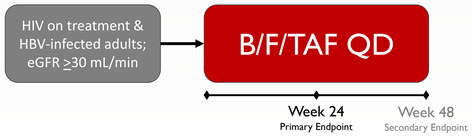
- Proportion of subjects with HIV-1 RNA <50 copies/mL at Week 24 as defined by the US FDA Snapshot Algorithm.
- Proportion of subjects with plasma HBV DNA <29 IU/mL at Week 24 using the missing = failure method.

Secondary Endpoints

- Proportion of subjects with HIV-1 RNA <50 copies/mL at Week 48.
- Proportion of subjects with HBV DNA <29 IU/mL at Week 48.
- Change from baseline in CD4 cell count at Week 24 and 48.
- Proportion of subjects with normalized ALT at Week 24 and 48.

Methodology

This open-label, single-arm, Phase 4, switch study from two clinical centers (Baltimore, MD and Philadelphia, PA) evaluated the efficacy, safety, and tolerability of treatment with FDC B/F/TAF in adults with HIV-1 and HBV coinfection. Eligible participants were switched from their current antiretroviral regimen (regardless of viral suppression) and receive FDC of bictegravir 50 mg/emtricitabine 200 mg/tenofovir alafenamide 25 mg taken orally once daily, without regard to food. Study treatment duration is 48 weeks.



Safety evaluations will consist of adverse event, physical examination (including vital signs), and clinical laboratory data.

Here, we present our interim week 24 data.

Results

A total of 28 participants were enrolled from May 2019 to December 2021. Median age was 51 years (range 34-71), majority were black (89%), male gender (86%), non-Hispanic (96%), and 65% had both HIV and HBV virally suppressed (Table 1). Two participants, one lost to follow-up and the other removed due to nonadherence prior to week 24, were included in the safety analysis and intention-to-treat (ITT) efficacy analysis.

Table 1. Participant Baseline Demographics

	N	Percent
Total Enrolled (N)	28	-
Age (years)		
Median	51.0	
Range	34-71	
Male gender	24	86%
Race		
Black or African American	25	89%
White or Caucasian	3	11%
Ethnicity		
Non-Hispanics	28	100%
African	8	29%
HIV RNA PCR (IU/mL)		
<50	20	71%
50-500	6	21%
>500	2	7%
CD4 Count (cells/µL)		
>500	12	43%
200-500	15	54%
<200	1	4%
HBV DNA PCR <29 IU/mL	22	79%
HBeAg positive	11	39%
Anti-HBe positive	6	21%
HCV antibody positive*	5	18%
HDV antibody positive	6	21%
Abnormal ALT (>44 IU/mL)	4	14%

*None had detectable HCV RNA at baseline.

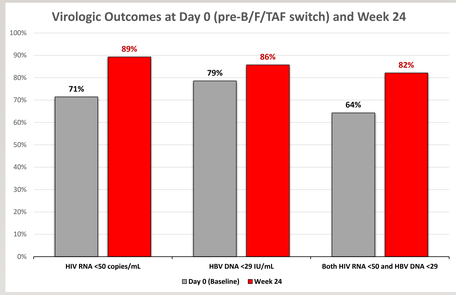
Safety Outcomes

Safety analysis set includes all participants who received at least one dose of study drug. Safety outcomes are as below:

- Thirty-five (35) adverse events (AEs) were reported, of which ten were related to study treatment.
- All AEs were either mild or moderate in severity.
- The most common AE, related or unrelated, was upper respiratory tract infection (4/28 or 14%).
- The most common treatment-related AE was nausea in 2 of 28 (7%) participants and were mild and transient. Other treatment-related AEs (1 each) included abdominal pain, diarrhea, headache, irritability, night sweats, peripheral edema, rash, and vivid dreams.
- All treatment-related AEs were grade 1 (mild) in severity.
- No participant discontinued study treatment due to an AE.
- No serious AEs were reported.
- No hepatitis flares were seen.

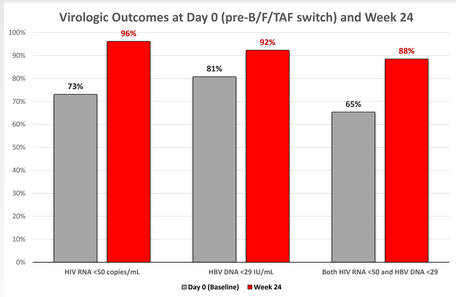
Primary Efficacy Endpoints

Intention-to-Treat Efficacy Analysis, N=28



The ITT population (N = 28) includes all participants who had at least one study drug. At baseline, 71% were HIV suppressed and 79% were HBV suppressed. At week 24, 25 (89%) were HIV suppressed and 24 (86%) were HBV suppressed. Twenty-three (82%) were HIV and HBV suppressed, which was higher than prior to B/F/TAF use.

Per Protocol Efficacy Analysis, N=28



Per protocol population (N = 26) includes all participants who had at least one dose of study drug and remained on study at week 24. Significantly higher number of participants were HIV suppressed (25/26 or 96%) and HBV suppressed (24/26 or 92%) at week 24, compared to prior to B/F/TAF switch. Twenty-three (88%) had both HIV and HBV suppressed at week 24 in this population.

Secondary Endpoints

- Four of 28 (14%) participants had elevated ALT at baseline, all of which normalized by week 24.
- No significant change in CD4 from baseline to Week 24.

Discussion

Enrolled in our study is a population with a unique but important demographic profile. Close to 90% are black, a historically underserved population. Almost 30% are migrants from Africa, and in an unexpected finding, our study had a good proportion of HDV positive participants.

Interim results show that there is a numerically higher degree of both HIV and HBV suppression at week 24 compared to prior to B/F/TAF switch. Similar to that seen in HIV monoinfected patients in registry trials[1-3] and a more recent HIV-HBV naïve study[4], B/F/TAF is well tolerated by our participants with none discontinuing due to AE.

The study population is small, mainly due to many coinfected individuals already having switched to B/F/TAF use in our clinics. Study was also affected by COVID-19 travel and research restrictions, particularly between March – August 2020 whereby screening and non-essential study visits were restricted.

Study is ongoing and the last participant is expected to complete their week 48 this year, and study outcomes will reveal the efficacy, safety and durability of B/F/TAF therapy in HIV-HBV coinfected patients.

Conclusion

B/F/TAF is efficacious, safe, and well tolerated in patients coinfected with HIV and HBV after 6 months of treatment, regardless of suppression prior to switch.

Ethical Considerations

BEST-HBV study is approved by the Institutional Review Board of both the University of Maryland School of Medicine (Baltimore site) and the Philadelphia Department of Health (Philadelphia site). All study participants provided written informed consent prior to any study procedure.

References

[1]Gallant J, Lazzarin A, Mills A, et al. (2017) Bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir, abacavir, and lamivudine for initial treatment of HIV-1 infection (GS-US-380-1489): a double-blind, multicentre, phase 3, randomised controlled non-inferiority trial. *Lancet.* 390:2063-2072.

[2]Sax PE, Pozniak A, Montes ML, et al. (2017) Coformulated bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir with emtricitabine and tenofovir alafenamide, for initial treatment of HIV-1 infection (GS-US-380–1490): a randomised, double-blind, multicentre, phase 3, non-inferiority trial. *Lancet.* 390:2073-2082.

[3]Rockstroh JK, Sax PE, Daar ES, et al. (2018) High HBV and HIV suppression with treatment of HIV/HBV coinfection in B/F/TAF studies. CROI (Boston, MA) Abstract 618, 2018 March 4-7. Session number P-K06.

[4]Avihingsanon A, Lu H, Leong CL, et al. (2022) Phase 3 randomized controlled trial of B/F/TAF vs DTG-F/TDF as initial treatment in adults with HIV/HBV coinfection. AIDS (Montreal, Canada) oral OALBX0105.

Acknowledgment

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