Predictors of Hepatitis B Treatment Response in People with HIV-1 and HBV Initiating Treatment

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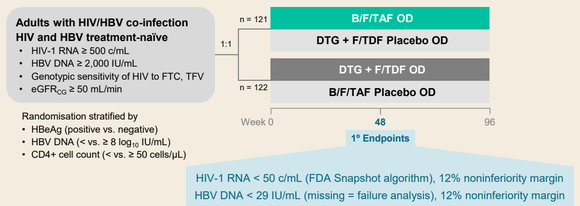
Introduction

- Chronic hepatitis B affects ~8% of people with HIV, and HIV/HBV co-infection rates can reach 20% in areas where both viruses are endemic[1-3]
- People with HIV and HBV should receive treatment to suppress both viruses
  - International guidelines recommend a TDF- or TAF-based ARV regimen in combination with 3TC or FTC as the NRTI backbone for most people with HIV/HBV co-infection[4-7]
- Better understanding of factors that can affect response to treatment is important to help optimise regimen selection
- The ALLIANCE study investigated B/F/TAF vs. DTG + F/TDF for HIV/HBV co-infection
- Primary results from the ALLIANCE study, presented at AIDS 2022, showed that B/F/TAF was non-inferior to DTG + F/TDF for achieving HIV-1 RNA < 50 c/mL and superior for achieving HBV DNA < 29 IU/mL[8]
- This subanalysis of the Week 48 results from the ALLIANCE study examines predictors of HBV response to treatment for people with HIV and HBV initiating treatment with B/F/TAF or DTG + F/TDF

3TC, lamivudine; ARV, antiretroviral; B, bictegravir; c/mL, copies per milliliter; DTG, dolutegravir; F/FTC, emtricitabine; HBV, hepatitis B virus; IU/mL, international units per milliliter; NRTI, nucleos(t)ide reverse transcriptase inhibitor; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate

ALLIANCE Study Design and Analyses



- **Pre-specified subgroup analysis of between-treatment differences in the proportion of people with HBV DNA < 29 IU/mL**
- **Multivariate analysis to identify baseline predictors of HBV DNA < 29 IU/mL, HBeAg losss and HBsAg loss**

ALT, alanine aminotransferase; B, bictegravir; c/mL, copies per mL; DTG, dolutegravir; eGFR$_{CG}$, estimated glomerular filtration rate by Cockcroft–Gault method; F/FTC, emtricitabine; FDA, U.S. Food and Drug Administration; HBeAg, hepatitis B envelope antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IU/mL, international units per milliliter; OD, once daily; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TFV, tenofovir

https://clinicaltrials.gov/ct2/show/NCT03547908 (accessed Jan, 2023)

Introduction, cont'd

Baseline Characteristics

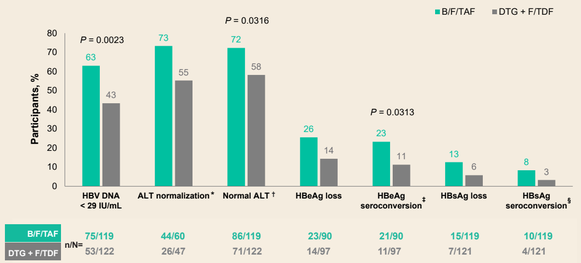
	B/F/TAF n = 121	DTG + F/TDF n = 122
HBV genotype, n (%)*		
A/D	22 (20)	33 (30)
B/C	84 (75)	74 (68)
HBV DNA		
Median, log$_{10}$ IU/mL (IQR)	8.0 (6.5, 8.4)	8.1 (6.6, 8.5)
≥ 8 log$_{10}$ IU/mL, n (%)	60 (50)	66 (54)
HBeAg positive, n (%)	92 (76)	97 (80)
ALT > ULN, n (%)†	60 (50)	47 (39)

The overall median age was 32 years, 95% were male at birth and 88% were from Asia
Median HIV-1 RNA was 4.7 log$_{10}$ c/mL and median CD4 cell count was 243 cells/μL

*B/F/TAF: n = 112, DTG + F/TDF: n = 109; †American Association for the Study of Liver Diseases (AASLD) criteria: 25 U/L (females), 35 U/L (males)
ALT, alanine aminotransferase; B, bictegravir; c/mL, copies per milliliter; DTG, dolutegravir; F, emtricitabine; HBeAg, hepatitis B envelope antigen; HBV, hepatitis B virus; IQR, interquartile range; IU/mL, international units per milliliter; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; ULN, upper limit of normal

Results

HBV Outcomes at Week 48 (M = F)

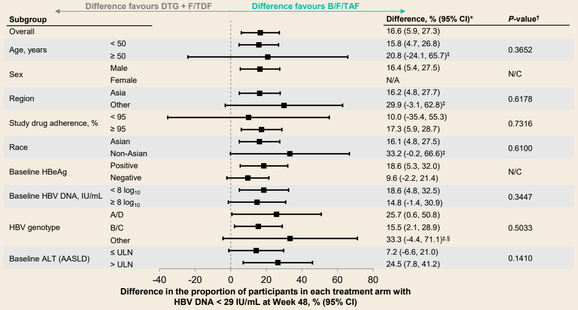


*Proportion of participants with ALT > ULN at baseline with a normal ALT [≤ 25 U/L (females), ≤ 35 U/L (males)] at Week 48; †Proportion of participants with normal ALT (by AASLD criteria) at Week 48; ‡Defined as loss of serum HBeAg and development of anti-HBeAg antibodies; §Defined as loss of serum HBsAg and development of anti-HBsAg antibodies

ALT, alanine aminotransferase; AASLD, American Association for the Study of Liver Diseases; B, bictegravir; DTG, dolutegravir; F, emtricitabine; HBeAg, hepatitis B envelope antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IU/mL, international units per milliliter; M = F, missing = failure; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; ULN, upper limit of normal

Results, cont'd

Treatment Difference in Proportion of Participants with HBV DNA < 29 IU/mL at Week 48, by Subgroup (M = F)



*The difference in proportion of participants with HBV DNA < 29 IU/mL between treatment groups (B/F/TAF vs. DTG + F/TDF) calculated based on the MH proportions adjusted by baseline HBeAg status (positive vs. negative) and baseline HBV DNA (< 8 log$_{10}$ IU/mL vs. ≥ 8 log$_{10}$ IU/mL), if not the subgroup factor; †P-value for the homogeneity test was from the Wald test of the interaction between treatment and subgroup based on a logistic regression model; ‡Proportion difference and 95% CI from normal approximation without stratification as they were not calculable by stratum-adjusted MH method; §'Other' HBV genotype excluded from the logistic regression model for P-value calculation due to small sample size. ALT, alanine aminotransferase; B, bictegravir; CI, confidence interval; DTG, dolutegravir; F, emtricitabine; HBeAg, hepatitis B envelope antigen; HBV, hepatitis B virus; IU/mL, international units per milliliter; M = F, missing = failure; MH, Mantel–Haenszel; N/A, not applicable; N/C, not calculable (due to lack of variance in subgroup[s]); TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; ULN, upper limit of normal

Baseline Predictors of HBV Treatment Response: Multivariate Logistic Regression Analysis (Full Analysis Set)

Stepwise logistic regression was conducted. The significance level for entry into the model = 0.025, the significance level for staying in the model = 0.05. Candidate independent variables included: demographics (group of age, sex, race and ethnicity), baseline HBV DNA, HBV genotype baseline ALT, baseline BMI, baseline HIV1-RNA, baseline CD4 cell count and HIV-1 disease status. The final multivariate model included treatment and variables selected by the stepwise method as independent variables

ALT, alanine aminotransferase; B, bictegravir; BMI, body mass index; CI, confidence interval; DTG, dolutegravir; F, emtricitabine; HBeAg, hepatitis B envelope antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IU/mL, international units per milliliter; OR, odds ratio; ref., reference; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; ULN, upper limit of normal

Conclusions

In adults with HIV and HBV initiating antiviral therapy for the first time, after 48 weeks:

- Significantly more participants on B/F/TAF versus DTG + F/TDF had HBV DNA < 29 IU/mL, normal ALT and HBeAg seroconversion
- B/F/TAF treatment led to a larger proportion of participants with HBV DNA < 29 IU/mL compared with DTG + F/TDF across all subgroups
- Several baseline factors were determined to be predictors of HBV DNA suppression, including B/F/TAF treatment, HBeAg-negative status, HBV DNA < 8 log$_{10}$ and ALT > ULN at baseline
  - ALT > ULN and CD4 ≥ 200 cells/μL at baseline were predictors of HBeAg and HBsAg loss
- The ALLIANCE study will continue in a blinded fashion through Week 96 to determine longer-term safety and efficacy

References: 1. Leumi S, et al. Clin Infect Dis 2020;71:2799-2806; 2. Kellerman SE, et al. J Infect Dis 2003;188:571-577; 3. Thio CL. Hepatology 2009;49:S138-S145; 4. WHO. https://www.who.int/publications/i/item/9789240031593 (accessed Jan, 2023); 5. EACS. https://www.eacsociety.org/media/final2021eacsguidelinesv11.0_oct2021.pdf (accessed Jan, 2023); 6. DHHS. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf (accessed Nov. 10, 2022); 7. Saag MS, et al. JAMA 2020;324:1651-1669; 8. Avihingsanon A, et al. AIDS 2022, Oral OALBX0105

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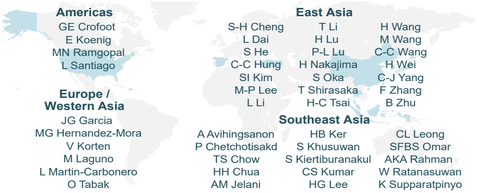

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