Week 48 Results of a Phase 3 Randomized Controlled Trial of B/F/TAF vs DTG + F/TDF as Initial Treatment in Adults with HIV/HBV Coinfection (ALLIANCE)

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Disclosures

- I have no relevant financial relationships with ineligible companies to disclose

B/F/TAF for People With HIV/HBV Coinfection

- Chronic hepatitis B (CHB) affects ~8% of people with HIV, and HIV/HBV coinfection rates can reach 25% in areas where both viruses are endemic[1-3]
  - Coinfection worsens morbidity and mortality; people with HIV/HBV coinfection have higher HBV DNA levels and have higher risk of cirrhosis and liver cancer than people with HBV monoinfection
- People with HIV/HBV coinfection 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 coinfection[4-7]
- TDF and TAF are approved for the treatment of HBV, and both are widely used as part of an ARV regimen for HIV treatment, but there are no randomized studies of TDF vs TAF-based ART in adults with HIV/HBV coinfection initiating treatment

3TC, lamivudine; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; FTC, emtricitabine; NRTI, nucleos(t)ide reverse transcriptase inhibitor; TDF, tenofovir disoproxil fumarate.

1. Leumi S, et al. Clin Infect Dis. 2020;71:2799-806; 2. Kellerman SE, et al. J Infect Dis, 2003;188:571-7; 3. Kourtis AP, et al. N Engl J Med. 2012;366:1749-52; 4. WHO. Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery and Monitoring: Recommendations for a Public Health Approach; 2021; 5. EACS Guidelines v11.0, October 2021; 6. DHHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV; Accessed 30 Jun 2022; 7. Saag MS, et al. JAMA, 2020;324:1651–69.

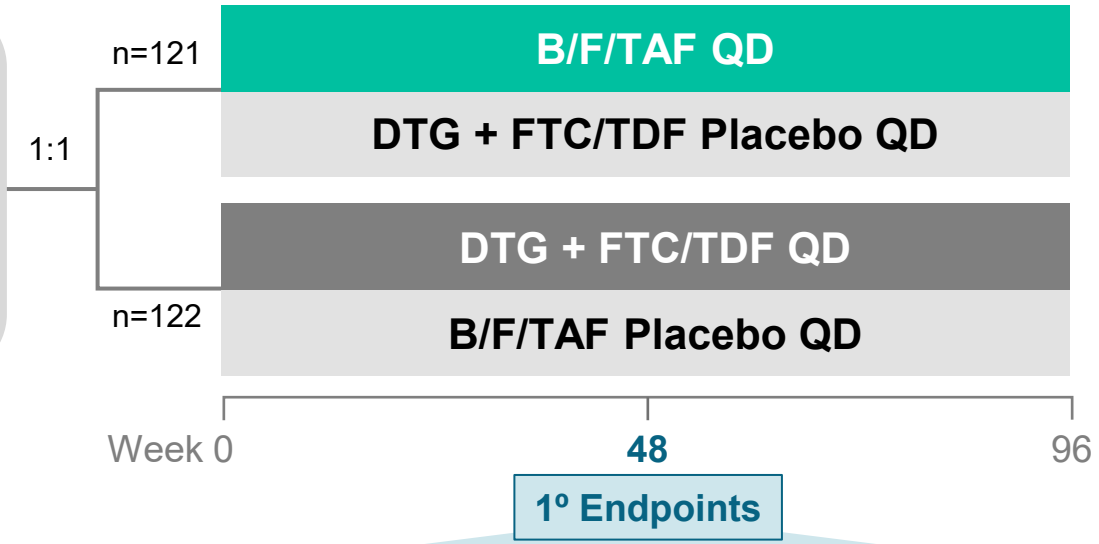
Study Design

Adults with HIV/HBV coinfection, Treatment-Naive to HIV and HBV

- HIV-1 RNA ≥500 c/mL
- HBV DNA ≥2000 IU/mL
- Genotypic sensitivity of HIV to FTC, TFV
- $eGFR_{CG}$ ≥50 mL/min

Randomization stratified by

- HBeAg (positive vs negative)
- HBV DNA (< vs ≥8 log_{10} IU/mL)
- CD4+ cell count (< vs ≥50 cells/μL)

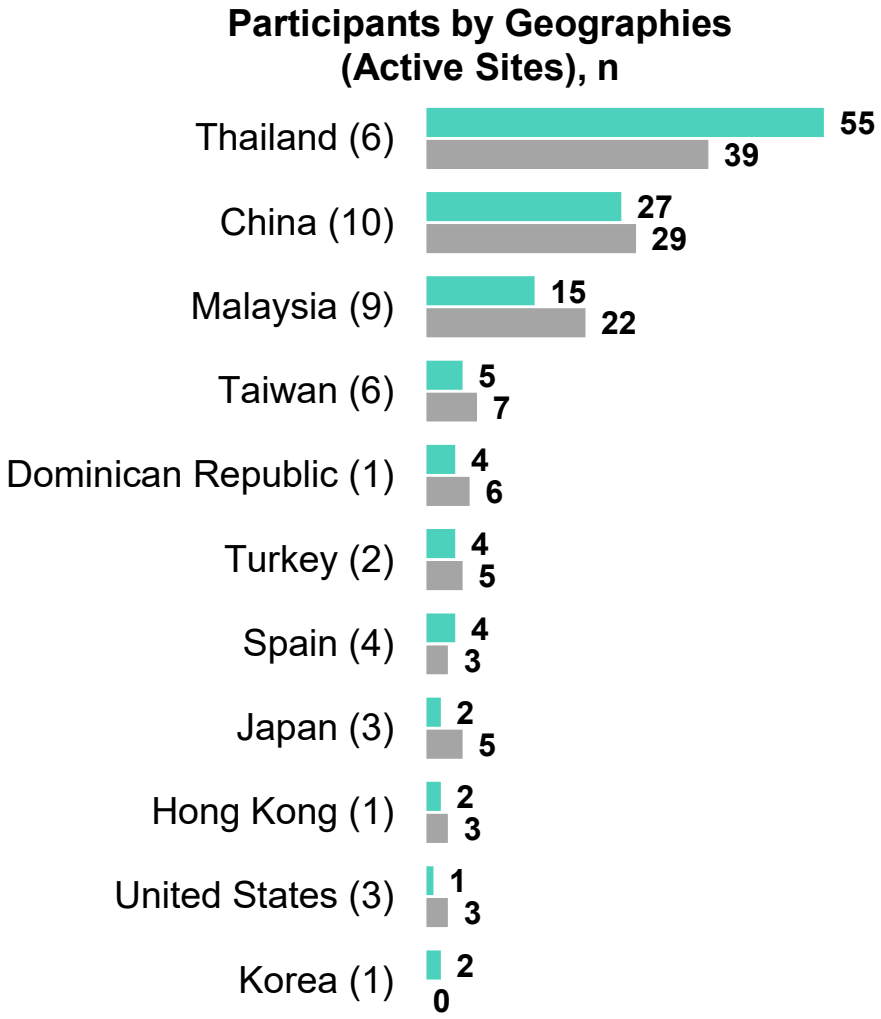


HIV-1 RNA <50 copies/mL (FDA Snapshot algorithm), 12% noninferiority margin

HBV DNA <29 IU/mL (missing = failure analysis), 12% noninferiority margin

DTG, dolutegravir; $eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault method; HBeAg, hepatitis B e antigen; TFV, tenofovir. ClinicalTrials.gov NCT03547908.

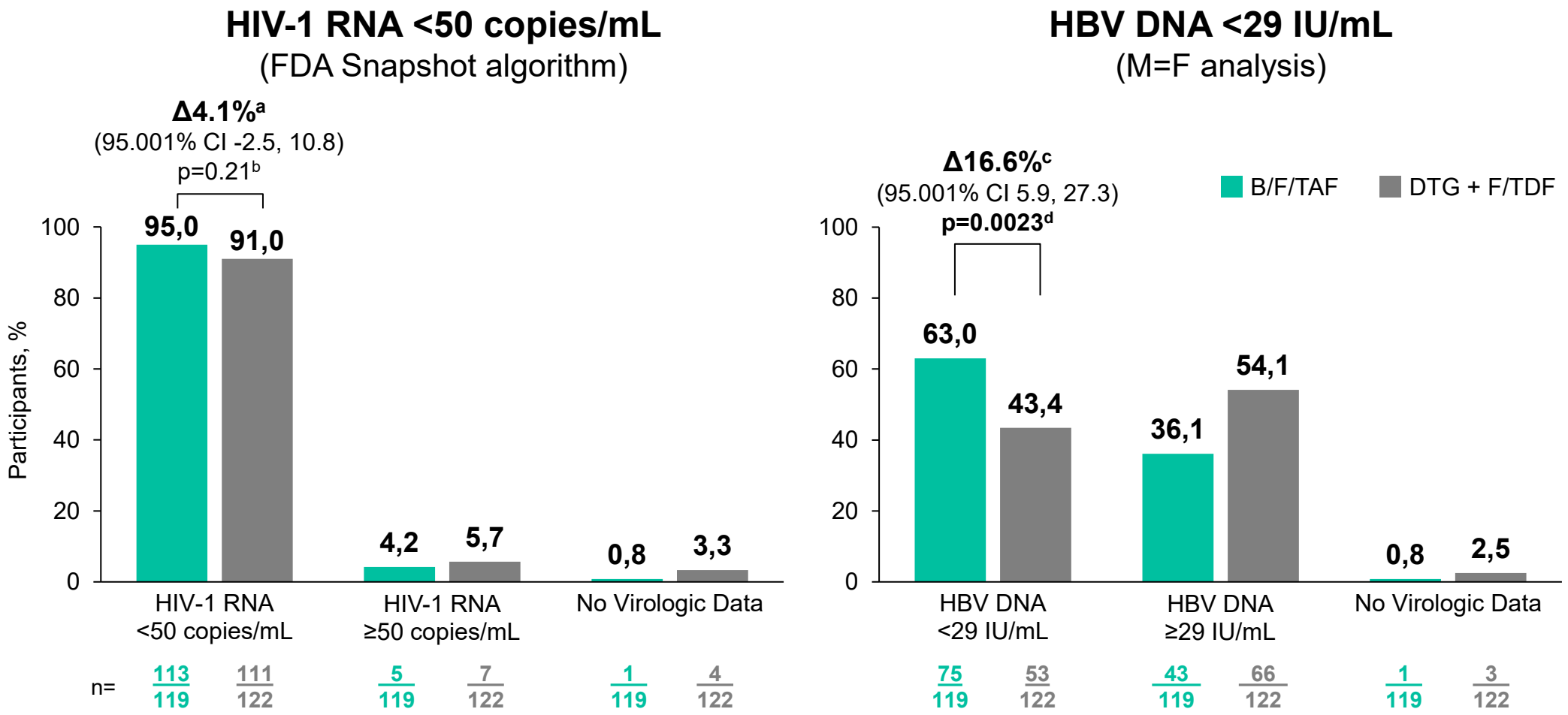
Enrollment and Baseline Characteristics



	B/F/TAF n=121	DTG + F/TDF n=122
Median age, y (IQR)	31 (27, 39)	32 (25, 38)
Female at birth, n (%)	9 (7)	2 (2)
Race/ethnicity, n (%)		
Asian	108 (89)	106 (87)
White	10 (8)	9 (7)
Black	2 (2)	6 (5)
Other	1 (1)	1 (1)
Median body mass index, kg/m^2 (IQR)	22.2 (19.9, 24.7)	21.7 (19.3, 23.7)
Median HIV-1 RNA, $\log_{10}$ copies/mL (IQR)	4.7 (4.2, 5.1)	4.7 (4.3, 5.0)
HIV-1 RNA >100,000 copies/mL, n (%)	38 (31)	34 (28)
Median CD4 cells/μL (IQR)	245 (127, 383)	236 (121, 380)
CD4 count <200 cells/μL, n (%)	46 (38)	52 (43)
Median HBV DNA, $\log_{10}$ IU/mL (IQR)	8.0 (6.5, 8.4)	8.1 (6.6, 8.5)
HBV DNA ≥8 $\log_{10}$ IU/mL, n (%)	60 (50)	66 (54)
HBeAg positive, n (%)	92 (76)	97 (80)
ALT >ULN, n (%)*	60 (50)	47 (39)

*American Association for the Study of Liver Diseases (AASLD) criteria: 25 U/L (females), 35 U/L (males). IQR, interquartile range; ULN, upper limit of normal.

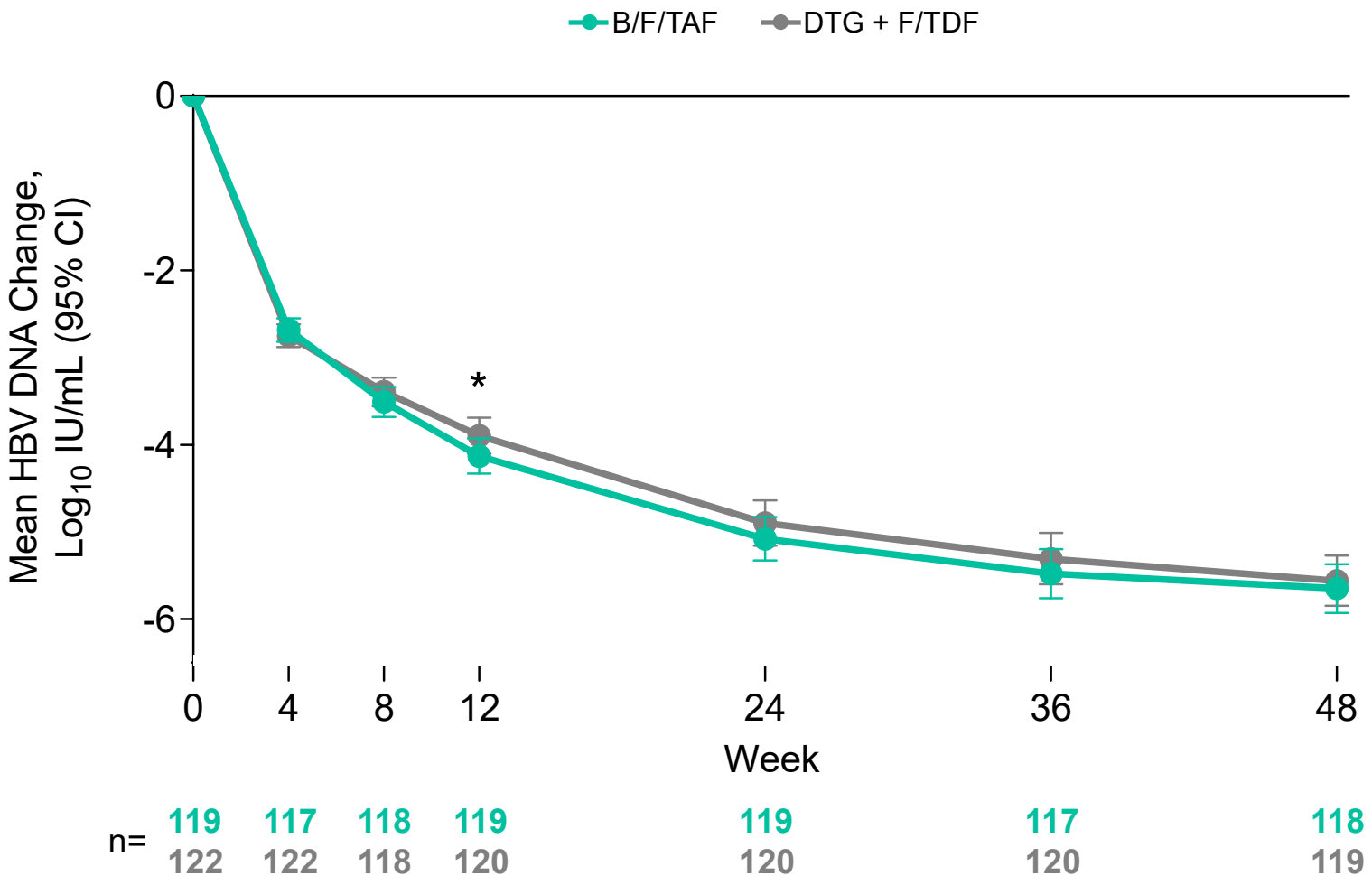
Virologic Outcomes at Week 48: Co-primary Endpoints



- Mean CD4 change from baseline, cells/μL (95% CI): B/F/TAF +200 (175, 226), DTG + F/TDF +175 (152, 198)

[a]Based on Mantel-Haenszel (MH) proportions adjusted by baseline HIV-1 RNA stratum (< vs ≥100,000 copies/mL); [b]Cochran-Mantel-Haenszel (CMH) test stratified by baseline HIV-1 RNA stratum; [c]Based on MH proportions adjusted by baseline HBeAg status (positive vs negative) and HBV DNA category (< vs ≥8 $\log_{10}$ IU/mL); [d]CMH test stratified by baseline HBeAg status and baseline HBV DNA category. Full analysis set. M=F, missing = failure, CI, confidence interval.

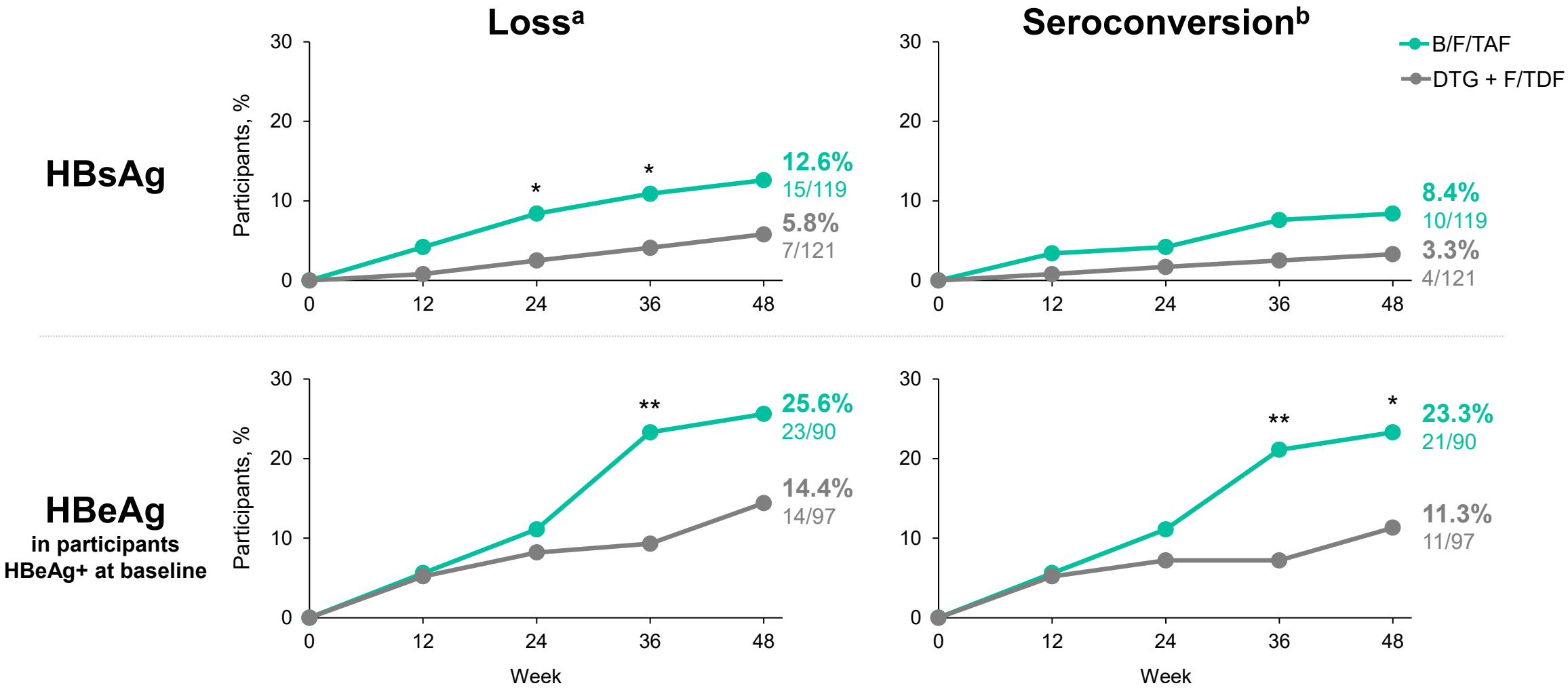
Virologic Outcomes at Week 48: Change in HBV DNA



*p<0.05 using analysis of variance (ANOVA) model adjusted by baseline HBeAg stratum and HBV DNA stratum.

HBs/eAg Loss and Seroconversion at Week 48

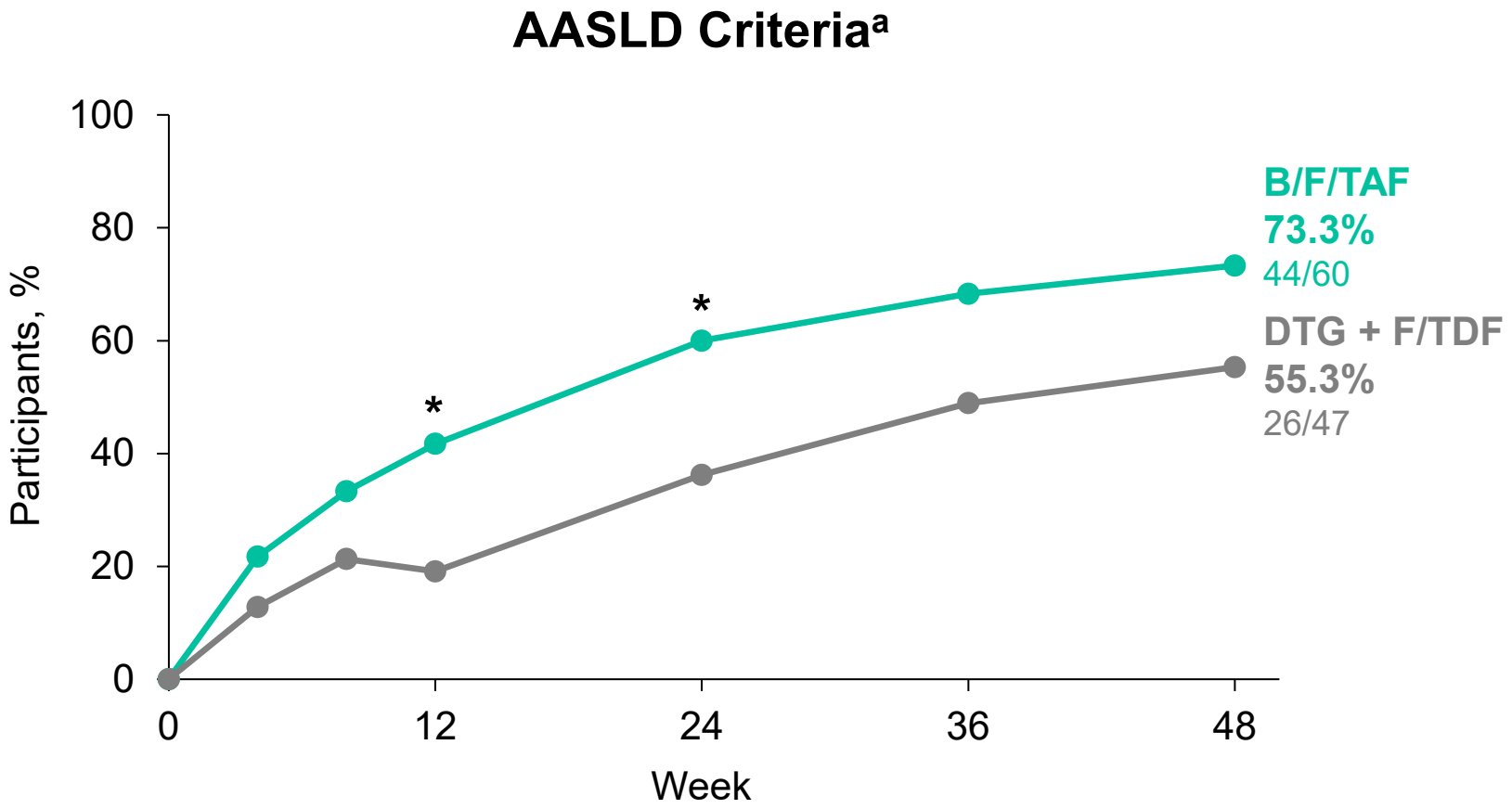
M=F Serologically Evaluable Full Analysis Set



*p<0.05, **p<0.01, CMH tests for HBsAg loss and seroconversion stratified by baseline HBeAg status (positive vs negative) and baseline HBV DNA (< vs ≥8 $\log_{10}$ IU/mL), tests for HBeAg loss and seroconversion stratified by baseline HBV DNA (< vs ≥8 $\log_{10}$ IU/mL); [a]Changes from HBs/eAg+ at baseline to − at a postbaseline visit with baseline HBs/eAb −/missing; [b]HBs/eAg loss and HBs/eAb changes from −/missing at baseline to + at a postbaseline visit.

ALT Normalization Through Week 48

M=F (Full Analysis Set with Baseline ALT > ULN)



*p<0.05, CMH tests stratified by baseline HBeAg status (positive vs negative) and baseline HBV DNA (< vs ≥8 log10 IU/mL); [a]ALT ULN 25 U/L (females), 35 U/L (males).

HIV Resistance Through Week 48

Participants, n	B/F/TAF n=119	DTG + F/TDF n=122
Met criteria for resistance testing[a]	3	4
NRTI resistance detected	0	1
INSTI resistance detected	0	0

- No treatment-emergent resistance to any components of B/F/TAF occurred in the resistance analysis population
- One participant on DTG + F/TDF developed NRTI-resistant mutations K70E at Week 24 and M184V/I at Week 36 (no K70E present), was resuppressed by the Week 36 retest, and then was lost to follow up

[a]HIV-1 RNA ≥ 200 copies/mL at confirmed virologic failure, Week 48, or last on-treatment visit. (Full Analysis Set). INSTI, integrase strand transfer inhibitor.

Adverse Events through Week 48: Overall Summary

	% Participants	
	B/F/TAF n=121	DTG + F/TDF n=122
Treatment-emergent AE	89	86
Grade 3 or 4	14	16
Treatment-emergent study drug-related AE	24	27
Grade 3 or 4	5	1
Treatment-emergent serious AE	12	12
Treatment-emergent study drug-related serious AE	1[a]	0
Treatment-emergent AE leading to discontinuation	1[b]	0
Death	1[c]	1[c]

[a]Cryptococcal meningitis on Day 32 (resolved on Day 40); [b]Hepatocellular carcinoma on Day 1115 (subsequently died in hospice); [c]Both due to unknown cause on Days 28 and 38, respectively.

All Grade and Study Drug-related AEs through Week 48

Preferred Term		% Participants B/F/TAF n=121	% Participants DTG + F/TDF n=122
Any treatment-emergent AE		89	86
All-Grade AEs, Terms ≥10%	Upper respiratory tract infection	17	11
	COVID-19	13	11
	Pyrexia	9	12
	ALT increased	7	11
	Nasopharyngitis	11	4
Any study drug-related AE		24	27
Study drug-related AEs, Terms ≥2%	Weight increased[a]	6	7
	ALT increased	1	5
	Headache	3	2
	Nausea	1	4
	Dizziness	2	2

[a]Preferred terms include 'weight increased' and 'abnormal weight gain.' Median BMI (IQR) change from baseline at Week 48, kg/m^2: B/F/TAF +1.3 (0.3, 2.7), DTG + F/TDF +0.8 (-0.5, 1.5).

Grade 3 or 4 Laboratory Abnormalities Through Week 48

Maximum Treatment-Emergent Toxicity Grade	% Participants	
	B/F/TAF n=120	DTG + F/TDF n=121
Any Grade 3 or 4	34	31
Grade 3 or 4 occurring in ≥2% in either group		
ALT increased[a]	20	13
AST increased[a]	13	12
LDL (fasting, increased)	8	2
Amylase increased[b]	5	7
Urine glucose increased[c]	3	2
Total cholesterol (fasting, increased)	3	0
Neutrophils decreased	0	2

[a]Were transient and did not result in discontinuation of therapy; [b]No cases of pancreatitis; [c]No cases of glycosuria occurred in non-diabetics without concomitant hyperglycemia

Conclusions

In adults with HIV-1/HBV coinfection initiating first-line antiviral therapy, after 48 weeks of treatment:

- B/F/TAF was noninferior to DTG + F/TDF (95% vs 91%) at achieving HIV-1 RNA < 50 c/mL
- B/F/TAF was superior to DTG + F/TDF (63% vs 43%) at achieving HBV DNA < 29 IU/mL
- B/F/TAF was associated with higher rates of HBeAg seroconversion compared to DTG + F/TDF (23% vs 11%), with numerically higher but not statistically significant differences between groups in HBsAg loss/seroconversion, HBeAg loss, and ALT normalization
- No participant developed treatment-emergent HIV-1 drug resistance while on B/F/TAF
- B/F/TAF and DTG + F/TDF were well tolerated with few study-drug related AEs or discontinuations

B/F/TAF is a safe and effective treatment for people with HIV-1/HBV coinfection

For 5-year outcomes in adults initiating B/F/TAF, see Sax P, et al. EPB150

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