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Long-term Analysis of B/F/TAF in Treatment-Naïve Adults Living With HIV Through Four Years of Follow-up

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Introduction

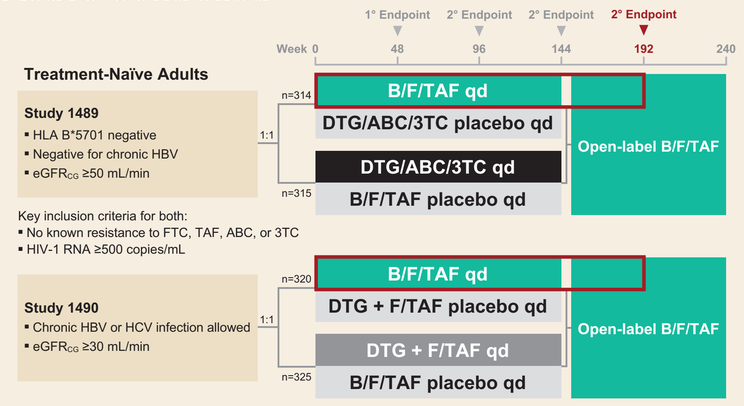
- Bictegravir (BIC)/emtricitabine (FTC)/tenofovir alafenamide (TAF; B/F/TAF) is a guidelines-recommended, single-tablet regimen for people living with HIV[1-3]
- B/F/TAF has a high barrier to resistance, favorable drug-drug interaction profile, and ability to be given once daily without food restrictions
- Safety and efficacy through Week 144 have been demonstrated in two Phase 3 studies (GS-US-380-1489 [ClinicalTrials.gov NCT02607930] and GS-US-380-1490 [NCT02607956]) of B/F/TAF compared with 3-drug dolutegravir (DTG)–containing regimens in treatment-naïve adults[4-8]
  - All participants were offered enrollment in an open-label extension (OLE) after completing 144 wk of the randomized portions of the studies

Objectives

- To assess pooled outcomes from Studies 1489 and 1490 in participants initially randomized to B/F/TAF through Week 192

Methods

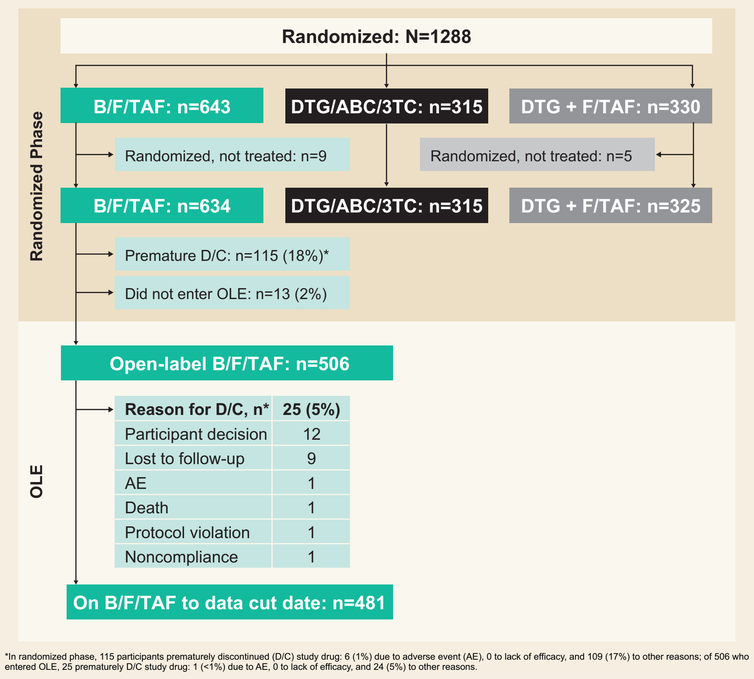
Study Designs: Randomized, Double Blind, Active Controlled



3TC, lamivudine; ABC, abacavir; $eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault equation; HBV, hepatitis B virus; HCV, hepatitis C virus; HLA, human leukocyte antigen.

Results

Participants Randomized to B/F/TAF: Disposition Through Week 192



Reason for D/C, n*	25 (5%)
Participant decision	12
Lost to follow-up	9
AE	1
Death	1
Protocol violation	1
Noncompliance	1

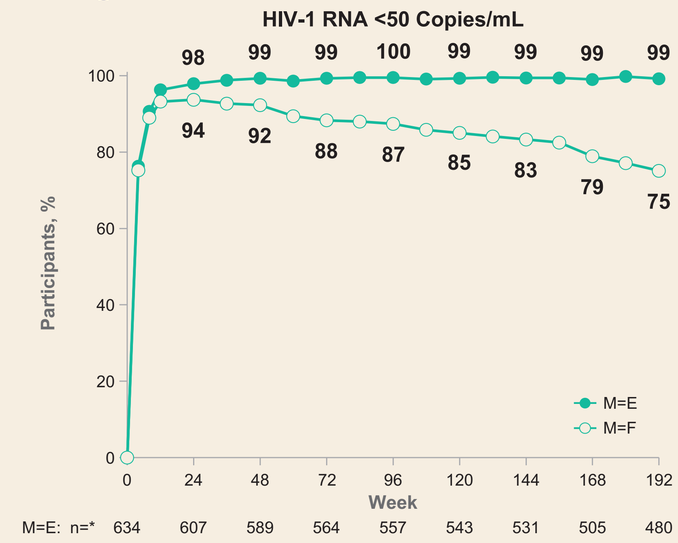
*In randomized phase, 115 participants prematurely discontinued (D/C) study drug: 6 (1%) due to adverse event (AE), 0 to lack of efficacy, and 109 (17%) to other reasons; of 506 who entered OLE, 25 prematurely D/C study drug: 1 (<1%) due to AE, 0 to lack of efficacy, and 24 (5%) to other reasons.

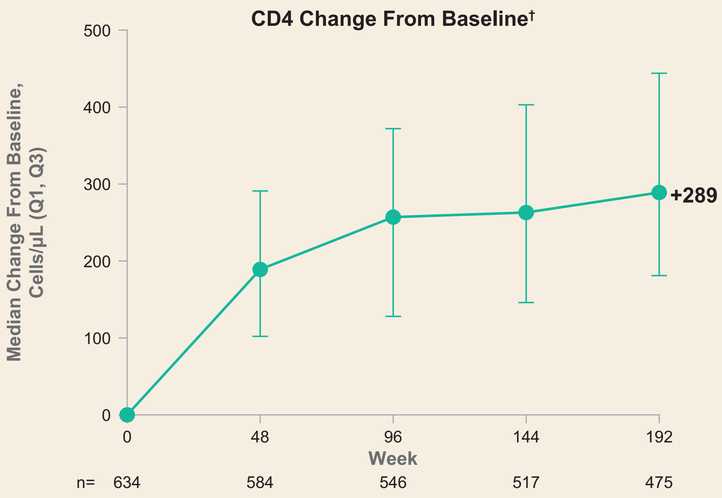
Baseline Characteristics

	Pooled B/F/TAF n=634
Median age, y (range)	32 (18–71)
Female at birth, n (%)	69 (11)
Race/ethnicity, n (%)	
Black or African descent	211 (33)
Hispanic/Latinx ethnicity	155 (24)
Median body weight, kg (Q1, Q3)	77 (68, 88)
Median body mass index, kg/m^2 (Q1, Q3)	25.1 (22.3, 28.6)
Median HIV-1 RNA, log_{10} copies/mL (Q1, Q3)	4.4 (4.0, 4.9)
HIV-1 RNA >100,000 copies/mL, n (%)	119 (19)
Median CD4 cells/μL (Q1, Q3)	442 (293, 590)
CD4 count <200 cells/μL, n (%)	80 (13)
Asymptomatic HIV infection, n (%)	572 (90)
Median $eGFR_{CG}$, mL/min (Q1, Q3)	122 (104, 143)

CD4, cluster of differentiation-4; Q, quartile.

Virologic Outcomes





*Participants with nonmissing HIV-1 RNA value; †While receiving B/F/TAF (observed data). M=E, missing=excluded; M=F, missing=failure.

- 99% of B/F/TAF participants maintained HIV-1 RNA <50 copies/mL (M=E at Week 192)
- At Week 192, 476 participants had HIV-1 RNA <50 copies/mL and 4 participants had HIV-1 RNA >50 copies/mL

Virologic Resistance

	All B/F/TAF			
Participants, n	Week 48	Week 96	Week 144	Week 192
Met criteria for resistance testing*	8	7	8	8
NRTI resistance detected	0	0	0	0
INSTI resistance detected	0	0	0	0

*Resistance testing performed for participants with confirmed HIV-1 RNA ≥50 copies/mL, with confirmation visit having ≥200 copies/mL or ≥200 copies/mL at last visit, without resuppression of HIV-1 RNA to <50 copies/mL while on study drug. INSTI, integrase strand transfer inhibitor; NRTI, nucleoside reverse-transcriptase inhibitor.

- No participant failed with resistance to any component of B/F/TAF

Treatment-Emergent Adverse Events Through Week 192

	B/F/TAF	
Participants, %	Overall: n=634 (baseline–Week 192)	OLE: n=506 (Week 144–192)
Any AE	94	70
AEs ≥10% overall		
Diarrhea	21	4
Headache	18	4
Nasopharyngitis	18	6
Upper respiratory tract infection	16	5
Syphilis	15	5
Arthralgia	13	3
Back pain	13	4
Nausea	13	3
Cough	13	5
Fatigue	11	2
Insomnia	10	2
Influenza	10	3
Any study drug-related AE	28	2
Study drug-related AEs ≥2% overall		
Headache	5	<1
Diarrhea	5	<1
Nausea	4	<1
Fatigue	3	<1
Dizziness	2	<1
Insomnia	2	0

Adverse Events Leading to Discontinuation Through Week 192*

	B/F/TAF: n=634
AEs leading to D/C Not related n=3 (<1%)	Cardiac arrest (Week 4; Day 28)
	Paranoia (Week 42; Day 299)
	Intervertebral discitis (Week 195; Day 1366)
AEs leading to D/C Study drug related n=4 (1%)	Chest pain (Week 0; Day 1)
	Abdominal distension (Week 0; Day 1)
	Sleep disorder, dyspepsia, and tension headache (Week 2; Day 15); depressed mood and insomnia (Week 9; Day 63)
	Depression (Week 48; Day 337)
Deaths n=6 (1%)	Cardiac arrest (Week 4; Day 28)
	Poorly differentiated gastric adenocarcinoma (Week 53; Day 376)
	Hypertensive heart disease (Week 58; Day 412)
	Self-inflicted wrist wound (Week 93; Day 656)
	Combined toxicity of chloroethane and methamphetamine (Week 110; Day 771)
	Sudden cardiac arrest (Week 151; Day 1060)

**Red shading* indicates AEs occurring during OLE.

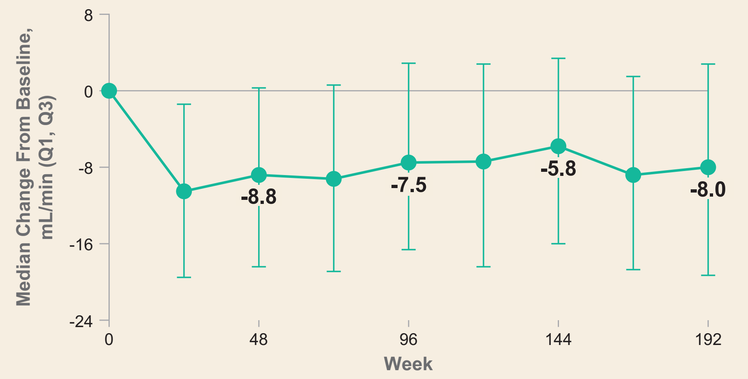
- Few AEs leading to B/F/TAF D/C were observed through 4 y of follow-up
- Only a small proportion of AEs leading to D/C occurred after Year 1

Laboratory Abnormalities Through Week 192

Participants, %	B/F/TAF n=634
Any Grade 3 or 4 laboratory abnormality	31
≥2%	
Increased creatine kinase*	10
Increased LDL (fasting)	5
Increased AST†	4
Increased ALT†	3
Decreased neutrophils	3
Increased amylase‡	3

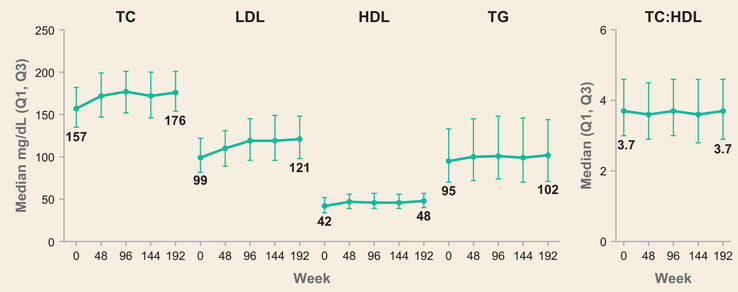
*Elevations asymptomatic, no cases of myositis, commonly occurred postexercise, and not deemed clinically significant; †No cases of drug-related hepatitis; ‡1 case of drug-related pancreatitis on Day 572 (resolved Day 574); participant did not D/C study drug. ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDL, low-density lipoprotein.

$eGFR_{CG}$ Changes



- No reported cases of proximal renal tubulopathy or D/Cs due to renal AEs were observed on B/F/TAF
- Initial decline followed by stable $eGFR_{CG}$ are consistent with inhibition of tubular creatinine secretion via organic cation transporter 2 by BIC

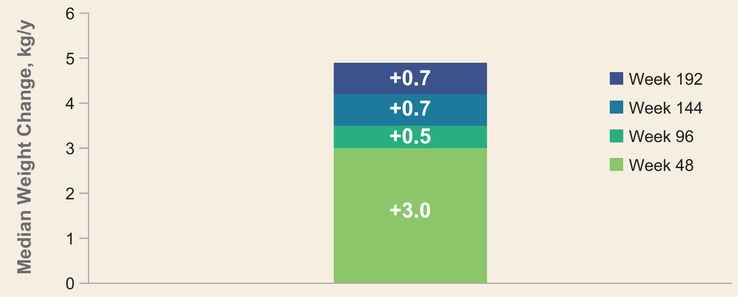
Fasting Lipid Changes



Participants, %	B/F/TAF: n=634
Taking lipid-lowering agents at baseline	5
Initiated lipid-lowering agents while on B/F/TAF	6

HDL, high-density lipoprotein; TC, total cholesterol; TG, triglycerides.

Weight Change



- Most of the weight change took place in the first year, followed by annual changes of +0.5–0.7 kg/y

Conclusions

- In treatment-naïve people living with HIV, through 4 y of follow-up among those originally randomized to B/F/TAF, we observed:
  - High rates of virologic suppression with no treatment-emergent resistance
  - Few AEs leading to D/C, no renal related D/Cs overall, and AEs were rare between Weeks 144 and 192
    - 9/634 participants (1%) experienced a treatment-emergent drug-related AE during the OLE
  - Small changes in lipid fractions, with minor change from baseline in TC:HDL ratio at Week 192
  - Weight gain of ~3 kg in the first year, followed by annual changes of +0.5–0.7 kg/y, consistent with data from previous studies in treatment-naïve populations, and similar to findings in the general population of increases in body mass index and weight of nearly 1 kg/y[9-17]
- These results confirm the long-term safety and efficacy of B/F/TAF

References: **1.** DHHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV; 12/18/19; **2.** EACS Guidelines Version 10.0 November 2019; **3.** Saag MS, et al. JAMA 2018;320:379-96; **4.** Gallant J, et al. Lancet 2017;390:2063-72; **5.** Orkin C, et al. Lancet HIV 2020;7:e389-400; **6.** Sax PE, et al. Lancet 2017;390:2073-82; **7.** Stellbrink H-J, et al. Lancet HIV 2019;6:e364-72; **8.** Wohl DA, et al. Lancet HIV 2019;6:e355-63; **9.** Hill JO, et al. Science 2003;299:853-5; **10.** Lakey W, et al. AIDS Res Hum Retroviruses 2013;29:435-40; **11.** Sax PE, et al. Clin Infect Dis 2020;71:1379-89; **12.** Sharma A, et al. PLoS One 2015;10:e0143740; **13.** Taramasso L, et al. Open Forum Infect Dis 2017;4:ofx239; **14.** Tate T, et al. Antivir Ther 2012;17:1281-9; **15.** WHO 2016. Centers for Disease Control and Prevention. Obesity and overweight. 2016; **16.** Workowski K, et al. CROI 2021, science spotlight 2268; **17.** Yuh B, et al. Clin Infect Dis 2015;60:1852-9.

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