EPB150

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

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Introduction

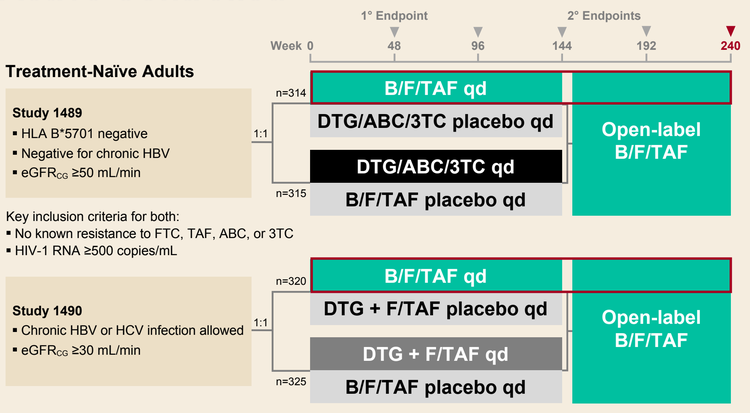
- Bictegravir (BIC)/emtricitabine (FTC)/tenofovir alafenamide (TAF; B/F/TAF) is a guidelines-recommended, single-tablet regimen for people living with HIV[1-3]
- B/F/TAF has a high barrier to resistance, favorable drug-drug interaction profile, and ability to be given once daily without food restrictions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

Objective

- To assess pooled outcomes from Studies 1489 and 1490 in participants initially randomized to B/F/TAF through Week 240 (end of study)

Methods

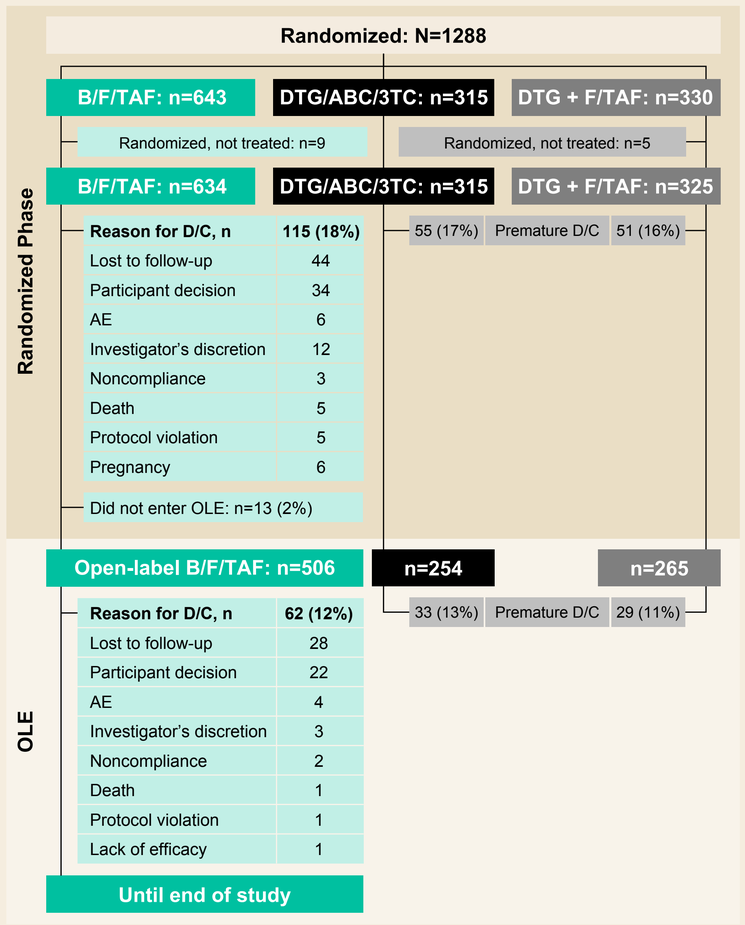
Study Designs: Randomized, Double Blind, Active Controlled



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 240



AE, adverse event; D/C, discontinuation.

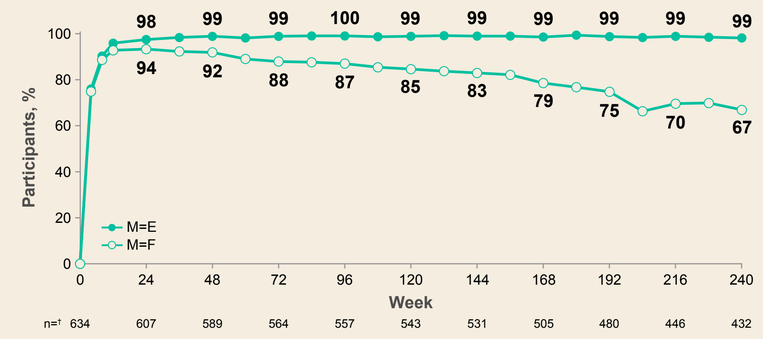
Baseline Characteristics

	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	155 (25)
Median body weight, kg (Q1, Q3)	77 (68, 88)
Median BMI, kg/m² (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)

*Baseline characteristics of participants who started open-label B/F/TAF (n=506) were similar to those of the randomized B/F/TAF population (n=634). BMI, body mass index; CD4, cluster of differentiation-4; Q, quartile.

Virologic Outcomes

HIV-1 RNA <50 Copies/mL*



*Calculated using U.S. Food and Drug Administration Snapshot algorithm; †Participants with nonmissing HIV-1 RNA value. M=E, missing = excluded; M=F, missing = failure.

- Using M=E, 99% of B/F/TAF participants maintained HIV-1 RNA <50 copies/mL
- At Week 240, 426 participants had HIV-1 RNA <50 copies/mL and 6 participants had HIV-1 RNA ≥50 copies/mL
- Median CD4 change from baseline at Week 240: +317 cells/µL

Virologic Failure at Week 240 (n=6)

Participant	% Adherence (blinded/ open label)*	Baseline HIV-1 RNA, Copies/mL	Baseline CD4, Cells/µL	Total B/F/TAF Duration, mo	HIV-1 RNA, Copies/mL	
					Week 240	Week 252
1	96/96	≤100,000	200–<350	61.2	897	<50
2	91/92	>100,000–400,000	200–<350	61.3	128	<50
3	99/99	≤100,000	350–<500	59.1	317	<50
4	93/93	>100,000–400,000	50–<200	59.0	53	<50
5	86/87	≤100,000	200–<350	59.2	141	<50
6†	99/98	>400,000	200–<350	53.9	133	Lost to follow-up

*Adherence measured by pill count; †Discontinued due to "lack of efficacy" before they were considered lost to follow-up.

- 5/6 participants resuppressed while maintaining B/F/TAF at Week 252; 1 was lost to follow-up after Week 240

Virologic Resistance Through Week 240

Participants, n	B/F/TAF: n=634
Met criteria for resistance testing*	9
NRTI resistance detected	0
INSTI resistance detected	0

*Final resistance analysis population included participants with confirmed HIV-1 RNA ≥200 copies/mL or ≥200 copies/mL at last visit, with no resuppression of HIV-1 RNA to <50 copies/mL while on study drug; includes only participants initially randomized to B/F/TAF. INSTI, integrase strand transfer inhibitor; NRTI, nucleos(t)ide reverse-transcriptase inhibitor.

- No resistance to any components of B/F/TAF occurred in any group of the final resistance analysis population

Treatment-Emergent Adverse Events Through Week 240

Participants, %		B/F/TAF Overall: n=634 (baseline–Week 240)	B/F/TAF OLE: n=506 (Weeks 144–240)
Any AE		95	82
AEs ≥10% overall	Diarrhea	22	4
	Headache	19	5
	Nasopharyngitis	18	7
	Upper respiratory tract infection	17	6
	Syphilis	17	8
	Arthralgia	14	6
	Back pain	14	7
	Nausea	13	3
	Cough	13	6
	Fatigue	11	2
	Anxiety	11	4
	Insomnia	11	3
	Influenza	10	4
	COVID-19	8	10
Any study drug-related AE		**28**	**4**
Study drug-related AEs ≥2% overall	**Headache**	**5**	**<1**
	Diarrhea	**5**	**<1**
	Nausea	**4**	**<1**
	Fatigue	**3**	**<1**
	Dizziness	**2**	**<1**
	Insomnia	**2**	**0**

- Overall AEs and study drug-related AEs were infrequent during OLE

Adverse Events Leading to Discontinuation Through Week 240*

	B/F/TAF: n=634
AEs leading to D/C Not related n=5 (<1%)	Cardiac arrest (Week 4; Day 28)
	Paranoia (Week 42; Day 299)
	Intervertebral discitis (Week 195; Day 1366)
	Toxicity to various agents (Week 221; Day 1549)†
	COVID-19 (Week 250; Day 1748)
AEs leading to D/C Study drug related n=5 (<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)
	Morbid obesity (Week 233; Day 1634)
Deaths n=9 (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)
	Toxicity to various agents (Week 221; Day 1549)†
	Unknown (Week 242; Day 1697)
	COVID-19 (Week 250; Day 1748)

Red shading indicates AEs occurring during OLE; †Amphetamine, methamphetamine, and fentanyl.

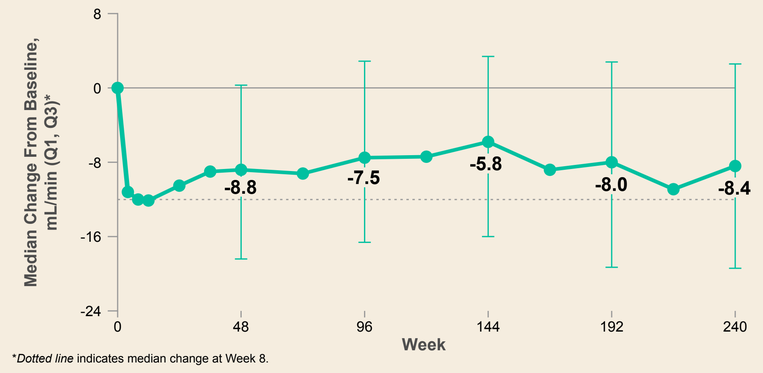
- Few participants (n=5) experienced a study drug-related AE leading to D/C through 5 y of follow up

Laboratory Abnormalities Through Week 240

Participants, %		B/F/TAF: n=634
Any Grade 3 or 4 laboratory abnormality		33
Grade 3 or 4 laboratory abnormalities in ≥2% of B/F/TAF group		
Increased creatine kinase*	10–<20x ULN	11
Increased LDL (fasting)	>190 mg/dL	6
Increased AST†	>5–10x ULN	4
Increased amylase‡	>2.0–5.0x ULN	4
Increased ALT†	>5–10x ULN	3
Decreased neutrophils	WBCs 1000–<1500/mm³	3
Increased TC (fasting)	>300 mg/dL	2
Urine RBC (hematuria)	>75 RBCs/HPF	2

*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; HPF, high-power field; LDL, low-density lipoprotein; RBC, red blood cell; TC, total cholesterol; ULN, upper limit of normal; WBCs, white blood cells.

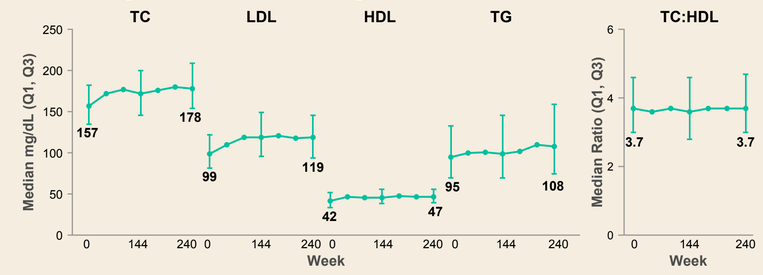
$eGFR_{CG}$ Changes



Dotted line indicates median change at Week 8.

- No cases of proximal renal tubulopathy or D/Cs due to renal AEs were observed with B/F/TAF
- Initial decline followed by stable $eGFR_{CG}$ is consistent with inhibition of tubular creatinine secretion via organic cation transporter-2 (OCT2) by BIC[9]

Fasting Lipids Changes

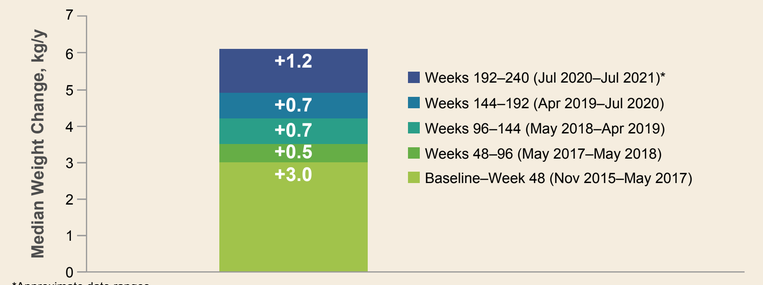


Participants, %	At Baseline	Week 48	Weeks 48–96*	Weeks 96–144*	Weeks 144–192*	Weeks 192–240*
Initiated lipid-lowering agents	5	2	2	1	2	<1

*Calculated as differences from Weeks 48 to 96, 96 to 144, 144 to 192, and 192 to 240. HDL, high-density lipoprotein; TG, triglycerides.

- Small changes in fasting lipids were observed from baseline to Week 240, with stable TC:HDL ratios and ≤2% of participants who initiated lipid-lowering agents by each subsequent year on study

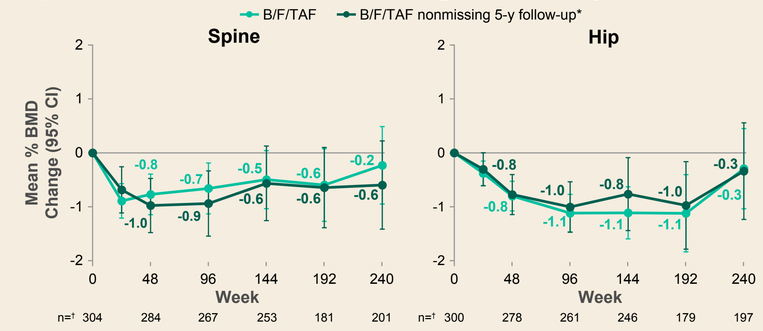
Weight Changes



*Approximate date ranges.

- Most of the weight change took place in the first year, followed by annual changes of +0.5–1.2 kg/y, consistent with previous observations in the general population[10]
- Weeks 192–240 occurred during the first 2 y of the COVID-19 pandemic, a period when accelerated weight gain has been reported[11]

Spine and Hip BMD Changes: Study 1489



*151 participants with spine and 147 with hip bone mineral density (BMD) data from baseline through Week 240; BMD measured by dual-energy x-ray absorptiometry in Study 1489 only; †Numbers of participants initially randomized to B/F/TAF. CI, confidence interval.

Conclusions

- In adults with HIV who initiated treatment with B/F/TAF and continued through 5 y of follow-up, we observed:
  - High rates of virologic suppression with no treatment-emergent resistance
  - <1% occurrence of study drug-related AEs leading to D/C and no renal-related D/Cs
  - Stable $eGFR_{CG}$ after an initial decline consistent with inhibition of tubular creatinine secretion via OCT2 by BIC and no cases of proximal renal tubulopathy
  - Small increases in fasting lipids and stable TC:HDL ratios with few participants initiating lipid-lowering agents
  - Median cumulative weight gain of 6.1 kg; ~3 kg in first 48 wk, followed by ~0.5–1.2 kg/y, consistent with annual weight gain data from previous studies in treatment-naïve populations[12-17] and the general population[10]
  - Minimal impact on the longitudinal trends of spine and hip BMD from baseline, validated by mean decreases that did not exceed 0.6% at Week 240 among participants with nonmissing data at all visits
- 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; 20 Jan 2022; **2.** EACS Guidelines Version 11.0 October 2021; **3.** Saag MS, et al. JAMA 2020;324:1651-69; **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.** Custodio JM, et al. IDWeek 2017, poster 1386; **10.** Hill JO, et al. Science 2003;299:853-5; **11.** Khubchandani J, et al. Diabetes Metab Syndr 2022;16:102392; **12.** Lakey W, et al. AIDS Res Hum Retroviruses 2013;29:435-40; **13.** Sax PE, et al. Clin Infect Dis 2020;71:1379-89; **14.** Sharma A, et al. PLoS One 2015;10:e0143740; **15.** Taramasso L, et al. Open Forum Infect Dis 2017;4:ofx239; **16.** Tate T, et al. Antivir Ther 2012;17:1281-9; **17.** Yuh B, et al. Clin Infect Dis 2015;60:1852-9.

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