B/F/TAF Five-Year Outcomes in Treatment-Naïve Adults

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Introduction

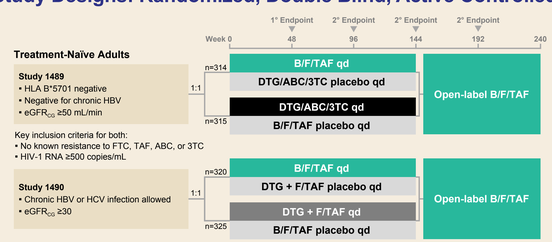
- B/F/TAF, the single-tablet coformulation of bictegravir (B; BIC), emtricitabine (F; FTC), and tenofovir alafenamide (TAF) is a guidelines-recommended regimen for people living with HIV[1-3]
- B/F/TAF has a high barrier to resistance, favorable drug-drug interaction profile, and ability to be given once daily without food restrictions
- Safety and efficacy through Week 144 have been demonstrated in two Phase 3 studies (GS-US-380-1489 [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 who completed 144 wk of the blinded treatment phase were given the opportunity to participate in an open-label extension (OLE) for an additional 96 wk

Objectives

- To assess 5-year outcomes (144 wk of blinded treatment plus 96 wk in OLE [aka Week 240]) from Studies 1489 and 1490
- The present analysis focuses on those participants originally randomized to B/F/TAF to gain further insight into long-term safety and efficacy

Methods

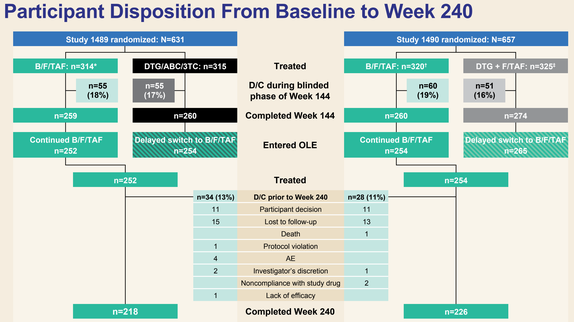
Study Designs: Randomized, Double Blind, Active Controlled



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

Participant Disposition From Baseline to Week 240



a2 participants randomized and not treated; †7 randomized and not treated; ‡5 randomized and not treated. AE, adverse event; D/C, premature discontinuation.

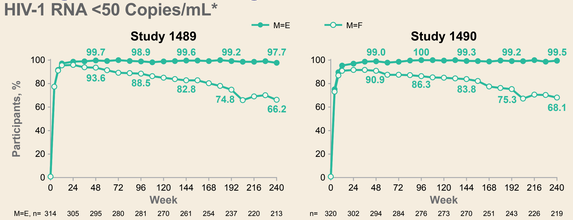
Characteristics at B/F/TAF Start*

	Study 1489 B/F/TAF: n=314	Study 1490 B/F/TAF: n=320
Median age, y (range)	31 (18–71)	33 (18–71)
Female sex at birth, n (%)	29 (9)	40 (13)
Race/ethnicity, n (%)		
Black or African descent	114 (37)	97 (30)
Hispanic/Latinx ethnicity	72 (23)	83 (26)
Median body weight, kg (IQR)	77 (68, 88)	76 (68, 87)
Median HIV-1 RNA, log_{10} copies/mL (IQR)	4.4 (4.0, 4.9)	4.4 (4.0, 4.9)
HIV-1 RNA >100,000 copies/mL, n (%)	53 (17)	66 (21)
Median CD4 cells/μL (IQR)	443 (299, 590)	440 (289, 591)
CD4 count <200 cells/μL, n (%)	36 (11)	44 (14)
Asymptomatic HIV infection, n (%)	286 (91)	286 (89)
Median $eGFR_{CG}$, mL/min (IQR)	126 (108, 146)	120 (101, 142)

*Includes only participants initially randomized to B/F/TAF. CD4, cluster of differentiation-4; IQR, interquartile range.

Virologic Outcomes Through Week 240

HIV-1 RNA <50 Copies/mL*



*Calculated using US FDA Snapshot algorithm; includes only participants initially randomized to B/F/TAF. M=E, missing = excluded; M=F, missing = failure.

- Efficacy was ≥98% (M=E) after Week 48 at each study visit through Week 240 in both studies for all participants
  - Among those with baseline CD4 <200 cells/μL from the pooled studies, 98% (49/50) had HIV-1 RNA <50 copies/mL at Week 240
- Median CD4 changes from B/F/TAF start to Week 240, cells/μL (IQR): Study 1489: +313 (179, 475); Study 1490: +331 (215, 467)

Virologic Resistance Through Week 240

Participants, n	Study 1489 B/F/TAF: n=314	Study 1490 B/F/TAF: n=320
Met criteria for resistance testing*	1	8
NRTI resistance detected	0	0
INSTI resistance detected	0	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

Adverse Events Through Week 240*

Participants, %	Study 1489 B/F/TAF: n=314	Study 1490 B/F/TAF: n=320
Any AE	97	93
>10% in either study		
Diarrhea	19	24
Headache	16	21
Nasopharyngitis	18	19
URTI	17	17
Syphilis	18	16
Arthralgia	14	14
Back pain	15	13
Cough	13	13
Nausea	14	11
Fatigue	13	9
Anxiety	14	8
Insomnia	11	11
Influenza	8	13
Pain in extremity	8	10
Rash	12	6
Oropharyngeal pain	10	8
Hypertension	10	7

*Includes only participants initially randomized to B/F/TAF. URTI, upper respiratory tract infection.

Adverse Events Through Week 240*

Study Drug-Related AEs

Participants, %	Study 1489 B/F/TAF: n=314	Study 1490 B/F/TAF: n=320
Any study drug-related AE†	32	24
Grade 3–4	1	2
>5% in either study		
Diarrhea	6	3
Headache	5	5
Nausea	5	3

AEs Leading to D/C‡

Study 1489 B/F/TAF: n=4/314 (1%)	Study 1490 B/F/TAF: n=6/320 (2%)
Intervertebral discitis (Day 1366)	*Chest pain* (Day 1)
Toxicity to various agents (Day 1549)	*Abdominal distension* (Day 1)
Obesity (Day 1634)	*Sleep disorder, dyspepsia, and tension headache* (Day 15); *depressed mood and insomnia* (Day 63)
COVID-19 (Day 1748)	Cardiac arrest (Day 28)
	Paranoia (Day 299)
	Depression (Day 337)

*Includes only participants initially randomized to B/F/TAF; †Mostly Grade 1 and rarely led to D/C; ‡*Italics* indicate AEs considered study drug related by investigator; *red shading* indicates events that occurred after Week 192; *each row* represents 1 participant.

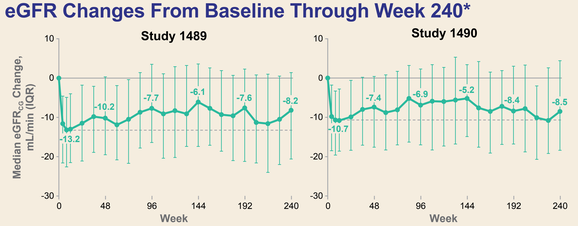
- Few participants (n=5) experienced a study drug-related AE that led to D/C

Laboratory Abnormalities Through Week 240*

Participants, %	Study 1489 B/F/TAF: n=314	Study 1490 B/F/TAF: n=320
Any Grade 3/4 laboratory abnormality	34	32
Grade 3/4 laboratory abnormalities ≥3% in either group		
Increased creatine kinase†	12	10
Increased LDL (fasting)	6	5
Increased AST‡	5	3
Increased amylase§	4	4
Increased ALT‡	3	4
Decreased neutrophils	3	4

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

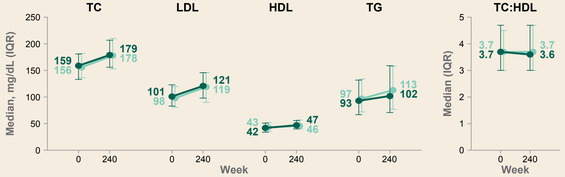
eGFR Changes From Baseline Through Week 240*



*Includes only participants initially randomized to B/F/TAF; *dotted lines* indicate median changes at Week 8.

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

Fasting Lipid Changes Through Week 240*

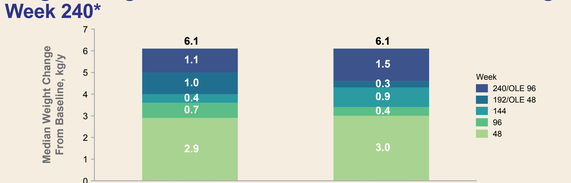


Participants on Lipid-Lowering Agents, %	At Baseline	Initiated				
		Week 48	Weeks 48–96†	Weeks 96–144†	Weeks 144–192†	Weeks 192–240†
Study 1489: n=314	4	3	2	1	2	1
Study 1490: n=320	7	2	2	1	2	1

*Includes only participants initially randomized to B/F/TAF; †Calculated as differences from Weeks 48 to 96, 96 to 144, 144 to 192, and 192 to 240. HDL, high-density lipoprotein; TC, total cholesterol; TG, triglycerides.

- Small changes in lipids were observed among participants randomized to B/F/TAF over 5 y, with stable TC:HDL ratios, and small numbers of participants who initiated lipid-lowering agents between baseline and Week 240

Weight Changes From Randomized Phase Baseline Through Week 240*

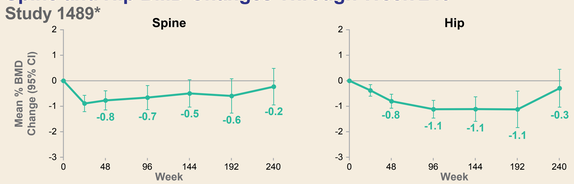


*Includes only participants initially randomized to B/F/TAF.

- Median cumulative weight gain from baseline to Week 240 was 6.1 kg for participants initially randomized to B/F/TAF
- Weight gains after Week 48 are consistent with what is seen in the general population[10]

Spine and Hip BMD Changes Through Week 240

Study 1489*



*Includes only participants initially randomized to B/F/TAF; bone mineral density (BMD) measured by dual-energy x-ray absorptiometry in Study 1489 only. CI, confidence interval.

Conclusions

- In treatment-naïve people living with HIV through 5 y of follow-up among those originally randomized to B/F/TAF, we observed:
  - High rates of virologic suppression with no treatment-emergent resistance in the final resistance analysis population
  - ≤1% occurrence of study drug-related AEs leading to D/C and no renal-related D/Cs
  - Stable $eGFR_{CG}$ after organic cation transporter-2–related initial declines and no reported cases of proximal renal tubulopathy
  - Small changes in fasting lipids, with stable TC:HDL ratios and few participants initiating lipid-lowering agents
  - Median cumulative weight gain of 6.1 kg; ~3 kg in first 48 wk, followed by ~0.3–1.5 kg/y, consistent with data from previous studies in treatment-naïve populations[11-16]
    - Weight gains after Week 48 are consistent with what is seen in the general population[10]
  - Minimal impact on longitudinal trends of spine and hip BMD from baseline, with mean decreases that did not exceed 0.29% at Week 240
- 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.** Custodio JM, et al. IDWeek 2017, poster 1386; **10.** Hill JO, et al. Science 2003;299:853-5; **11.** Lakey W, et al. AIDS Res Hum Retroviruses 2013;29:435-40; **12.** Sax PE, et al. Clin Infect Dis 2020;71:1379-89; **13.** Sharma A, et al. PLoS One 2015;10:e0143740; **14.** Taramasso L, et al. Open Forum Infect Dis 2017;4:ofx230; **15.** Tate T, et al. Antivir Ther 2012;17:1281-9; **16.** Yuh B, et al. Clin Infect Dis 2015;60:1852-9. **Acknowledgments:** We extend our thanks to the participants, their partners and families, and all 1489 and 1490 investigators. Special thanks to the 1489 and 1490 study teams. These studies were funded by Gilead Sciences, Inc. Editorial and production assistance were provided by BioScience Communications, New York, NY, funded by Gilead.