2268

Four-Year Outcomes of B/F/TAF in Treatment-Naïve Adults

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Introduction

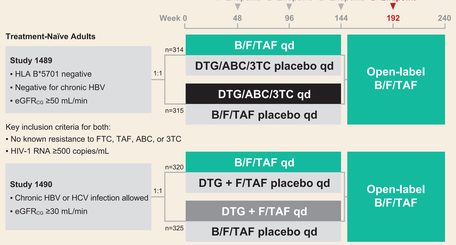
- Bictegravir (B; BIC), emtricitabine (F; FTC), and tenofovir alafenamide (TAF; B/F/TAF) is a guidelines-recommended, single-tablet regimen for people living with HIV[1-3]
- B/F/TAF has a high barrier to resistance, favorable drug-drug interaction profile, and ability to be given once daily without food restrictions
- Safety and efficacy through Week 144 have been demonstrated in two Phase 3 studies (GS-US-380-1489 [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

Objective

- To assess 4-y outcomes (Week 48 of the OLE phase/Week 192) from Studies 1489 and 1490

Methods

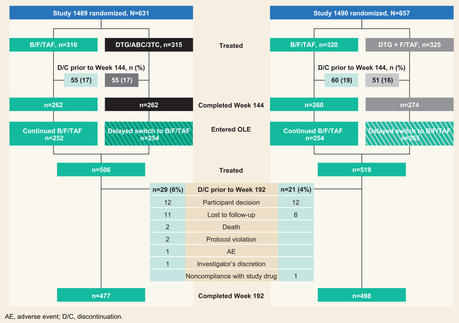
Study Designs: Randomized, Double Blind, Active Controlled



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 192



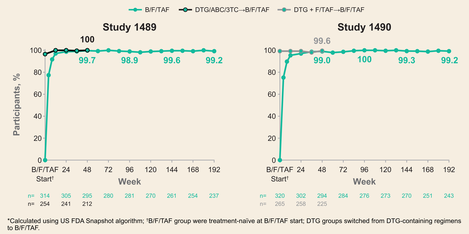
AE, adverse event; D/C, discontinuation.

Characteristics at B/F/TAF Start

	Study 1489		Study 1490	
	B/F/TAF n=314	DTG/ABC/3TC to B/F/TAF n=254	B/F/TAF n=320	DTG + F/TAF to B/F/TAF n=266
Median age, y (range)	31 (18–71)	36 (22–71)	33 (19–71)	39 (21–80)
Female at birth, n (%)	29 (9)	29 (11)	40 (13)	26 (10)
Race/ethnicity, n (%)				
Black or African descent	114 (36)	94 (37)	97 (30)	80 (30)
Hispanic/Latinx ethnicity	72 (23)	54 (21)	83 (26)	73 (28)
Median body weight, kg (IQR)	77 (68, 88)	83 (73, 94)	76 (68, 87)	82 (71, 96)
Median HIV-1 RNA, $\log_{10}$ copies/mL (IQR)	4.4 (4.0, 4.9)	1.9 (1.5, 3.7)	4.4 (4.0, 4.9)	1.7 (1.4, 3.9)
HIV-1 RNA >100,000 copies/mL, n (%)	53 (17)	3 (1)	66 (21)	0
Median CD4 cells/μL (IQR)	443 (299, 590)	766 (599, 1023)	440 (289, 591)	730 (550, 958)
CD4 count <200 cells/μL, n (%)	36 (11)	0	44 (14)	3 (1)
Asymptomatic HIV infection, n (%)	286 (91)	229 (90)	286 (89)	234 (88)
Median eGFR$_{CG}$, mL/min (IQR)	126 (108, 146)	116 (99, 138)	120 (101, 142)	111 (95, 135)

CD4, cluster of differentiation-4; IQR, interquartile range.

Virologic Outcomes Through Week 192 on B/F/TAF
HIV-1 RNA <50 Copies/mL, Missing = Excluded*



*Calculated using US FDA Snapshot algorithm; †B/F/TAF group were treatment-naive at B/F/TAF start; DTG groups switched from DTG-containing regimens to B/F/TAF.

- Efficacy was ≥98% after Week 48 at each study visit through Week 192 in both studies for all participants
- HIV-1 RNA <50 copies/mL was maintained in participants who switched from DTG-containing regimens to B/F/TAF at Weeks 144–192

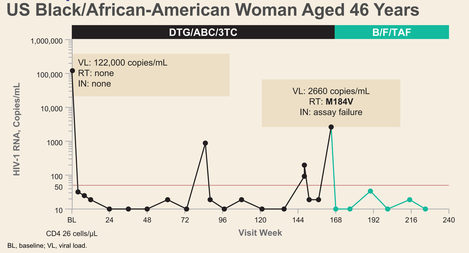
Virologic Resistance Through Week 192

	Week 144 to Unblinding				OLE B/F/TAF			
	Study 1489		Study 1490		Study 1489		Study 1490	
Participants, n	B/F/TAF n=263	DTG/ABC/3TC n=269	B/F/TAF n=266	DTG + F/TAF n=261	B/F/TAF n=252	DTG/ABC/3TC to B/F/TAF n=254	B/F/TAF n=254	DTG + F/TAF to B/F/TAF n=245
Met criteria for resistance testing*	0	4[†]	0	1	0	1	0	1
NRTI resistance detected	0	1 (M184V)[‡]	0	0	0	0	0	0
INSTI resistance detected	0	0	0	0	0	0	0	0

*Resistance testing performed for 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; †1 DTG/ABC/3TC participant was missing data at final virologic failure time point; ‡1 DTG/ABC/3TC participant developed M184V and had assay failure for integrase (IN). INSTI, IN strand transfer inhibitor; NRTI, nucleoside reverse-transcriptase (RT) inhibitor.

- No resistance to any components of B/F/TAF occurred in any group

Participant With Resistance
US Black/African-American Woman Aged 46 Years



BL, baseline; VL, viral load.

Adverse Events Through Week 192*

Participants, %		Study 1489 B/F/TAF: n=314	Study 1490 B/F/TAF: n=320
Any AE		96	92
>10% in either group	Diarrhea	19	23
	Headache	16	20
	Nasopharyngitis	17	18
	URTI	16	15
	Syphilis	15	14
	Nausea	14	11
	Arthralgia	13	13
	Cough	13	12
	Back pain	13	12
	Fatigue	12	9
	Anxiety	11	6
	Rash	11	5
	Insomnia	11	10
	Influenza	8	11
Any study drug-related AE		32	24
>5% in either group	Headache	5	5
	Diarrhea	6	3
	Nausea	5	3

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

- Participants who switched from DTG/ABC/3TC or DTG + F/TAF to B/F/TAF experienced similar AEs as in all B/F/TAF groups

Adverse Events Leading to Discontinuation Through Week 192*

AEs Leading to D/C		Deaths	
Study 1489: B/F/TAF n=314	Study 1490: B/F/TAF n=320	Study 1489: B/F/TAF n=314	Study 1490: B/F/TAF n=320
n=1 (<1%)	n=6 (2%)	n=2 (<1%)	n=4 (1%)
Intervertebral discitis (Day 1366)	Cardiac arrest (Day 28)	Combined toxicity of chloroethane and methamphetamine (Day 771)	Cardiac arrest (Day 28)
	Paranoia (Day 299)	Self-inflicted wrist wound (Day 656)	Poorly differentiated gastric adenocarcinoma (Day 376)
	Chest pain (Day 1)		Sudden cardiac arrest (Day 1060)
	Depression (Day 337)		Hypertensive heart disease (Day 412)
	Abdominal distension (Day 1)		
	Sleep disorder, dyspepsia, and tension headache (Day 15); *depressed mood and insomnia* (Day 63)		

*Italics indicate AEs considered study drug-related by investigator; *red shading* indicates AEs that occurred after Week 144.

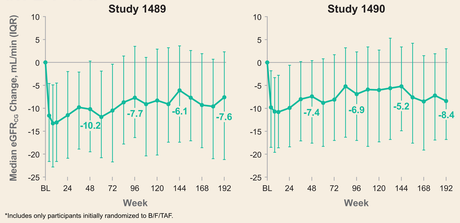
- 1 participant (<1%) who switched from DTG/ABC/3TC to B/F/TAF and 1 (<1%) who switched from DTG + F/TAF to B/F/TAF experienced an AE that led to D/C

Laboratory Abnormalities Through Week 192*

Participants, %	Study 1489 B/F/TAF: n=314	Study 1490 B/F/TAF: n=320
Any Grade 3 or 4 laboratory abnormality ≥3%	32	29
Increased lipase	20	3
Increased creatine kinase	11	9
Increased LDL (fasting)	5	5
Increased AST	5	3
Increased ALT	3	3
Decreased neutrophils	3	3
Increased amylase	3	3

*Includes only participants initially randomized to B/F/TAF. ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDL, low-density lipoprotein.

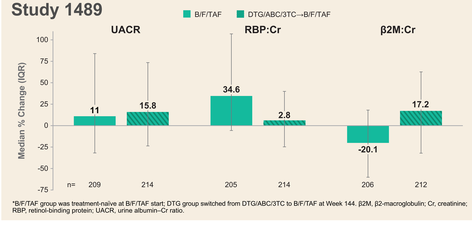
eGFR Changes From Baseline Through Week 192 on B/F/TAF*



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

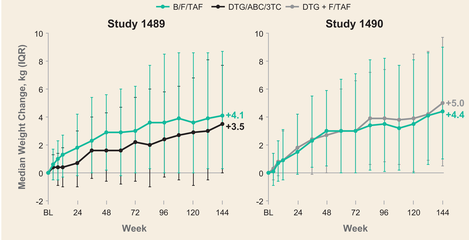
- No reported cases of proximal renal tubulopathy or D/C due to renal AEs were observed on B/F/TAF
- Changes in eGFR$_{CG}$ are consistent with inhibition of tubular creatinine secretion via organic cation transporter-2 by BIC

Renal Biomarker Changes Through Week 192 on B/F/TAF*
Study 1489

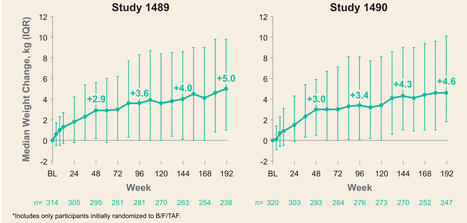


*B/F/TAF group was treatment-naïve at B/F/TAF start; DTG group switched from DTG/ABC/3TC to B/F/TAF at Week 144. β2M, β2-macroglobulin; Cr, creatinine; RBP, retinol-binding protein; UACR, urine albumin–Cr ratio.

Weight Changes From Baseline Through Week 144 of Blinded Phase



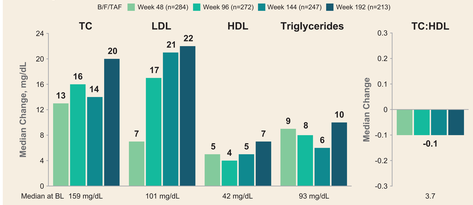
Weight Changes From Baseline Through Week 192 on B/F/TAF*



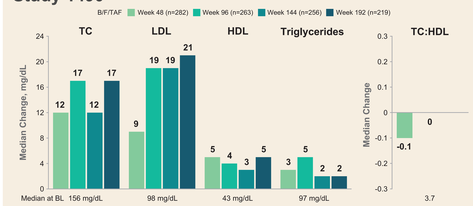
*Includes only participants initially randomized to B/F/TAF.

- Median weight change for participants who switched from a DTG-based regimen and subsequently received 48 wk of B/F/TAF, kg (IQR): DTG/ABC/3TC to B/F/TAF, +2.4 (-0.3, 4.7); DTG + F/TAF to B/F/TAF, +1.1 (-1.3, 3.9)

Fasting Lipid Changes Through Week 192 on B/F/TAF*
Study 1489



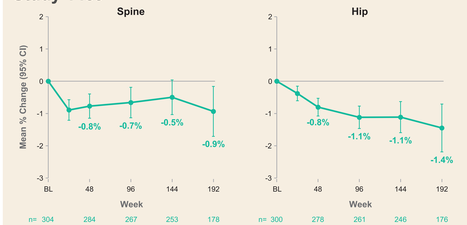
Study 1490



Participants, %	Study 1489 B/F/TAF n=314	Study 1490 B/F/TAF n=320
Taking lipid-lowering agents at B/F/TAF start	4	7
Initiated lipid-lowering agents while on B/F/TAF	7	6

*Includes only participants initially randomized to B/F/TAF. HDL, high-density lipoprotein; TC, total cholesterol.

Spine and Hip BMD Changes Through Week 192 on B/F/TAF*
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 4 years 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 and no renal related D/Cs
  - Weight gain of ~3 kg in first 48 wk, followed by approximately 1 kg/year, consistent with data from previous studies in treatment-naïve populations[9-14]
  - Small declines in spine and hip BMD from BL, with mean change of ≤ -1.4% over 4 years of treatment
- 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.** Lakey W, et al. AIDS Res Hum Retroviruses 2013;29:435-40; **10.** Sax PE, et al. Clin Infect Dis 2020;71:1379-89; **11.** Sharma A, et al. PLoS One 2015;10:e0143740; **12.** Taramasso L, et al. Open Forum Infect Dis 2017;4:ofx239; **13.** Tebe T, et al. Antivir Ther 2012;17:1281-9; **14.** 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 GS-US-380-1489 and GS-US-380-1490 investigators. Special thanks to the 1489 and 1490 study teams. These studies were funded by Gilead Sciences, Inc.