144-Week Efficacy and Safety of B/F/TAF in Treatment-Naive Adults Age ≥50 Years

Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404
800-445-3235

Anthony Mills,[1] Samir K. Gupta,[2] Cynthia Brinson,[3] Kimberly Workowski,[4] Amanda Clarke,[5] Andrea Antinori,[6] Jeffrey L. Stephens,[7] Ellen Koenig,[8] Jose R. Arribas,[9] David M. Asmuth,[10] Douglas Ward,[11] Jürgen K. Rockstroh,[12] Hailin Huang,[13] Hal Martin,[13] Diana M. Brainard[13]

[1]Men's Health Foundation, West Hollywood, CA; [2]Indiana University School of Medicine, Indianapolis, IN; [3]Central Texas Clinical Research, Austin, TX; [4]Emory University, Atlanta, GA; [5]Brighton & Sussex University Hospitals NHS Trust, Brighton, UK; [6]Lazzaro Spallanzani Istituto Nazionale Malattie Infettive, Roma, Italy; [7]Mercer University, Macon, GA; [8]Instituto Dominicano de Estudios Virológicos, Santo Domingo, Dominican Republic; [9]Hospital Universitario La Paz, Madrid, Spain; [10]University of California, Davis; [11]Dupont Circle Physicians Group, Washington, DC; [12]Universitätsklinikums Bonn, Germany; [13]Gilead Sciences, Inc., Foster City, CA

Introduction

- Nearly half of people living with HIV in the USA and Europe are age ≥50 y, and that proportion is expected to grow[1,2]
- Identifying highly effective and safe antiretroviral regimens in the context of medical comorbidities and drug-drug interactions is important in older adults
- The single-tablet regimen bictegravir, emtricitabine, and tenofovir alafenamide (B/F/TAF) is a guidelines-recommended regimen, with demonstrated safety, efficacy, and a high barrier to resistance[3-5]
- B/F/TAF may be a beneficial option for older adults due to its safety, tolerability, and relative lack of drug interactions

Objective

- To compare Week 144 results pooled from two Phase 3 studies of B/F/TAF compared with dolutegravir (DTG)–containing regimens in treatment-naïve adults age ≥ vs <50 y

Methods

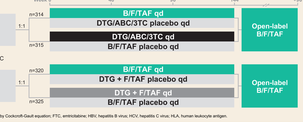
Study Designs: Randomized, Double Blind, Active Controlled

Treatment-Naive Adults

Study 1489 (NCT02607930)
- HLA B*5701 negative
- Negative for chronic HBV
- eGFR$_{CG}$ ≥50 mL/min

Study 1490 (NCT02607956)
- Chronic HBV or HCV infection allowed
- eGFR$_{CG}$ ≥30 mL/min

Key inclusion criteria for both:
- No known resistance to FTC, TAF, ABC, or 3TC
- HIV-1 RNA ≥500 copies/mL



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

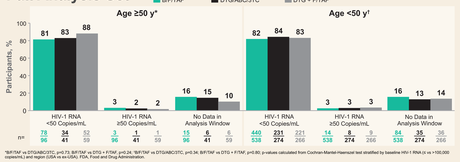
Results

Baseline Characteristics

	Age ≥50 y (n=196)			Age <50 y (n=1078)		
	B/F/TAF n=96	DTG/ABC/3TC n=41	DTG + F/TAF n=59	B/F/TAF n=538	DTG/ABC/3TC n=274	DTG + F/TAF n=266
Median age, y (range)	55 (50–71)	54 (50–68)	54 (50–77)	30 (18–49)	30 (18–49)	31 (18–49)
Male, %	84	73	86	90	92	89
Race/ethnicity, %						
Black or African descent	32	27	20	34	37	33
Hispanic/Latino ethnicity	11	15	20	27	22	26
Median HIV-1 RNA, log$_{10}$ copies/mL (IQR)	4.48 (4.00–4.83)	4.27 (3.74–5.01)	4.45 (3.90–4.92)	4.41 (4.00–4.86)	4.53 (4.06–4.85)	4.45 (4.04–4.83)
HIV-1 RNA >100,000 copies/mL, %	24	27	20	18	14	16
Median CD4 cells/µL (IQR)	436 (235–601)	534 (291–741)	405 (229–610)	442 (299–590)	444 (331–599)	447
CD4 count <200 cells/µL, %	20	12	15	11	10	9
Asymptomatic HIV infection, %	90	83	80	90	92	91
Median eGFR$_{CG}$, mL/min (IQR)	99 (84–114)	102 (83–131)	104 (84–122)	126 (109–147)	125 (110–146)	125 (106–152)

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

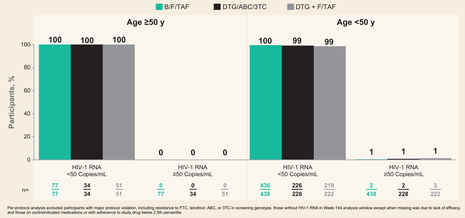
Virologic Outcomes at Week 144: FDA Snapshot
Full Analysis Set



*B/F/TAF vs DTG/ABC/3TC, p=0.73; B/F/TAF vs DTG + F/TAF, p=0.24; †B/F/TAF vs DTG/ABC/3TC, p=0.34; B/F/TAF vs DTG + F/TAF, p=0.80. p-values calculated from Cochran-Mantel-Haenszel test stratified by baseline HIV-1 RNA (≤ vs >100,000 copies/mL) and region (USA vs ex-USA). FDA, Food and Drug Administration.

- There were no significant differences in efficacy between B/F/TAF and comparators in the age ≥ and <50-y subgroups

Virologic Outcomes at Week 144: FDA Snapshot
Per-Protocol Analysis Set



Per-protocol analysis excluded participants with major protocol violation, including resistance to FTC, tenofovir, ABC, or 3TC in screening genotype, those without HIV-1 RNA in Week 144 analysis window except when missing was due to lack of efficacy, and those on contraindicated medications or with adherence to study drug below 2.5th percentile.

- There were no differences in efficacy between B/F/TAF and comparators in the age ≥ and <50-y subgroups in the per-protocol analysis of participants on study drug with HIV-1 RNA results in the analysis window

Virologic Resistance at Week 144: All Ages

	Overall (all ages)		
	B/F/TAF n=634	DTG/ABC/3TC n=315	DTG + F/TAF n=325
Met criteria for resistance testing*	8†	6‡	7‡
Assay failure	0	0	0
NRTI resistance detected	0	0	0
INSTI resistance detected	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 participant in B/F/TAF group, 1 in DTG/ABC/3TC group, and 1 in DTG + F/TAF group were age ≥50 y. INSTI, integrase strand transfer inhibitor; NRTI, nucleoside reverse-transcriptase inhibitor.

- No resistance to any components of the treatment regimens occurred in any treatment group

Adverse Events Through Week 144

All Grades, % ≥10% in Any Overall Group	Age ≥50 y			Age <50 y		
	B/F/TAF n=96	DTG/ABC/3TC n=41	DTG + F/TAF n=59	B/F/TAF n=538	DTG/ABC/3TC n=274	DTG + F/TAF n=266
Nasopharyngitis	20	22	25	13	16	18
Diarrhea	19	22	8	19	18	18
URTI	16	17	12	13	19	17
Back pain	15	17	12	9	11	12
Nausea	11	10	5	11	26	15
Syphilis	10	12	8	12	16	10
Headache	6	15	10	17	18	19
Fatigue	7	7	7	10	13	12
Insomnia	6	12	5	9	11	8
Oropharyngeal pain	1	10	3	7	11	6

URTI, upper respiratory tract infection.

Study Drug-Related Adverse Events Through Week 144

All Grades, % ≥5% in Any Group	Age ≥50 y			Age <50 y		
	B/F/TAF n=96	DTG/ABC/3TC n=41	DTG + F/TAF n=59	B/F/TAF n=538	DTG/ABC/3TC n=274	DTG + F/TAF n=266
Diarrhea	4	10	3	5	3	3
Nausea	5	7	2	4	19	6
Headache	4	0	0	5	6	4
Flatulence	2	0	5	<1	<1	2
Hypercholesterolemia	2	0	5	<1	0	0

Adverse Events Leading to Discontinuation Through Week 144

Age ≥50 y			Age <50 y		
B/F/TAF n=96	DTG/ABC/3TC n=41	DTG + F/TAF n=59	B/F/TAF n=538	DTG/ABC/3TC n=274	DTG + F/TAF n=266
n=2 (2%)	n=2 (5%)	n=4 (7%)	n=4 (1%)	n=3 (1%)	n=2 (1%)
Cardiac arrest (Day 28)	Steatorrhea* (Day 134)	Erythema and pruritus (Day 112)	Dyspepsia,* tension headache,* depressed mood,* insomnia,* and sleep disorder* (Day 65)	Nausea* and generalized rash* (Day 4)	Supraventricular tachycardia (Day 597)
Atypical chest pain* (Day 31)	Renal failure (Day 621)	Depression* (Day 420)			
		Lipoatrophy* (Day 464)	Paranoia (Day 302)	Thrombocytopenia* (Day 50)	Large B-cell lymphoma (Day 1009)
		Depression* (Day 532)	Abdominal distension* (Day 304)	Depression* (Day 248)	
			Depression* (Day 337)		

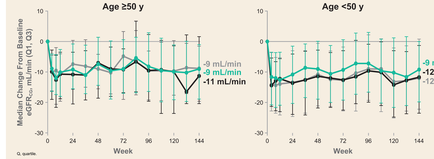
*Considered study drug-related by investigator.

Laboratory Abnormalities Through Week 144

Grade 3 or 4, % ≥3% in Any Group	Age ≥50 y			Age <50 y		
	B/F/TAF n=96	DTG/ABC/3TC n=41	DTG + F/TAF n=59	B/F/TAF n=538	DTG/ABC/3TC n=274	DTG + F/TAF n=266
Any Grade 3 or 4 lab abnormality	26	29	27	25	25	22
Decreased neutrophils	2	5	0	3	4	2
Increased AST	2	0	2	4	4	3
Increased creatine kinase	0	2	0	8	8	5
Increased amylase*	3	2	7	3	5	3
Fasting LDL increased	5	12	12	4	4	5
Fasting hyperglycemia	3	5	8	<1	<1	3
Glycosuria†	3	7	7	<1	<1	3
Nonfasting hyperglycemia	2	0	3	<1	<1	1

*Adverse events of pancreatitis (acute or chronic) reported in B/F/TAF: age ≥50 y (n=2) and <50 y (n=1), DTG/ABC/3TC: ≥50 y (n=1) and <50 y (n=1), and DTG + F/TAF: ≥50 y (n=2) and <50 y (n=1). †Includes diabetes and hyperglycemia; glycosuria, no participant had normoglycemic glycosuria. AST, aspartate aminotransferase; LDL, low-density lipoprotein.

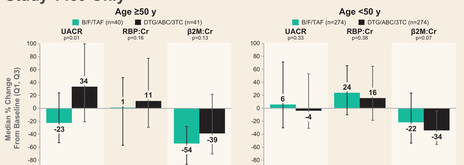
Changes From Baseline in eGFR$_{CG}$ Through Week 144



Q, quartile.

- No discontinuations due to renal adverse events in B/F/TAF or DTG + F/TAF groups
- 1 discontinuation due to renal failure in DTG/ABC/3TC group, but not related to study drug
- No reported cases of proximal renal tubulopathy in any group
- Changes in eGFR$_{CG}$ are consistent with inhibition of tubular creatinine secretion via organic cation transporter-2 by DTG and BIC

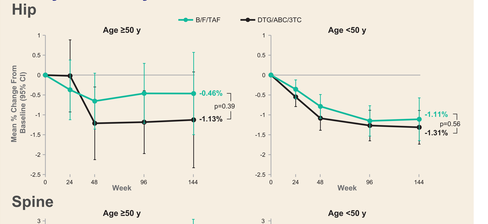
Changes From Baseline in Renal Biomarkers: Week 144
Study 1489 Only



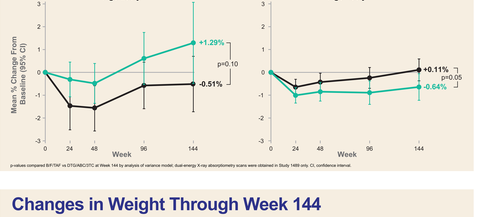
Difference in % change from baseline for each marker tested between treatment groups by Wilcoxon rank-sum test. β2M:Cr, β2-microglobulin:creatinine; RBP:Cr, retinol-binding protein:creatinine; UACR, urine albumin:creatinine.

Changes in Bone Mineral Density Through Week 144: Study 1489 Only

Hip

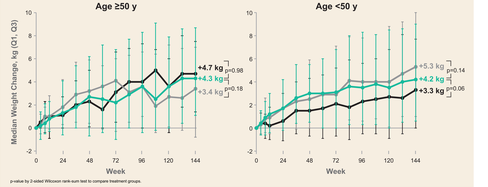


Spine



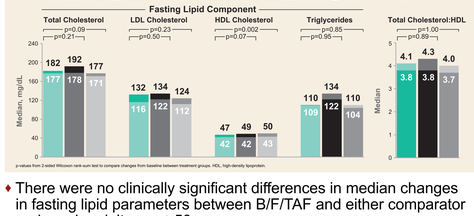
p-values compared B/F/TAF vs DTG/ABC/3TC at Week 144 by analysis of variance model; dual-energy X-ray absorptiometry scans were obtained in Study 1489 only. CI, confidence interval.

Changes in Weight Through Week 144



p-value by 2-sided Wilcoxon rank-sum test to compare treatment groups.

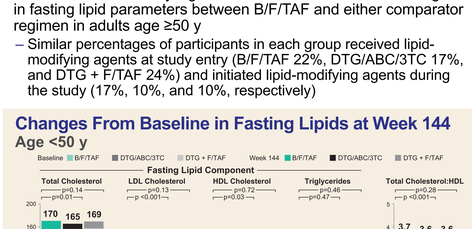
Changes From Baseline in Fasting Lipids at Week 144
Age ≥50 y



p-values from 2-sided Wilcoxon rank-sum test to compare changes from baseline between treatment groups. HDL, high-density lipoprotein.

- There were no clinically significant differences in median changes in fasting lipid parameters between B/F/TAF and either comparator regimen in adults age ≥50 y
  - Similar percentages of participants in each group received lipid-modifying agents at study entry (B/F/TAF 22%, DTG/ABC/3TC 17%, and DTG + F/TAF 24%) and initiated lipid-modifying agents during the study (17%, 10%, and 10%, respectively)

Changes From Baseline in Fasting Lipids at Week 144
Age <50 y



p-values from 2-sided Wilcoxon rank-sum test to compare changes from baseline between treatment groups.

- No clinically relevant changes from baseline were noted for fasting lipid parameters in the overall population
  - Similar percentages of participants in each group received lipid-modifying agents at study entry (B/F/TAF 2%, DTG/ABC/3TC 0%, and DTG + F/TAF 2%) and initiated lipid-modifying agents during the study (3%, 4%, and 4%, respectively)

Conclusions

- B/F/TAF was noninferior to either DTG-based regimen at Week 144
- Efficacy in adults age ≥50 y was comparable across regimens and similar to adults age <50 y
  - 20% of adults age ≥50 y in the B/F/TAF arm had baseline CD4 count <200 cells/µL
- No treatment-emergent resistance was observed in any treatment arm
- There were few adverse events leading to discontinuations
  - Adverse events were comparable between adults age ≥ and <50 y
  - There were no renal related discontinuations for participants on B/F/TAF or DTG + F/TAF
- Changes from baseline in bone mineral density were comparable between B/F/TAF and DTG/ABC/3TC in adults age ≥50 y and similar to changes in those age <50 y
- Changes in eGFR$_{CG}$ occurred early and were stable through Week 144, consistent with inhibition of tubular creatinine secretion by DTG and BIC
- There were no clinically significant differences in median changes from baseline in fasting lipids in participants age ≥50 y

References: 1. Centers for Disease Control and Prevention. https://www.cdc.gov/hiv/group/age/olderamericans/. 9/18; 2. Tavoschi L, et al. Lancet HIV 2017;4:e514-21; 3. AIDSinfo. https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/0. 12/19; 4. EACS Guidelines Version 10.0 November 2019. https://www.eacsociety.org/files/2019_guidelines-10.0_final.pdf; 5. Saag MS, et al. JAMA 2018;320:379-96. **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.