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

Video Link

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Introduction

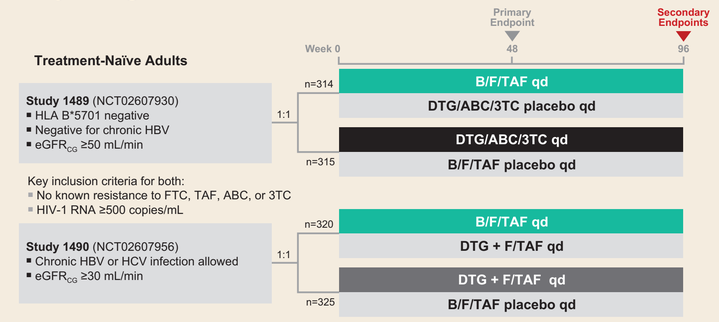
- Nearly half of people living with HIV in the USA and Europe are aged ≥50 y, and that proportion is expected to grow as people age on antiretroviral therapy[1,2]
- Identifying highly effective and safe antiretroviral regimens in the context of medical comorbidities and drug-drug interactions is of heightened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

Objective

- To compare the long-term safety and efficacy of B/F/TAF vs dolutegravir (DTG)-containing regimens in treatment-naive adults and the subset aged ≥50 y, in a pooled analysis from two phase 3 studies at Week 96

Methods

Study Designs: Randomized, Double Blind, Active Controlled



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

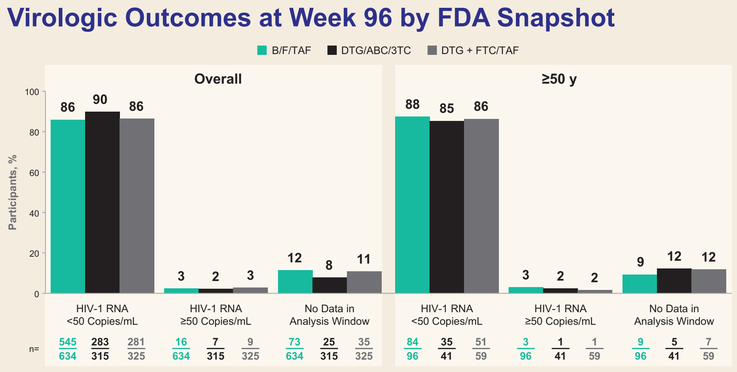
Results

Baseline Characteristics

	Overall Study Participants			Adults Aged ≥50 y		
	B/F/TAF n=634	DTG/ABC/3TC n=315	DTG + F/TAF n=325	B/F/TAF n=96	DTG/ABC/3TC n=41	DTG + F/TAF n=59
Median age, y (range)	32 (18–71)	32 (18–68)	34 (18–77)	55 (50–71)	54 (50–68)	54 (50–77)
Male, %	89	90	89	84	73	86
Race/ethnicity, %						
Black or African descent	33	36	31	32	27	20
Hispanic/Latino ethnicity	24	21	25	11	15	20
Median HIV-1 RNA, log_{10} copies/mL (IQR)	4.42 (4.00–4.88)	4.51 (4.04–4.87)	4.45 (4.03–4.84)	4.48 (4.00–4.93)	4.27 (3.74–5.01)	4.45 (3.90–4.92)
HIV-1 RNA >100,000 copies/mL, %	19	16	17	24	27	20
Median CD4 cell count, cells/μL (IQR)	442 (293–590)	450 (324–608)	441 (297–597)	436 (235–601)	534 (291–741)	405 (229–610)
CD4 count <200 cells/μL, %	13	10	10	20	12	15
Asymptomatic HIV infection, %	90	91	89	90	83	80
Median eGFRCG, mL/min (IQR)	122.4 (104.1–143.4)	123.0 (107.0–144.3)	120.6 (102.8–145.1)	99.0 (83.7–114.0)	101.9 (83.2–130.5)	104.0 (84.2–121.8)

IQR, interquartile range.

Virologic Outcomes at Week 96 by FDA Snapshot



FDA, Food and Drug Administration.

- There were no significant differences in efficacy between B/F/TAF and comparators in the overall population and age ≥50-y subgroup (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]):
  - Overall: B/F/TAF vs DTG/ABC/3TC, p=0.10; B/F/TAF vs DTG + F/TAF, p=0.88
  - Age ≥50 y: B/F/TAF vs DTG/ABC/3TC, p=0.83; B/F/TAF vs DTG + F/TAF, p=0.81

Virologic Resistance at Week 96

	Overall		
	B/F/TAF n=634	DTG/ABC/3TC n=315	DTG + F/TAF n=325
Met criteria for resistance testing*	7†	5†	6†
Assay failure	0	0	1
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 was aged ≥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

Overall Safety Through Week 96

	Overall			Aged ≥50 y		
AE, %	B/F/TAF n=634	DTG/ABC/3TC n=315	DTG + F/TAF n=325	B/F/TAF n=96	DTG/ABC/3TC n=41	DTG + F/TAF n=59
Any grade	91	96	89	91	93	85
Grade 3 or 4	13	12	12	20	15	12
Study drug related	24*	40*	28	23	37	29
Grade 3 or 4	1	1	0	4	2	0
Serious AE	14	12	10	20	22	14
Study drug related	1	<1	1	2	2	2
AE leading to study drug discontinuation	1	2	2	2	5	7
Deaths†	1 (n=5)	0	1 (n=3)	4 (n=4)	0	3 (n=2)

*p <0.001: B/F/TAF vs DTG/ABC/3TC based on Fisher exact test.
†Deaths in B/F/TAF group included (italic denotes event in adult aged ≥50 y): recreational drug use (n=1), suicide (n=1), cardiac arrest (n=1), poorly differentiated gastric adenocarcinoma (n=1), and hypertensive heart disease with congestive heart failure(n=1); deaths in DTG + F/TAF group included unknown (n=1), lymphoma (n=1), and pulmonary embolism (n=1).
AE, adverse event.reverse-transcriptase inhibitor.

Results (Cont'd)

Adverse Effects Through Week 96

	Overall			Aged ≥50 y		
All Grades >10% in Any Overall Group, %	B/F/TAF n=634	DTG/ABC/3TC n=315	DTG + F/TAF n=325	B/F/TAF n=96	DTG/ABC/3TC n=41	DTG + F/TAF n=59
Diarrhea	17	16	16	16	22	8
Headache	15	16	15	6	15	8
Nausea	10*	24*	11	11	10	3
Nasopharyngitis	11	12	16	16	17	25
Upper respiratory tract infection	10	16	13	14	15	5
Fatigue	8	11	10	5	7	7
Syphilis	8	12	7	9	7	5
Back pain	7	10	8	10	12	12

*p <0.001: B/F/TAF vs DTG/ABC/3TC based on Fisher exact test.

Study Drug-Related Adverse Events Through Week 96

	Overall			Aged ≥50 y		
All Grades ≥5% in Any Overall Group, %	B/F/TAF n=634	DTG/ABC/3TC n=315	DTG + F/TAF n=325	B/F/TAF n=96	DTG/ABC/3TC n=41	DTG + F/TAF n=59
Nausea	4*	17*	5	5	7	2
Headache	5	5	3	4	0	0
Diarrhea	5	4	3	4	10	3

*p <0.001: B/F/TAF vs DTG/ABC/3TC based on Fisher exact test.

Adverse Events Leading to Discontinuation Through Week 96*

Overall		
B/F/TAF n=634	DTG/ABC/3TC n=315	DTG + F/TAF n=325
n=6 (1%)	n=5 (2%)	n=5 (2%)
Atypical chest pain (Day 31)†	Nausea,† generalized rash (Day 4)†	*Erythema, pruritus* (Day 112)
Sleep disorder,† dyspepsia,† tension headache,† depressed mood,† insomnia (Day 65)†	Thrombocytopenia (Day 50)†	*Depression* (Day 420)†
Cardiac arrest (Day 28)	*Steatorrhea* (Day 134)†	*Lipoatrophy* (Day 464)†
Paranoia (Day 302)	Depression (Day 248)†	*Depression* (Day 532)†
Abdominal distension (Day 304)†	*Renal failure* (Day 621)	Supraventricular tachycardia (Day 597)
Depression (Day 337)†		

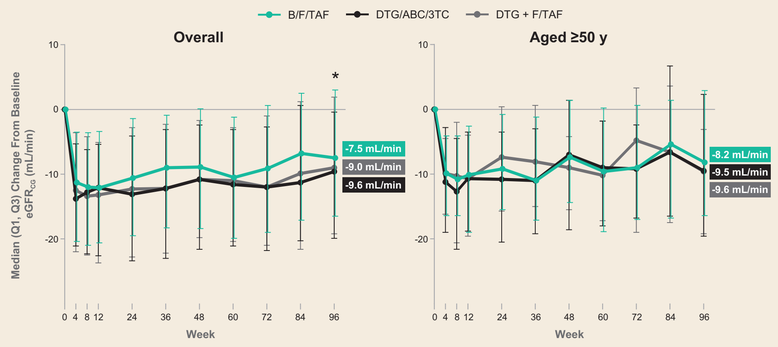
*Italic denotes adult aged ≥50 y; †Considered study drug-related by investigator.

Laboratory Abnormalities Through Week 96

	Overall			Aged ≥50 y		
Grade 3 or 4 ≥3% in Any Overall Group, %	B/F/TAF n=634	DTG/ABC/3TC n=315	DTG + F/TAF n=325	B/F/TAF n=96	DTG/ABC/3TC n=41	DTG + F/TAF n=59
Any Grade 3 or 4 lab abnormality	22	20	19	23	22	24
Decreased neutrophils	3	4	1	2	5	0
Increased AST	3	3	3	2	0	2
Increased creatine kinase	6	5	3	0	0	0
Increased amylase*	2	3	3	3	2	7
Fasting LDL increased	3	4	4	5	8	8
Fasting hyperglycemia	1	1	3	2	5	8
Glycosuria†	1	1	3	2	5	7

*AEs of pancreatitis reported in B/F/TAF (n=1; 0.2%) and DTG/ABC/3TC (n=2; 0.6%);.†Includes diabetes and hyperglycemic glycosuria, no participant had normoglycemic glycosuria. AST, aspartate aminotransferase; LDL, low-density lipoprotein.

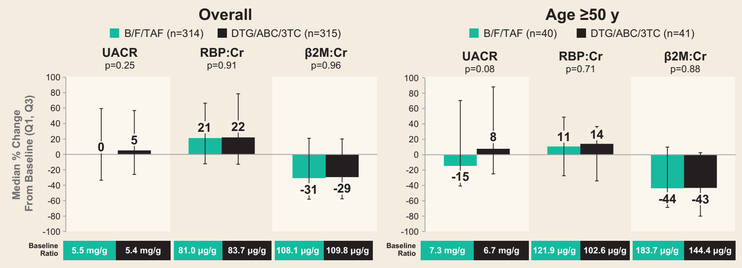
Changes From Baseline in eGFR Through Week 96



*p=0.002: difference at Week 96 between B/F/TAF and DTG/ABC/3TC (calculated from 2-sided Wilcoxon rank-sum test).
Q, quartile.

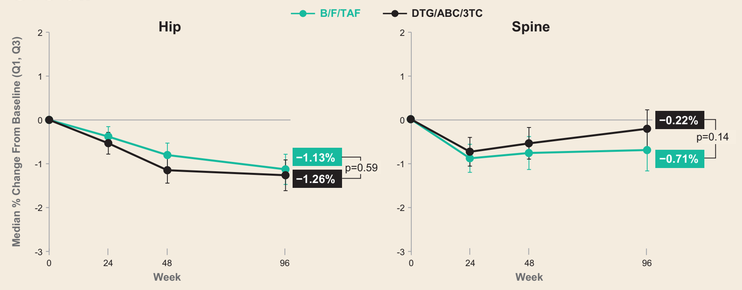
- No discontinuations due to renal AEs in the B/F/TAF or DTG + F/TAF groups
- One discontinuation due to renal failure in DTG/ABC/3TC group, not related to study drug
- No reported cases of proximal renal tubulopathy in any group
- Changes in eGFR are consistent with inhibition of tubular creatinine secretion via organic cation transporter-2 by DTG or BIC

Changes From Baseline in Renal Biomarkers at Week 96 (Study 1489 only)*



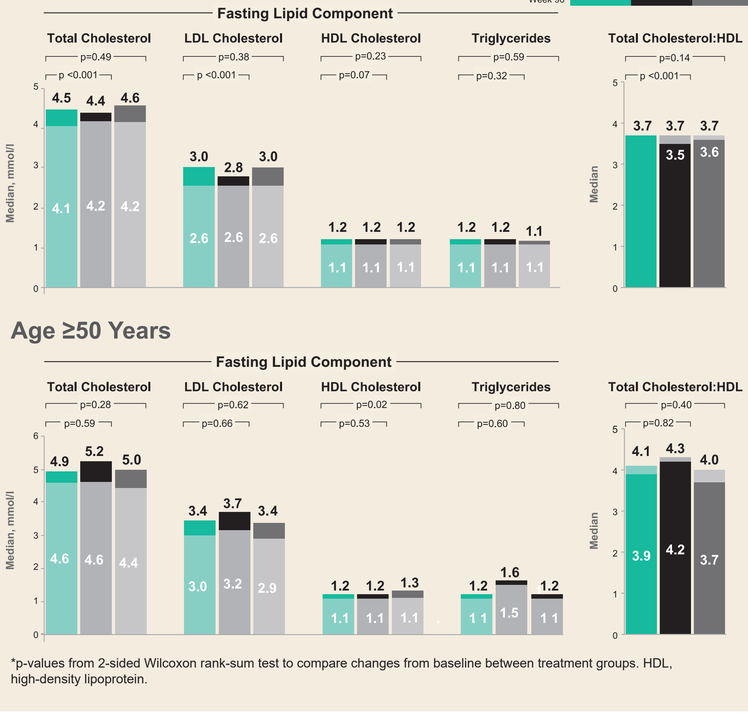
*Difference in % change from baseline for each marker tested between treatment groups by Wilcoxon rank-sum test. β2M, β2-microglobulin; Cr, creatinine; RBP, retinol-binding protein; UACR, urine albumin:Cr ratio.

Changes in BMD Through Week 96 (Study 1489 only)*



*p-values compared B/F/TAF vs DTG/ABC/3TC at Week 96 by analysis of variance model; dual-energy X-ray absorptiometry scans were obtained in Study 1489 only.
BMD, bone mineral density; CI, confidence interval.

Changes from Baseline in Fasting Lipids at Week 96*



*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 relevant differences in changes in lipids in the overall population
  - Similar percentages of participants in each group received lipid-modifying agents at study entry (B/F/TAF 5.2%, DTG/ABC/3TC 2.2%, and DTG + F/TAF 5.5%) and initiated treatment during the study (3.8%, 3.8%, and 3.7%, respectively)
- There were no statistically significant differences in changes in lipids in adults aged ≥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 treatment during the study (12%, 10%, and 10%, respectively)

Conclusions

- Initial treatment for HIV-1 with B/F/TAF was noninferior to either DTG-based regimen at Week 96 by FDA snapshot algorithm, with high rates of virologic suppression in all treatment arms
  - Efficacy in adults aged ≥50 y was comparable to that in the overall study population
- There was no treatment-emergent resistance observed in any treatment arm
- There were few AEs leading to discontinuations
  - Reported AEs for adults aged ≥50 y were comparable to those for the overall study population
- B/F/TAF was associated with fewer treatment-related AEs than DTG/ABC/3TC (p <0.001)
  - Nausea and treatment-related nausea were less common with B/F/TAF vs DTG/ABC/3TC (p <0.001) in the overall population
- Changes from baseline in BMD and renal markers were comparable between treatment arms, with no cases of proximal renal tubulopathy
  - Bone and renal safety findings were consistent in adults aged ≥50 y
- There were no clinically significant differences in median changes from baseline in total cholesterol, LDL, and total cholesterol:HDL ratio between treatments in the overall population and age ≥50-y subgroup, and no differences in the proportions of participants initiating lipid-lowering therapy

References & Acknowledgements

1. Centers for Disease Control and Prevention. HIV Among People Aged 50 and Older. 9/18/18. https://www.cdc.gov/hiv/group/age/olderamericans/. **2.** Tavoschi L, et al. Lancet HIV 2017;4:e514-21.

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