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Week 72 Outcomes and COVID-19 Impact From the BRAAVE 2020 Study: a Randomized Switch to B/F/TAF in Black American Adults With HIV

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Introduction

- Black Americans are disproportionately impacted by HIV in the USA, but are underrepresented in medical research
- In Phase 3 international clinical trials of bictegravir (BIC)/emtricitabine/tenofovir alafenamide (B/F/TAF), 33% of treatment-naïve and 26% of treatment-experienced participants identified as Black Americans[1-3]
- As previously presented, the BRAAVE 2020 study (ClinicalTrials.gov NCT03631732) demonstrated that guideline-recommended B/F/TAF was noninferior to continuing current HIV treatment in Black American adults through Week 24 with high efficacy through Week 48[4,5]; participants could continue B/F/TAF until Week 72
- The single-tablet regimen B/F/TAF is a US DHHS, EACS, and IAS-USA guidelines-recommended regimen,[6-8] with demonstrated safety and efficacy, and a high barrier to resistance
- Here, we present final Week 72 results, subgroup analyses, and COVID-19 impact

Objectives

- To evaluate the efficacy and safety of switching to B/F/TAF compared with continuing the baseline regimen in HIV-1–infected, virologically suppressed participants living in the USA who self-identify as Black American

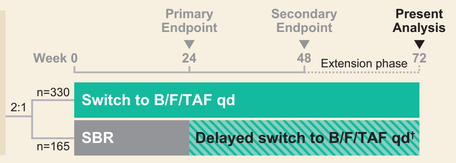
COVID-19 Operational Impact

- Some visits between Weeks 48 and 72 occurred during the COVID-19 pandemic and during shelter in place
- Pandemic response plans allowed for virtual visits if clinical sites were closed to in-person visits or transportation was shut down
- Local labs were used in place of a central lab
- Efficacy results only include data from the study central lab

Methods

BRAAVE Study Design

Adults with HIV-1 virologically suppressed on regimen of 2 NRTIs + 3rd agent*
- Self-describe as Black American or mixed race including Black American
- HIV-1 RNA <50 copies/mL for ≥6 mo
- $eGFR_{CG}$ ≥50 mL/min
- Preexisting resistance to NNRTIs, PIs, and/or NRTIs permitted (except K65R, ≥3 TAMs, or T69 insertions)
- Preexisting INSTI resistance excluded

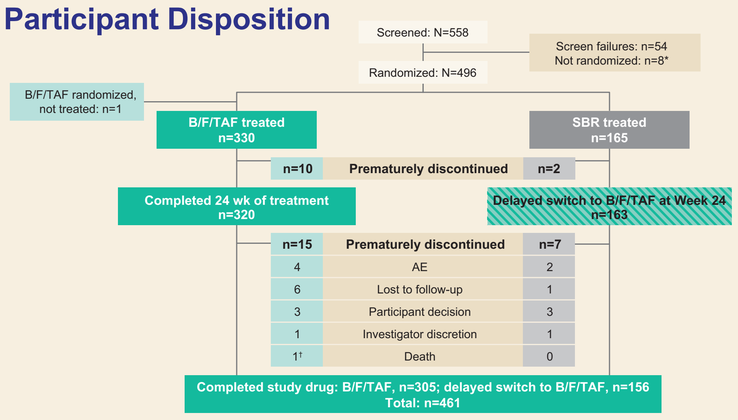


*Allowed 3rd agents: any US Food & Drug Administration (FDA)–approved protease inhibitor (PI), nonnucleoside reverse-transcriptase inhibitor (NNRTI; except etravirine), integrase strand transfer inhibitor (INSTI; except BIC), or maraviroc; †Corresponds to 48 wk after switch for delayed-switch-to-B/F/TAF group. $eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault; NRTIs, nucleoside reverse-transcriptase inhibitors; SBR, stay on baseline regimen; TAMs, thymidine analog mutations.

- Phase 3b, randomized, open-label, multicenter, active-controlled study
- Primary efficacy endpoint: proportion with HIV-1 RNA ≥50 copies/mL at Week 24 by FDA Snapshot
- Secondary efficacy endpoints: proportions of participants with HIV-1 RNA ≥ and <50 copies/mL at Week 48

Results

Participant Disposition



*Met all eligibility criteria, but were not randomized: withdrew consent (n=3), lost to follow-up (n=3), outside of visit window (n=1), and other (n=1); †Due to gunshot. AE, adverse event.

Baseline Characteristics

	B/F/TAF n=330	SBR n=165
Median age, y (range)	49 (18–79)	49 (19–70)
Female at birth, %	31	33
Gender identity, %		
Cisgender	96	96
Transgender	2	4
Other	2	0
Sexual orientation, %		
Heterosexual and female at birth	29	32
Heterosexual and male at birth	19	25
Gay or bisexual and female at birth	1	2
Gay or bisexual and male at birth	49	41
Hispanic/Latinx ethnicity, %	5	3
Median CD4 count, cells/μL (Q1, Q3)	747 (570, 922)	758 (494, 969)
Median $eGFR_{CG}$, mL/min (Q1, Q3)	110 (88, 132)	107 (86, 132)
Median weight, kg (Q1, Q3)	88 (79, 103)	89 (76, 104)
Median body mass index, kg/m² (Q1, Q3)	29.2 (25.9, 34.0)	29.3 (25.7, 34.3)
Hepatitis B coinfection, %	5	2

CD4, cluster of differentiation-4; Q, quartile.

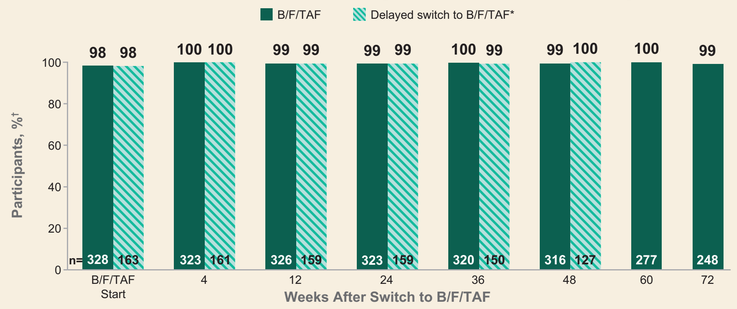
Baseline Regimens and Resistance

%	B/F/TAF n=330	SBR n=165
Baseline NRTI backbone		
F/TAF	68	65
F/TDF	17	21
ABC/3TC	13	15
Other	1	0
Baseline 3rd agent*		
INSTI	61	60
NNRTI	30	31
PI	9	8
CCR5 antagonist	0	1
Baseline ARV resistance†		
NRTI resistance	13	16
M184V/I	9	12
NNRTI resistance	21	19
PI resistance	11	15

*Includes: INSTIs dolutegravir, elvitegravir, and raltegravir; NNRTIs doravirine, efavirenz, etravirine, nevirapine, and rilpivirine; PIs ritonavir (*r*)– and cobicistat (c)–boosted darunavir, atazanavir/c, and unboosted atazanavir; lopinavir/*r* and nelfinavir; and chemokine coreceptor-5 (CCR5) antagonist maraviroc; †Assessed by cumulative historical or retrospective baseline proviral DNA genotype. 3TC, lamivudine; ABC, abacavir; ARV, antiretroviral; TDF, tenofovir disoproxil fumarate.

Virologic Outcome

HIV-1 RNA <50 Copies/mL, Missing=Excluded, Full-Analysis Set

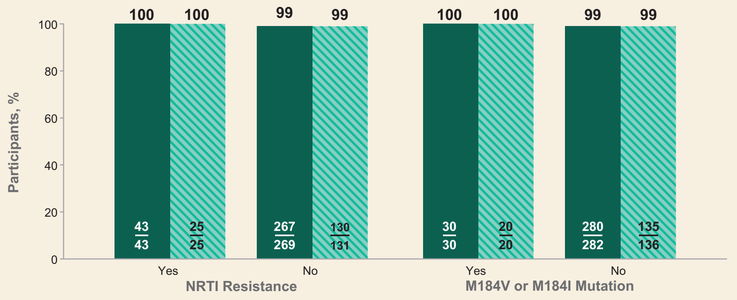


*Study Week 72 corresponds to 48 wk after switch; †Denominator for percentage is no. of participants in B/F/TAF full-analysis set with nonmissing HIV-1 RNA value at each visit.

- HIV-1 RNA <50 copies/mL was maintained in participants who remained on B/F/TAF and those who switched (delayed-switch group) to B/F/TAF

Virologic Outcomes Through Week 72: Resistance Subgroups*

HIV-1 RNA <50 Copies/mL at Last Visit



*Includes participants with ≥1 on-treatment HIV-1 RNA measurement and baseline resistance assessed by cumulative historical or proviral DNA genotype: B/F/TAF, n=312; SBR, n=156; †Study Week 72 corresponds to 48 wk after switch.

- Participants with NRTI resistance, including M184V/I, maintained virologic suppression on B/F/TAF
- No treatment-emergent resistance was detected in any treatment group

Adverse Events and Abnormal Laboratory Values

	B/F/TAF: n=330	Delayed Switch: n=163
Median study drug exposure, wk (Q1, Q3)	72 (71.4, 72.3)	48.0 (47.3, 48.3)

Randomized Phase Through Week 24 (previously presented)

	B/F/TAF: n=330	SBR: n=165
All-grade AEs (≥3% in either arm), %		
Upper respiratory tract infection	6	4
Arthralgia	4	1
Diarrhea	3	3
Cough	3	4
Headache	3	<1
Bronchitis	2	4
Grade 3 or 4 lab abnormalities (≥2% in either arm), %		
Nonfasting hyperglycemia*	2	1
Glycosuria*	3	<1

All Participants Who Received B/F/TAF at Any Time

	All B/F/TAF: n=493†
All-grade AEs (≥5%), %	
Upper respiratory tract infection	9
Syphilis	6
Headache	6
Pain in extremity	6
Arthralgia	5
Hypertension	5
Nasopharyngitis	5
Grade 3 or 4 lab abnormalities (≥2%), %	
Nonfasting hyperglycemia*	4
Glycosuria*	5
Fasting LDL increased	3
Fasting hyperglycemia	3
Urine red blood cells (hematuria: quantitative or dipstick)‡	3

*Occurred in participants with medical diagnosis of diabetes; †Includes all participants in B/F/TAF and delayed-switch groups; ‡Each in women during menses. LDL, low-density lipoprotein.

Adverse Events by Sex at Birth and Age

%	Sex at Birth		Age	
	Female: n=156	Male: n=337	<50 y: n=254	≥50 y: n=239
Any AE	**78**	**79**	**81**	**77**
All-grade AEs (>5% in any subgroup)				
Upper respiratory tract infection	10	8	9	8
Syphilis	1	8	9	2
Pain in extremity	5	6	4	7
Headache	6	5	6	5
Nasopharyngitis	3	6	7	3
Arthralgia	6	4	4	6
Cough	6	4	4	5
Chest pain	6	4	4	5
Urinary tract infection	7	1	4	3
Hypertension	5	5	6	4
Diarrhea	4	5	6	4
Back pain	3	4	6	3

- The numbers of participants experiencing AEs were similar by sex-at-birth and age groups

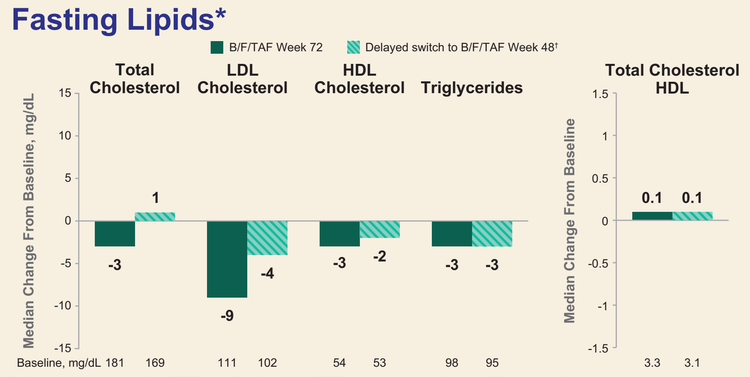
Adverse Events Leading to Study Drug Discontinuation

All B/F/TAF: n=493*
Total AEs leading to study drug discontinuation: n=12
Diarrhea†
Nightmare†
Headache†
Diarrhea,† dry mouth,† psychomotor hyperactivity, agitation, anxiety, and insomnia
Migraine†
Acute kidney injury (secondary to obstruction)
Abdominal distention† and flatulence†
Headache† and hyperhidrosis
Hemorrhage of intracranial aneurysm with multiple sequelae
After Week 48:
Change of bowel consistency† and flatulence†
COVID-19
COVID-19

*Includes all participants treated with ≥1 dose of B/F/TAF; each *row* represents 1 participant; †Reported as treatment related by investigator.

- As previously presented, 6 discontinuations occurred between baseline and Week 24; 3 discontinuations occurred between Weeks 24 and 48: 2 randomized to B/F/TAF and 1 delayed switch[1]
- 3 discontinuations occurred after Week 48: 2 participants with COVID-19, and 1 with change of bowel consistency and flatulence

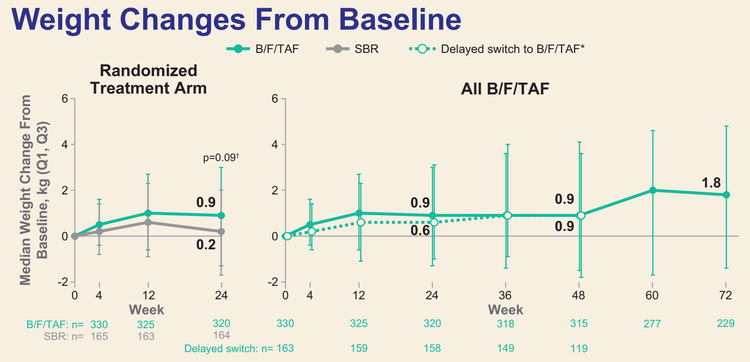
Fasting Lipids*



*Baseline is median value at time of 1st B/F/TAF dose; †Study Week 72 for B/F/TAF corresponds to 48 wk after switch. HDL, high-density lipoprotein.

- Taking lipid-lowering agents at baseline: 27% for B/F/TAF vs 23% for delayed switch
- Initiated lipid-lowering agents through Week 72 while on B/F/TAF: 6% for B/F/TAF vs 4% for delayed switch

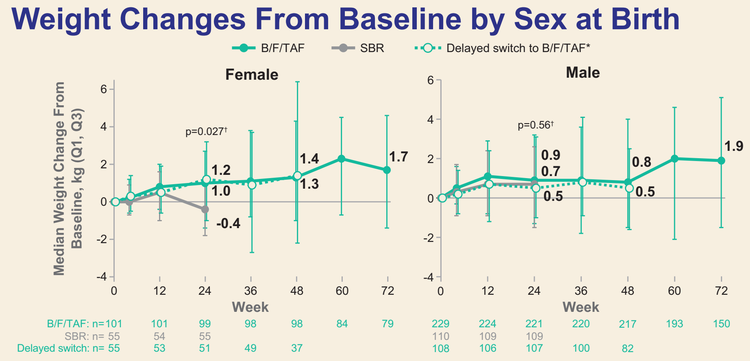
Weight Changes From Baseline



*Baseline: time of 1st B/F/TAF dose; †From 2-sided Wilcoxon rank-sum test comparing B/F/TAF vs SBR at Week 24.

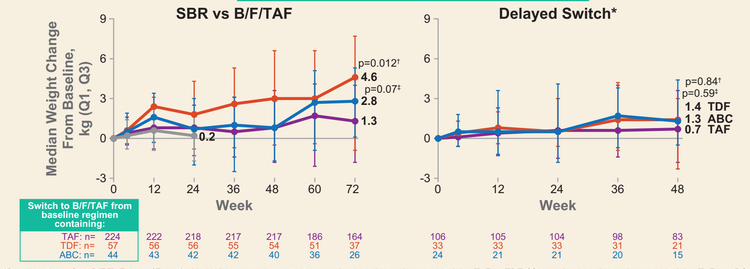
- Median (Q1, Q3) weight changes from baseline at Week 24: 0.9 kg (-1.3, 3.0) for B/F/TAF and 0.2 kg (-1.7, 2.0) for SBR

Weight Changes From Baseline by Sex at Birth



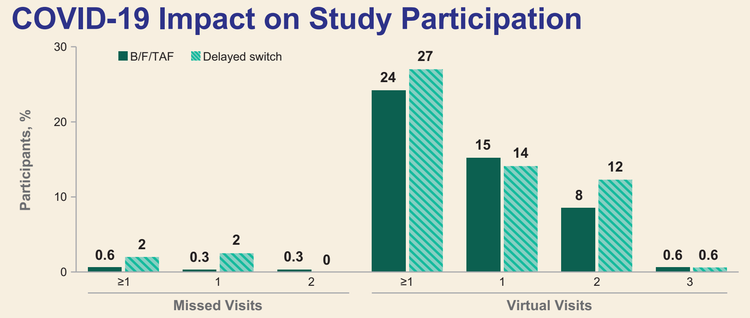
*Baseline: time of 1st B/F/TAF dose; †From 2-sided Wilcoxon rank-sum test comparing B/F/TAF vs SBR at Week 24.

Weight Changes Over Time by Baseline NRTIs



*Baseline: time of 1st B/F/TAF dose; †From 2-sided Wilcoxon rank-sum test comparing baseline regimens containing TAF vs TDF; ‡Comparing baseline regimens containing TAF vs ABC.

COVID-19 Impact on Study Participation



- Participants had high study engagement with few missed visits despite the COVID-19 pandemic
  - 124 participants (25%) completed virtual visits in lieu of site visits
  - 6 participants (1%) missed visits (in person and/or virtual) due to COVID-19-related challenges
  - The last participant visit was 19 Aug 2020
  - 5 participants were reported to have COVID-19 and 2 died

Conclusions

- For Black Americans living with HIV, switching to B/F/TAF was highly effective and safe through 72 wk regardless of age, sex at birth, or preexisting NRTI resistance
  - No participant had treatment-emergent resistance to study drugs
- Small reductions in median changes from baseline in total cholesterol and triglycerides were observed after switching to B/F/TAF
- Weight changes were similar between groups at Week 24 and stable from Weeks 24 to 72
  - More weight gain was observed in participants switching from TDF and ABC compared with TAF
- Black American participants had high study engagement, with few missed visits and high adherence despite the COVID-19 pandemic

References: 1. Daar ES, et al. Lancet HIV 2018;5:e347-56; **2.** Kityo C, et al. J Acquir Immune Defic Syndr 2019;82:321-8; **3.** Molina J-M, et al. Lancet HIV 2018;5:e357-65; **4.** Hagins D, et al. JAIDS May 18, 2021 [epub]; **5.** Saag MS, et al. JAMA 2018;320:379-96; **6.** Clinical Info HIV.gov. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV, 7/10/19; **7.** European AIDS Clinical Society Guidelines Version 10.0, November 2019; **8.** Sax PE, et al. Clin Infect Dis 2020 Jul 15;ciaa988; **9.** AIDSVu.org. Map.

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