Week-48 Outcomes From the BRAAVE 2020 Study: a Randomized Switch to B/F/TAF in African-American Adults With HIV

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Introduction

- African-Americans have the highest rates of HIV/AIDS in the USA, but are underrepresented in medical research
- The single-tablet regimen bictegravir (BIC; B), emtricitabine (FTC; F), and tenofovir alafenamide (TAF; B/F/TAF) is a US DHHS, EACS, and IAS–USA guidelines-recommended regimen,[1-3] with demonstrated safety and efficacy, and a high barrier to resistance
- In Phase 3 international clinical trials of B/F/TAF, 33% of treatment-naïve and 26% of treatment-experienced participants identified as African-American or Black[4-7]

Objectives

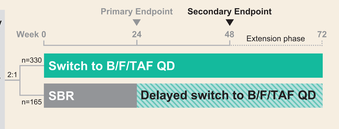
- To evaluate the efficacy and safety of switching to B/F/TAF compared with continuing the baseline regimen in HIV-1–infected, virologically suppressed participants living in the USA who self-identify as African-American or Black

Methods

BRAAVE Study Design*

Adults with HIV-1 virologically suppressed on a regimen of 2 NRTIs + 3rd agent[†]

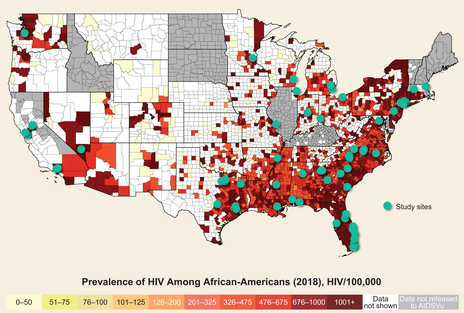
- Self-describe as African-American, Black, or mixed race including Black
- HIV-1 RNA <50 copies/mL for ≥6 mo
- eGFR$_{CG}$ ≥50 mL/min
- Preexisting resistance to NNRTIs, PIs, and/or NRTI permitted (except K65R, ≥3 TAMs, or T69 insertions)
- Preexisting INSTI resistance excluded



*NCT03631732; †Allowed 3rd agents: any FDA-approved protease inhibitor (PI), non-nucleoside reverse transcriptase inhibitor (NNRTI; except etravirine), integrase strand transfer inhibitor (INSTI; except BIC), or maraviroc. eGFR$_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault; NRTI, nucleoside reverse transcriptase inhibitor; SBR, stay on baseline regimen; TAMs, thymidine analog mutations.

- Phase 3, 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 with HIV-1 RNA ≥ and <50 copies/mL at Week 48

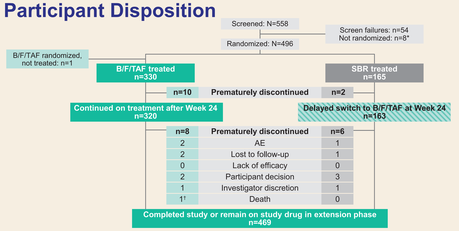
HIV-1 Prevalence Among African-Americans and BRAAVE Study Sites[8]



- Prevalence of HIV-1 among African-Americans by county of residence
- BRAAVE 2020 Study: 82 sites screened and enrolled participants

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/m^2 (Q1, Q3)	29.2 (25.9, 34.0)	29.3 (25.7, 34.3)
Hepatitis B coinfection, %	5	2

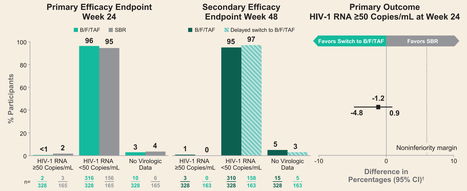
CD4, cluster of differentiation-4; Q, quartile.

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, nalfinavir, rilpivirine, and rilpivirine; PIs ritonavir (r)- and cobicistat (c)-boosted darunavir and atazanavir, and unboosted atazanavir; lopinavir/r; and chemokine coreceptor-5 (CCR5) antagonist maraviroc; †Resistance assessed by cumulative historical or retrospective baseline proviral DNA genotypes. 3TC, lamivudine; ABC, abacavir; ARV, antiretroviral; TDF, tenofovir disoproxil fumarate.

Virologic Outcomes: Full Analysis Set*



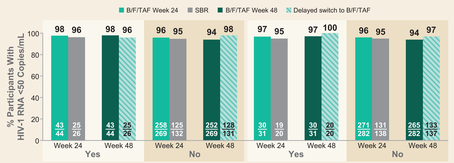
*2 participants had baseline INSTI resistance discovered after randomization based on historical data and were excluded from primary analysis; both were randomized to B/F/TAF and had HIV-1 RNA <50 copies/mL at Weeks 24 and 48; †Differences between treatment groups (B/F/TAF − SBR) in percentages of participants with HIV-1 RNA ≥50 copies/mL and 95% confidence interval (CI) were calculated based on exact method.

- Switching to B/F/TAF was noninferior to SBR
- High rates of virologic suppression were maintained at Week 48 in the B/F/TAF and delayed-switch groups

Treatment Difference in HIV-1 RNA <50 Copies/mL at Week 24 by Subgroup

*n=313; †n=158.

Virologic Outcomes at Week 24 and 48: Resistance Subgroups*



*Includes participants with baseline resistance assessed by cumulative historical or proviral DNA genotypes: B/F/TAF, n=313; SBR, n=158.

- Participants with NRTI resistance, including M184V/I, maintained virologic suppression on B/F/TAF
- No treatment-emergent resistance was detected in any treatment group
- For additional resistance details, see *Andreatta K, et al. IDWeek 2020, oral 109*

Adverse Events and Abnormal Laboratory Values

	B/F/TAF n=330	SBR n=165	Delayed Switch n=163
Median study drug exposure, wk (Q1, Q3)	61 (56, 68)	24 (24, 24)	38 (32, 44)

Randomized Phase Through Week 24 (previously presented)

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

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

All-Grade AEs (≥4%), %	All B/F/TAF† n=493
Upper respiratory tract infection	8
Syphilis	5
Diarrhea	4
Headache	4
Nasopharyngitis	4
Hypertension	4
Grade 3/4 Laboratory Values ≥2%, %	
Nonfasting hyperglycemia*	4
Fasting LDL increased	2
Glycosuria*	4
Urine RBC (hematuria: quantitative or dipstick)‡	2

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

Adverse Events Leading to Study Drug Discontinuation

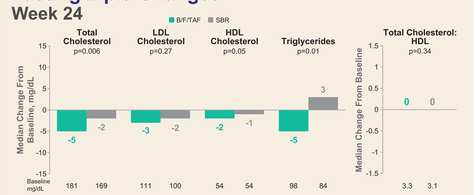
All B/F/TAF n=493*
AEs leading to study drug discontinuation: n=9
Diarrhea†
Nightmare†
Headache†
Diarrhea,† dry mouth,† psychomotor hyperactivity, agitation, anxiety, insomnia
Migraine†
Acute kidney injury (secondary to obstruction)
Abdominal distention,† flatulence†
Headache,† hyperhidrosis
Hemorrhage of intracranial aneurysm with multiple sequelae

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

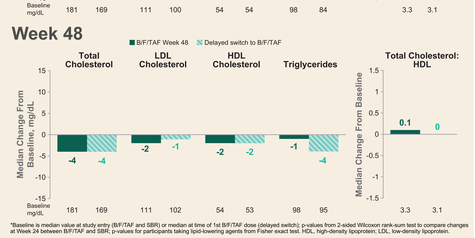
- 6 discontinuations occurred between baseline and Week 24
- 3 discontinuations occurred between Weeks 24 and 48: 2 randomized to B/F/TAF and 1 delayed switch

Fasting Lipid Changes*

Week 24



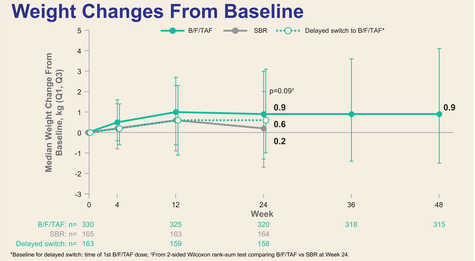
Week 48



*Baseline is median value at study entry (B/F/TAF and SBR) or median at time of 1st B/F/TAF dose (delayed switch); p-values from 2-sided Wilcoxon rank-sum test to compare changes at Week 24 between B/F/TAF and SBR; p-values for participants taking lipid-lowering agents from Fisher exact test. HDL, high-density lipoprotein; LDL, low-density lipoprotein.

- Taking lipid-lowering agents at baseline: B/F/TAF 27% vs SBR 23% (p=0.38)
- Initiated lipid-lowering agents through Week 24: B/F/TAF 2% vs SBR 1% (p=0.28)
- Initiated lipid-lowering agents through Week 48: B/F/TAF 3%

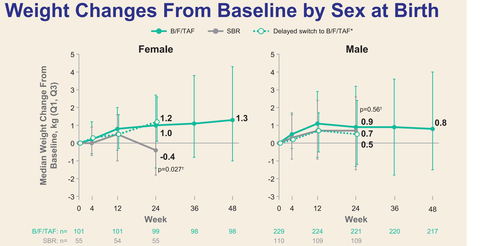
Weight Changes From Baseline



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

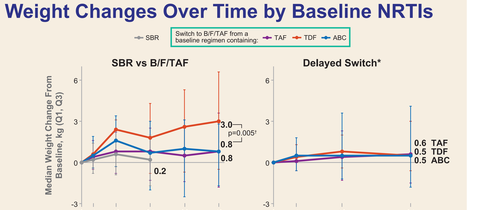
- Median (Q1, Q3) weight changes from baseline at Week 24: B/F/TAF 0.9 kg (-1.3, 3.0) and SBR 0.2 kg (-1.7, 2.0)

Weight Changes From Baseline by Sex at Birth



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

Weight Changes Over Time by Baseline NRTIs



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

Conclusions

- For African-Americans living with HIV:
  - Switching to B/F/TAF was noninferior to remaining on the baseline regimen of a 3rd agent + 2 NRTIs at Week 24; high efficacy was demonstrated through Week 48; <1% of participants switched to B/F/TAF had HIV RNA ≥50 copies/mL at Week 48
    - Virologic suppression was maintained in participants with preexisting NRTI resistance
  - No treatment-emergent resistance was observed
  - Switching to B/F/TAF was safe and well tolerated, and AEs were comparable between treatment groups
- 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 48
    - More weight gain was observed in participants switching off of TDF compared with other baseline NRTIs
- B/F/TAF is safe and effective for African-Americans switching from a variety of regimens, including those with preexisting NRTI resistance

References: 1. Clinical Info HIV.gov. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. 7/10/19; 2. European AIDS Clinical Society. Guidelines Version 10.0. November 2019; 3. Saag MS, et al. JAMA 2018;320:379-96; 4. Daar ES, et al. Lancet HIV 2018;5: e347-56; 5. Kityo C, et al. J Acquir Immune Defic Syndr 2019;82:321-8; 6. Molina JM, et al. Lancet HIV 2018;5: e357-65; 7. Sax PE, et al. Clin Infect Dis 2020 Jul 15:ciaa886; 8. AIDSVu.org. May.

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