Phase 3 Randomized, Controlled Trial of Switching to Fixed-Dose Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) from Boosted Protease Inhibitor-Based Regimens in Virologically Suppressed Adults: Week 48 Results

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Introduction

- Integrase strand transfer inhibitors (INSTIs) are guideline recommended as components of 1st-line antiretroviral therapy in combination with 2 nucleoside reverse transcriptase inhibitors (NRTIs)[1-3]
- Emtricitabine (FTC, F) /tenofovir alafenamide (TAF)–based regimens have demonstrated improved bone and renal safety compared with FTC/tenofovir disoproxil fumarate (TDF)–based regimens, with no discontinuations due to renal tubulopathy including Fanconi syndrome over 3 years[4]
- Bictegravir (BIC, B) is a novel, unboosted, potent INSTI with a high in vitro barrier to resistance and low potential for drug-drug interactions[5,6]
- BIC is coformulated into a single-tablet regimen with F/TAF (B/F/TAF) for once-daily dosing without regard to food
- In 2 treatment naïve Phase 3 studies, B/F/TAF was safe and efficacious through Week 48 compared to dolutegravir-containing regimens[7,8]
  - No patient developed resistance to study medications

1. AIDSinfo. http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf;
2. EACS. http://www.eacsociety.org/files/guidelines_8.2-english.pdf; 3. Gunthard HF, et al. JAMA 2016;316:191-210; 4. Arribas JR, et al. J Acquir Immune Defic Syndr 2017;75:211-8; 5. Gallant JE, et al. J Acquir Immune Defic Syndr 2017;75:61-6; 6. Tsiang M, et al. Antimicrob Agents Chemother 2016.60:7086-97; 7. Gallant J, et al Lancet 2017; 8. Sax PE, et al. Lancet 2017.

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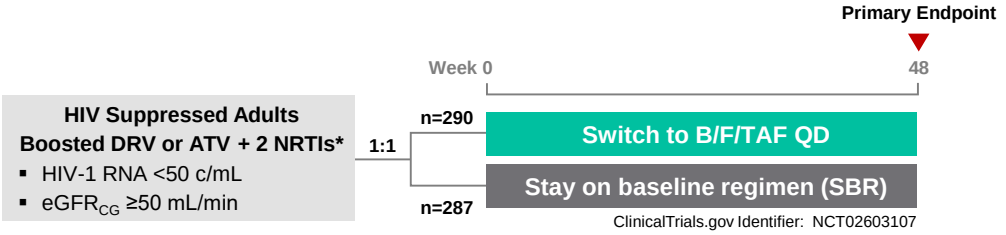
Study Design5

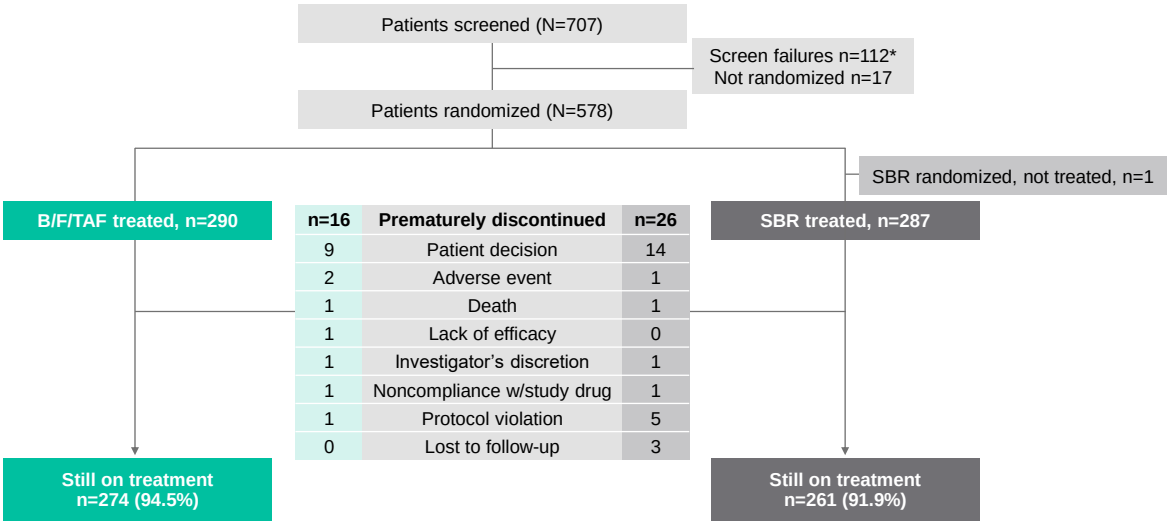


* Suppressed on regimen for ≥6 months;
NRTIs: ABC/3TC or FTC/TDF
RTV or COBI boosted

- Phase 3, randomized, open-label, multicenter, active-controlled study
  - North America, Europe, Australia
- Primary endpoint:
  - Proportion of patients with HIV-1 RNA ≥50 copies/mL at Week 48 based on FDA snapshot algorithm with a non-inferiority margin of 4%

3TC, lamivudine; ABC, abacavir; ATV, atazanavir; COBI, cobicistat; C, copies; DRV, darunavir; $eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault; FTC, emtricitabine; NRTI, nucleoside reverse transcriptase inhibitor; RTV, ritonavir; TDF, tenofovir disoproxil fumarate.

Patient Disposition



n=16	Prematurely discontinued	n=26
9	Patient decision	14
2	Adverse event	1
1	Death	1
1	Lack of efficacy	0
1	Investigator's discretion	1
1	Noncompliance w/study drug	1
1	Protocol violation	5
0	Lost to follow-up	3

*Did not meet all eligibility criteria.

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Baseline Characteristics

	B/F/TAF n=290	SBR n=287
Median age, y	48	47
Male, %	84	82
Race/ethnicity, %		
Black or African descent	27	25
Hispanic/Latino	21	16
Median CD4 count, cells/µL	617	626
HBV co-infection / HCV co-infection, n	8 / 5	6 / 5
Median $eGFR_{CG}$, mL/min	107	105
Baseline ARV regimen, %		
FTC/TDF, ABC/3TC	84, 16	85, 15
DRV, ATV	57, 43	54, 46

ARV, antiretroviral; HBV, hepatitis B virus; HCV, hepatitis C virus.

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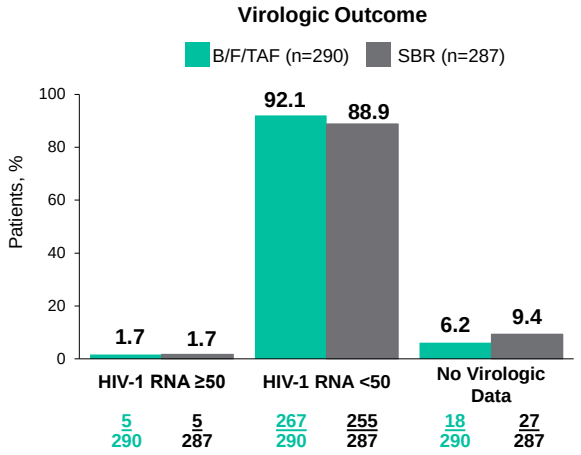
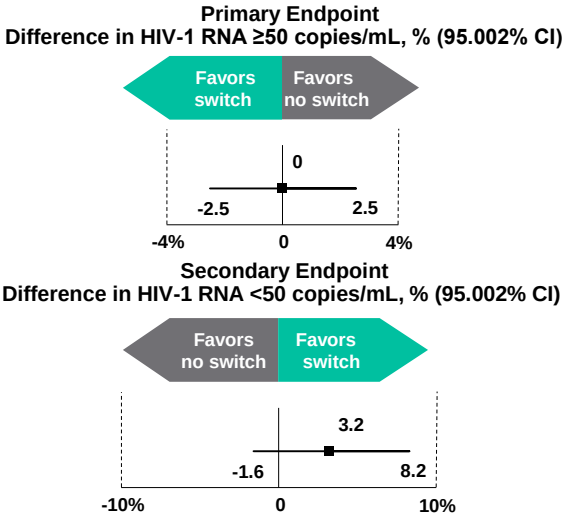
Virologic Outcome at Week 48





- Switching to B/F/TAF was noninferior to maintaining baseline protease inhibitor regimen

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Virologic Outcome at Week 48

Participants, % (n)	B/F/TAF n=290	SBR n=287	Difference (95.002% CI, p value)
HIV-1 RNA (VL) ≥50 copies/mL	**1.7% (5)**	**1.7% (5)**	**0** (-2.5, 2.5, p=1.00)
VL ≥50 copies/mL in Week 48 window	0.7% (2)	0.7% (2)	
D/C due to lack of efficacy	0.3% (1)	0	
D/C due to AE or death and last VL ≥50 copies/mL	0	0	
D/C due to other reasons and last VL ≥50 copies/mL	0.7% (2)	1% (3)	
VL <50 copies/mL	**92.1% (267)**	**88.9% (255)**	**3.2%** (-1.6, 8.2, p=0.2)
No virologic data in Week 48 window	**6.2% (18)**	**9.4% (27)**	
D/C due to AE/death and last VL <50 copies/mL	1.0% (3)	0.7% (2)	
D/C due to other reasons and last VL <50 copies/mL	3.4% (10)	6.6% (19)	
On study drug, but missing data in window	1.7% (5)	2.1% (6)	

VL, viral load.

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Resistance Analysis Population

Patients, n	B/F/TAF n=290	SBR n=287
Analyzed for Resistance (PR, RT, IN)	1	3
Any Emergent Resistance	0	1 (L74V)

- One patient on ABC/3TC + DRV/r developed virologic failure with treatment-emergent L74V in RT
- No patients developed resistance to B/F/TAF

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Adverse Events Leading to Study Drug Discontinuation

Patients, n	B/F/TAF n= 290	SBR n= 287
Any AE leading to D/C	2	1
Acetabular fracture/Acute kidney Injury	0	1
Rash	1	0
Schizophrenia	1	0

- No B/F/TAF patients discontinued for renal adverse events
- 2 deaths occurred; neither was related to study medication:
  - B/F/TAF: 63 year old smoker with COPD died of metastatic lung cancer
  - SBR: 54 year old died of blunt force trauma to the head

COPD: chronic obstructive pulmonary disease

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Adverse Events (≥5%) Through Week 48

All Grade, %	B/F/TAF n=290	SBR n=287
Headache	12	4
Diarrhea	8	6
Nasopharyngitis	7	12
Upper respiratory tract infection	7	8
Back pain	5	6
Arthralgia	4	5

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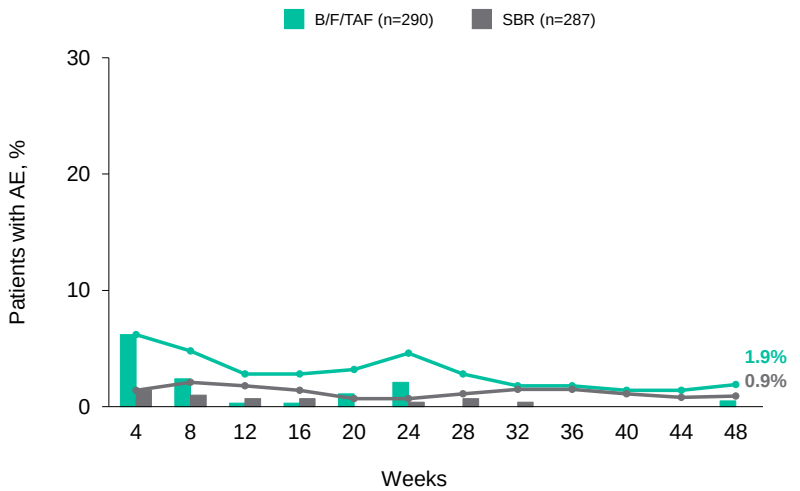
Headache: Incidence and Prevalence



Bar indicates incidence of patients with new onset at each 4-wk window.
Line indicates patients with ongoing events in the 4-wk window.

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Laboratory Abnormalities (≥2% in either arm) Through Week 48

Grade 3 or 4, %	B/F/TAF n=290	SBR n=287
LDL elevation	3.9	4.0
Amylase elevation	2.1	2.1
Glycosuria	2.1	1.1
ALT elevation	2.1	1.4
Total bilirubin	0.7	15.4
Total cholesterol	0.7	2.2
Hematuria	1.7	2.7

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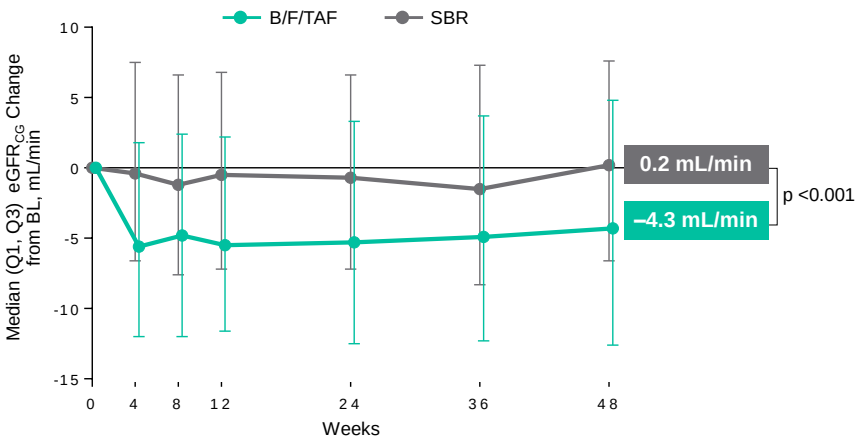
Change Baseline in $eGFR_{CG}$ Through Week 48



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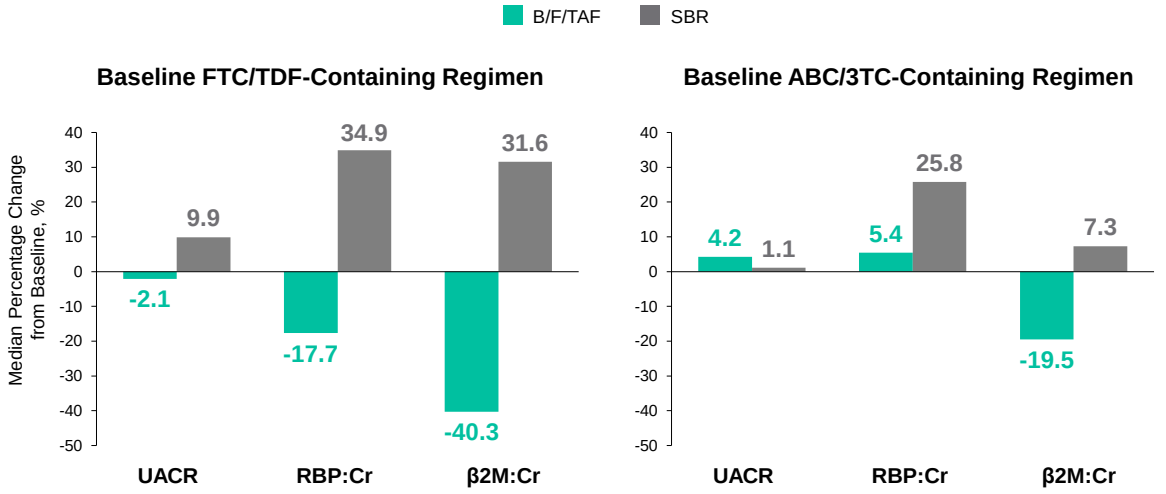
Percent Change from Baseline in Quantitative Proteinuria at Week 48



UACR: urine albumin to creatinine ratio; RBP: retinol binding protein to creatinine ratio;β2M:Cr: beta-2-microglobulin to creatinine ratio

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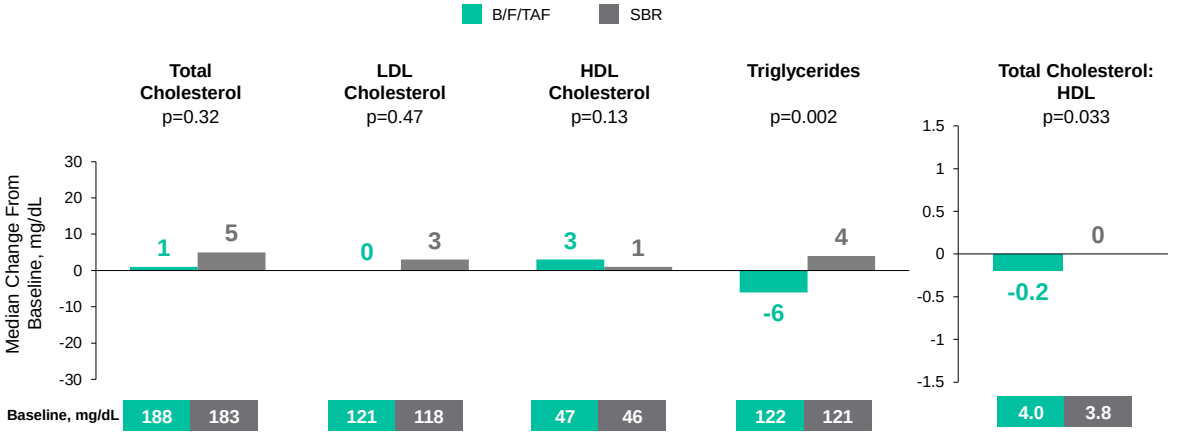
Fasting Lipid Changes at Week 48



- Taking lipid lowering agents at baseline: B/F/TAF 16.2%, SBR 15.7%, p=0.91
- Initiated lipid lowering agents during the study: B/F/TAF 2.8%, SBR 3.5%, p=0.64

p-values from the 2-sided Wilcoxon rank sum test to compare the 2 treatment groups.

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Conclusions: Week 48

- **Switching to B/F/TAF was non-inferior to remaining on a boosted protease inhibitor + 2 NRTIs**
  - 1.7% of subjects in each arm had HIV-1 RNA ≥ 50 copies/mL
  - 92.1% of subjects treated with B/F/TAF maintained virologic suppression vs 88.9% in the SBR arm
- **No treatment emergent resistance was observed in patients who switched to B/F/TAF**
  - 1 subject who continued DRV/r + ABC/3TC developed abacavir resistance
- **B/F/TAF was well tolerated**
  - Adverse events were comparable between arms at week 48
    - mild headache was reported more with B/F/TAF but was mostly transient and low grade
  - Less than 1% of patients discontinued due to an adverse event in both arms
  - No difference in Grade 3 or 4 laboratory abnormalities was observed between arms except for > total bilirubin abnormalities in SBR arm due to ATV use
  - Statistically significant improvements in triglycerides and total cholesterol:HDL ratio in subjects who switched to B/F/TAF

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