Efficacy, safety and tolerability of switching to bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in HIV-1 infected virologically-suppressed older adults in a real-world setting

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BACKGROUND:

- Approximately 50% of people living with HIV (PLWH) in the United States are ≥50 years old[1]. This aging population is at increased risk of additional comorbidities and drug-drug interactions (DDIs) between antiretrovirals (ARVs) and non-HIV medications
- B/F/TAF is a potent, well-tolerated single tablet regimen (STR) with few DDIs
- Clinical trials of B/F/TAF demonstrated potent efficacy and a favorable safety and tolerability profile in PLWH aged ≥ 65 years[2, 3]
- Real-world data from larger, diverse cohorts of older PLWH would be useful to validate these results outside of a clinical trial setting

METHODS:

- Retrospective cohort study to describe the efficacy, safety and tolerability of B/F/TAF in adults aged ≥50 years old through 48 weeks
- Eligible participants included PLWH who were switched to daily B/F/TAF as a complete ARV regimen between February 2018-August 2019 and were aged ≥50 years old at the time of switch
- Key inclusion criteria included:
  a. Documented plasma HIV-1 RNA<50 copies/mL x 2, (at least three months apart) within the year prior to switch
  b. Attendance at a minimum of two clinic visits in the year prior to switch
  c. No prior history of virologic failure on an integrase strand transfer inhibitor (INSTI) containing regimen or documented primary INSTI resistance
  d. Attendance at ≥2 clinic visits during the study period with a minimum of 2 HIV-1 RNA measurements following switch to allow for an efficacy estimate
- A documented plasma HIV-1 RNA>50 copies/mL in the year prior to switch was exclusionary
- Demographics, lab values and clinical parameters were extracted from the charts of all eligible patients through Week 48 of treatment with B/F/TAF
- The primary endpoint of the study was the proportion of patients with plasma HIV-1 RNA<50 copies/mL at Week 48
- Secondary efficacy endpoints included subgroup analyses of virologic outcomes at Week 48 by baseline regimen prior to switch
- Other secondary endpoints included (a) change in CD4+ cell count through Week 48 (b) change in lipids through Week 48 and (c) the impact of switching to B/F/TAF on DDIs
- Safety and tolerability of B/F/TAF through 48 weeks were also assessed

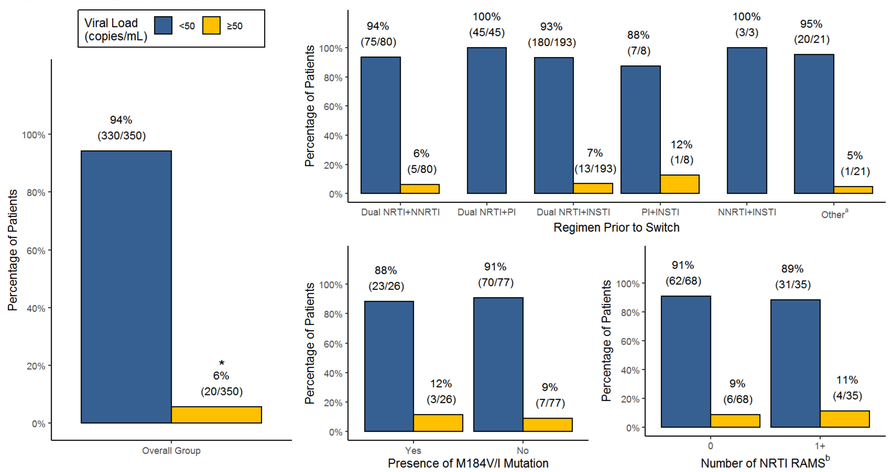
RESULTS:

Table 1. Baseline demographic and clinical characteristics

Characteristic	N=350
Median Age (range)	57 (50, 81)
Sex	
Male, n (%)	281 (80)
Female, n (%)	69 (20)
Race/Ethnicity	
Caucasian, n (%)	199 (57)
Black, n (%)	56 (16)
Hispanic, n (%)	80 (23)
Asian, n (%)	5 (1)
Other, n (%)	9 (3)
BMI, median (range)	27.8 (17.4, 48.3)
Weight, median (range), pounds	**185 (89, 346.3)**
CD4⁺ cell count, median (range), cells/mm^3	664 (58, 2327)
Co-infection	
HBV, n (%)	14 (4)
HCV, n (%)	10 (3)
Chronic comorbid conditions, median (range)	5 (0, 20)
Charlson comorbidity index score, median (range)	2 (1, 8)
10-year survival percentage, median (range)	90 (0-96)
Concomitant medications, median (range)	4 (0, 23)
Duration of HIV infection, median (range), years	20 (1, 40)
Number of ARV regimens prior to switch, median (range)	4 (1, 11)
Documented duration of virologic suppression prior to switch, median (range), years	11 (0, 27)
Prior ARV Experience	
>2 NRTIs, n (%)	288 (82)
≥1 NNRTI, n (%)	250 (71)
≥ 2 PIs, n (%)	93 (27)
1 INSTI, n (%)	171 (49)
>1 INSTI, n (%)	64 (18)
Regimen prior to switch	
Dual NRTI+NNRTI, n (%)	80 (23)
Dual NRTI+PI, n (%)	45 (13)
Dual NRTI+INSTI, n (%)	193 (55)
PI+INSTI, n (%)	8 (2)
NNRTI+INSTI, n (%)	3 (1)
Other, n (%)	21 (6)
Rationale for switch to B/F/TAF	
Simplification, n (%)	123 (35)
DDI Avoidance, n (%)	93 (27)
TDF to TAF switch, n (%)	70 (20)
Comorbidities, n (%)	27 (7.5)
Side Effects, n (%)	31 (9)
Other, n (%)	6 (1.5)
Historical genotypic resistance available, n (%)	**103 (29)**
≥1 NRTI RAM, n (%)	35 (34)
≥1 NNRTI RAM, n (%)	33 (32)
≥1 PI RAM, n (%)	37 (36)
≥1 INSTI RAM[b], n (%)	2 (2)
Pattern of NRTI RAMs[a]	
None, n (%)	77 (75)
M184V/I alone, n (%)	10 (10)
M184V/I+ 1 NRTI RAM, n (%)	6 (5)
M184V/I + > 1 NRTI RAM, n (%)	10 (10)

Abbreviations. BMI, Body Mass Index; HBV, hepatitis B; HCV, hepatitis C; ARV, antiretroviral; PI, protease inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; INSTI, integrase strand transfer inhibitor; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; DDI, drug-drug interaction; TDF; tenofovir disoproxil fumarate; RAMs, resistance associated mutations
[a]Total with available historical genotypes used as denominator
[b]Two patients with minor INSTI RAMs

Figure 1. Subgroup Analysis of Virologic Outcomes at Week 48



Abbreviations. NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; INSTI, integrase strand transfer inhibitor; RAMs, resistance associated mutations
[a] Other includes regimens with 3 antiretroviral drug classes
[b] Total with available historical genotypes used as denominator
*20 patients experienced HIV-1 RNA >50 copies/mL at Week 48, 19 had HIV-1 RNA between 50-200 copies/mL and 1 had HIV-1 RNA between 200-400 copies/mL. Two patients had documented non-adherence while 18/20 had 100% adherence documented. None underwent genotypic testing. 1 discontinued B/F/TAF due to lack of efficacy. 10/19 re-suppressed on B/F/TAF.

RESULTS cont'd:

There was no significant change in median CD4⁺ cell count from baseline to Week 48 (+7 cells/mm^3, 95% confidence interval (CI): [-9; 29], p=0.304)

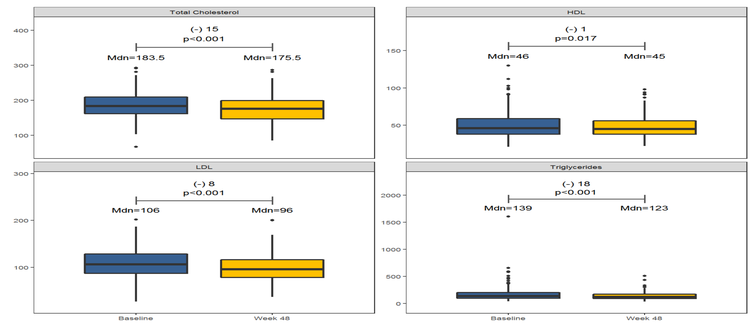
Table 2. Avoidance of Drug-Drug Interactions (DDIs) following switch to B/F/TAF

Baseline ARV	Concomitant Medication	DDI resolution following switch to B/F/TAF N (%)
Ritonavir or cobicistat containing regimen	Statins	81 (23)
Ritonavir or cobicistat containing regimen	PDE5 inhibitors	25 (7)
Ritonavir or cobicistat containing regimen	Factor Xa inhibitors	3 (1)
Ritonavir or cobicistat containing regimen	P2Y12 inhibitors	4 (1)
Ritonavir or cobicistat containing regimen	Warfarin	1 (0.3)
Ritonavir or cobicistat containing regimen	Inhaled or intranasal steroids	**16 (5)**
Ritonavir or cobicistat containing regimen	HCV NS3/4A protease inhibitor	1 (0.3)
Rilpivirine	PPIs	6 (2)
Rilpivirine	H2 blockers	3 (1)

Abbreviations. B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; ARV, antiretroviral; PDE5, phosphodiesterase type 5; PPI, proton pump inhibitor; H2, histamine type 2

A total of 140 potential DDIs were identified in 121 (35%) patients taking a boosting agent or rilpivirine at baseline that were resolved upon switching to B/F/TAF

Figure 2. Changes in lipid parameters through Week 48



Switching to B/F/TAF was associated with significant declines in total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides. At baseline, 179 (51%) patients were on lipid-lowering therapy. During the study period, 42 (12%) initiated lipid lowering therapy and 11 (3%) discontinued lipid lowering therapy

Table 3. Safety and Tolerability

Characteristic	B/F/TAF (N=350) N (%)
Drug-Related Adverse Events (AEs)[a]	51 (15)
Grade 2-5 Drug-Related AEs	16 (5)
Leading to B/F/TAF discontinuation[b]	8 (2)
Grade 3-4 lab abnormalities[c]	25 (7)
Serious AEs	0
Death	0

[a]The most common drug-related AEs were fatigue (4%), weight gain (3%), and arthralgia (3%)
[b] These included diarrhea (2), dizziness (2), arthralgia (2), creatinine elevation (1) and abdominal pain (1)
[c] These included hypertriglyceridemia (14), hyperglycemia (9), hypercholesterolemia (1), and transaminitis (1)

Median (range) percent change from baseline in weight was +1.2% (-12.6-35.8%) with B/F/TAF at Week 48. Absolute median increase in weight was 2.3 lb. 63 (19%) experienced ≥5% weight gain and 15 (5%) experienced ≥ 10% weight gain. 23 (7%) experienced ≥5% weight loss and 6 (2%) experienced ≥ 10% weight loss

CONCLUSIONS:

- In this real-world cohort, switching to B/F/TAF was associated with high virologic suppression at 94%, improvement in lipid parameters, and avoidance of DDIs in a large proportion of patients
- B/F/TAF was well-tolerated with low rates of Grade 2-5 drug-related AEs (5%) and discontinuations due to drug-related AEs (2%)
- These data support use of B/F/TAF as a treatment option in older PLWH

References
[1] Centers for Disease Control and Prevention. HIV Surveillance Report, 2018 (Updated); vol. 31. Available at http://www.cdc.gov/hiv/library/reports/surveillance/. Published May 2020.
[2] Ramgopal M., et al., Pooled analysis of 4 international trials of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in adults aged >65 or older demonstrating safety and efficacy: Week 48 results. Abstract OA80403. IAC 2020 July 6-10; Virtual
[3]Maggiolo F., et al., A Phase 3b, multicenter, open-label study switching from an Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide(E/C/F/TAF) or a Tenofovir disoproxil fumarate containing regimen to Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) in virologically-suppressed, HIV-1 infected subjects aged ≥65 years. Abstract MOPEB238. IAS 2019 July 21-24, Mexico City, Mexico

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