Switching to Bictegravir/Emtricitabine/Tenofovir Alafenamide in Treatment-Experienced People With HIV (PWH) With Baseline Symptoms of Depression/Anxiety and/or Insomnia in the Observational BICSTaR Study

Poster eP.B2.073

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Key Findings

- Participants with pre-existing depression/anxiety and/or insomnia (D/A/I) remained stable through 24 months following switch to B/F/TAF as indicated by:
  - Few changes to D/A/I-related comedications
  - Few B/F/TAF discontinuations (3%) due to drug-related D/A/I AEs
- 21% (26/123) of participants who had baseline (BL) D/A/I AEs also experienced D/A/I AEs (16% were non-drug related and 6% were drug related)
- Virologic effectiveness remained high through 24 months
- Self-reported symptoms associated with D/A/I remained stable over the course of B/F/TAF treatment, as did physical component summary (PCS) scores. Small improvements were observed in mental component summary (MCS) scores and treatment satisfaction over 24 months

Conclusion

- In this cohort of people with HIV (PWH) receiving comedications for pre-existing D/A/I, switching to B/F/TAF:
  - Maintained high virologic effectiveness through 24 months, with few drug-related D/A/I AEs leading to discontinuation of B/F/TAF
  - Resulted in stable HIV symptom scores, mental well-being and treatment satisfaction

Introduction

- Neuropsychiatric symptoms are common among PWH
  - PWH with neuropsychiatric symptoms that require medical treatment often experience a high rate of AEs, resulting in low adherence to their ART and a high risk of treatment failure[1–3]
  - Limited published data are available on the effectiveness and safety of INSTIs in PWH who have neuropsychiatric comorbidities[4–6]
- The guideline-recommended single tablet regimen B/F/TAF[7–9] includes the INSTI bictegravir and is widely used in clinical practice
- BICSTaR is a prospective, multinational, observational cohort study evaluating the real-world effectiveness and safety of B/F/TAF in ART treatment-naïve (TN) and treatment-experienced (TE) PWH
  - In planned interim analyses, BICSTaR has demonstrated the real-world effectiveness and tolerability of B/F/TAF through 3 years (see EACS poster eP.A.081)[10]

Objective

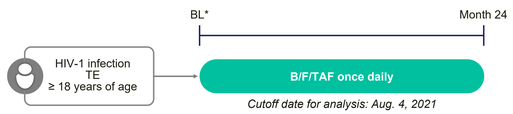
- To assess outcomes through 24 months in TE PWH with pre-existing D/A/I at the time of switching to B/F/TAF in a pooled analysis of the BICSTaR Europe, Canada and Israel cohorts

Methods

- This descriptive analysis included 123 (13% of 963*) participants with BL D/A/I comedication(s)
- D/A/I comedication(s) were used as a proxy to define BL D/A/I status
  - Participants who received ≥ 1 comedication at BL were classified as having D/A/I according to the reported comedication indication
  - If participants had ≥ 2 conditions, they were counted once in the analysis
  - Comedication for five participants was not specifically labeled as D/A/I, but as "neuropsychiatric disorder". The participants were included in this analysis as the drugs prescribed were indicated for D/A/I only
- Study outcomes examined at 24 months in PWH and BL D/A/I were:
  - D/A/I AEs and drug-related D/A/I AEs
    - D/A/I AEs were primarily defined according to MedDRA classification (Preferred Terms), but to ensure as many potential D/A/I AEs were captured as possible, AEs were considered to be related to D/A/I if the MedDRA high-level group term was in the following list: anxiety disorders and symptoms, sleep disorders and disturbances, depressed mood disorders and disturbances, suicidal behaviors, and self/injurious behaviors not elsewhere classified
  - Change in D/A/I comedication(s) (started, stopped or changed† regimen)
  - HIV-1 RNA < 50 c/mL
  - Patient-reported outcomes (PROs): changes in HIV-SI (mental health–related symptoms only), SF-36 PCS/MCS scores‡ and HIVTSQ (treatment satisfaction)

*N = number of participants with 24-month data; †Change defined as one medication stopped, and within 3 months, another medication for the same indication started; ‡The analysis of HIV-SI and PCS/MSC scores included participants with questionnaire data at BL and Month 12 or Month 24, respectively.

Study Design



*This analysis included participants with BL D/A/I comedication(s) only

Results

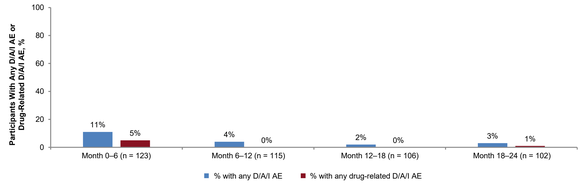
Baseline Characteristics

Characteristic	With D/A/Is at BL (N = 123)
Sex, n (%)	
Male	104 (85)
Female	19 (15)
Race,* n (%)	
White	104 (85)
Black	7 (6)
Asian	4 (3)
Other	6 (5)
Age	
Median (Q1, Q3), years	52 (43, 59)
≥ 50 years, n (%)	69 (56)
Any other ongoing comorbidity, n (%)	123 (100)
Hyperlipidemia	36 (29)
Hypertension	30 (24)
HIV-1 RNA viral load, n (%)	
n	108
< 50 c/mL	101 (94)
< 200 c/mL	5 (5)
> 100,000 c/mL	1 (< 1)
Time from HIV diagnosis to B/F/TAF initiation, years, median (Q1, Q3)	12 (7, 18)
CD4, n	107
Median (Q1, Q3), cells/µL	650 (407, 854)
CD4/CD8 ratio, n	96
Median (Q1, Q3)	0.8 (0.6, 1.1)
CD4 nadir, n	112
Median (Q1, Q3), cells/µL	245 (118, 383)
Ongoing neuropsychiatric conditions, n (%)	
Depression/anxiety	93 (76)
Insomnia	41 (33)
Depression/anxiety plus insomnia	11 (9)
Number of ongoing neuropsychiatric comedications, n (%)	123 (99†)
1	83 (67)
2	30 (24)
≥ 3	10 (8)
Prior ART, n (%)	
INSTI	84 (68)
DTG	43 (35)
EVG	21 (16)
RAL	20 (16)
PI	21 (17)
NNRTI	24 (20)

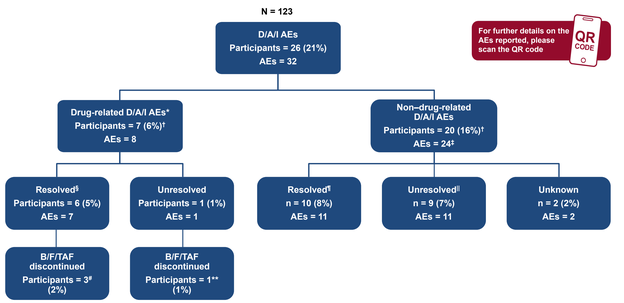
*Race data were not permitted to be collected for 2 participants; †Percentages do not equal 100% due to rounding.

- BL characteristics of participants with D/A/I were generally similar to those reported for the overall study population[11]

Proportion of Participants With D/A/I AEs Through 24 Months Over Time



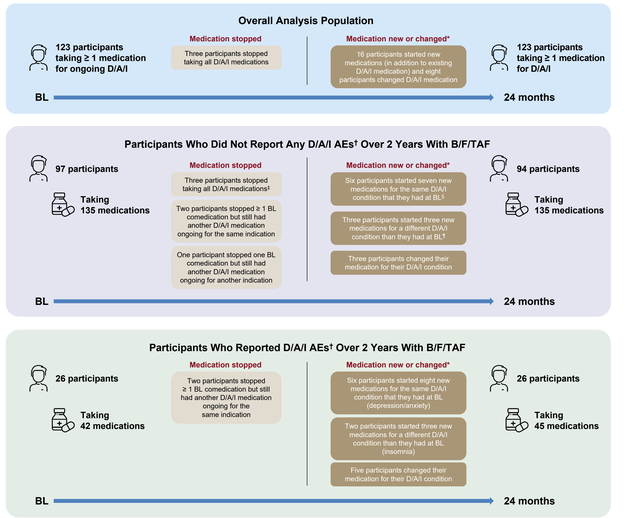
D/A/I AEs Reported Through 24 Months



*No drug-related serious D/A/I AEs were reported; †One participant had both drug-related and non–drug-related AEs; ‡None were due to HIV, six were due to an underlying condition, 14 to intercurrent illness, one due to comedication, two due to stress and one due to jetlag; §One participant had two AEs that resolved with sequalae; ‖One participant had one AE that resolved with sequalae; ¶Four were described as "resolving"; **One participant switched to DTG/RPV, one participant switched to RAL and F/TAF, and one participant switched to F/RPV/TAF; ††Switched to DOR/lamivudine/TDF.

- For three participants, drug-related D/A/Is resolved while still receiving B/F/TAF

Change in D/A/I Comedications in Participants



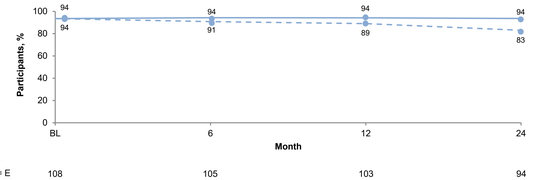
*Change defined as one medication stopped, and within 3 months, another medication for the same indication started; †Drug-related and non–drug-related D/A/I, included no worsening of D/A/I AE; ‡Two of whom switched medications before stopping; §Two participants started three medications for insomnia, one participant started one medication for depression/anxiety, and three participants started three medications for depression; ¶One participant started one medication for depression/anxiety and two participants started two medications for insomnia.

Drug-Related D/A/I AEs and Changes in D/A/I-Related Comedications

	BL D/A/I condition	B/F/TAF start date	B/F/TAF stop date	Worsening of BL D/A/I or new D/A/I AE	BL D/A/I comedication stopped (date)	BL D/A/I comedication unchanged	BL D/A/I comedication changed* or comedication added to BL comedication (date)	
							Same D/A/I indication	Different D/A/I indication
1	D/A	November 2018	Lost to follow-up since November 2019	Worsening anxiety	Venlafaxine (Sep. 9, 2019)	–	Bupropion (Aug. 19, 2019)	None changed or added
2	D	August 2019	–	Worsening depression	–	Citalopram	None changed or added	None changed or added
3	D	July 2018	Ongoing	Worsening depression	Duloxetine (Aug. 31, 2018)	–	Escitalopram (Sep. 14, 2018) Bupropion (Nov. 7, 2018)	None changed or added
4	D	February 2019	Ongoing	New colorful dreams	–	Duloxetine	None changed or added	None changed or added
5	D/A	May 2019	January 2020	New sleeping disorder	–	Oxazepam, alprazolam, bupropion	None changed or added	None changed or added
6	D	July 2019	–	New anxiety + worsening depression	–	Escitalopram	None changed or added	None changed or added
7	D	August 2018	October 2018	New insomnia + worsening depression	–	Citalopram	None changed or added	None changed or added

*Change defined as one medication stopped, and within 3 months, another medication for the same indication started.

Virologic Suppression (HIV-1 RNA < 50 c/mL) Through 24 Months in Participants With D/A/I



n = number of participants with available viral load data.
*Denominator includes those participants discontinuing B/F/TAF prior to the visit window, and in such cases viral load was imputed as ≥ 50 c/mL.

- Virologic effectiveness remained high through 24 months

PRO Measures at BL, and Change in Score at 12 and 24 Months

PRO measure	BL*	Change at 12 months*	BL†	Change at 24 months†
HIV-SI score‡				
Felt sad, down or depressed, median (Q1, Q3) / N	2.0 (0.0, 3.0) / 82	0.0 (-1.0, 0.0) / 82	1.0 (0.0, 2.0) / 77	0.0 (-1.0, 1.0) / 77
Min, max	0.0, 4.0	-4.0, 4.0	0.0, 4.0	-4.0, 3.0
Felt nervous or anxious, median (Q1, Q3) / N	1.0 (0.0, 3.0) / 79	0.0 (-1.0, 0.0) / 79	1.0 (0.0, 2.0) / 73	0.0 (-1.0, 0.0) / 73
Min, max	0.0, 4.0	-3.0, 3.0	0.0, 4.0	-3.0, 3.0
Difficulty falling/staying asleep, median (Q1, Q3) / N	2.0 (0.0, 3.0) / 82	0.0 (-1.0, 0.0) / 82	2.0 (0.0, 3.0) / 76	0.0 (-1.0, 0.0) / 76
Min, max	0.0, 4.0	-4.0, 4.0	0.0, 4.0	-4.0, 4.0
SF-36 score§				
MCS score, median (Q1, Q3) / N	44.1 (33.8, 51.4) / 77	+1.7 (-3.7, 7.3) / 77	44.0 (35.2, 51.4) / 75	+0.7 (-2.9, 7.9) / 75
Min, max	15.1, 61.2	-28.3, 38.4	15.1, 61.2	-33.6, 34.2
PCS score, median (Q1, Q3) / N	53.1 (46.4, 57.2) / 77	+0.8 (-3.3, 4.1) / 77	53.1 (47.0, 57.5) / 75	-0.9 (-4.3, 2.4) / 75
Min, max	31.1, 65.0	-20.4, 19.3	31.1, 65.0	-18.6, 15.6
HIVTSQ score¶				
Median (Q1, Q3) / N	NA	NA	53.0 (49.5, 59.5) / 35	+3.0 (0.0, 7.5) / 35
Min, max	NA	NA	8.0, 60.0	-26.0, 46.0

*For participants with data available at both BL and 12 months; †For participants with data available at both BL and 24 months; ‡HIV-SI individual symptoms scored as 0 (do not have symptom), 1 (have symptom, but no bother), 2 (have symptom, little bother), 3 (have symptom, bother), 4 (have symptom, bothers me a lot); §SF-36 measured on a scale of 0–100, where > 50 is better than average function; ¶HIVTSQ measured on a scale of 0–60, with 60 representing highest treatment satisfaction.

Limitations

- Baseline D/A/I diagnoses were not documented; medication for D/A/I was used as a proxy for diagnosis
- Some people with drug-resistant D/A/I may not be taking medication and some people with D/A/I are not treated with medication; therefore, this methodology could potentially underestimate the proportion of participants with D/A/I
- As BICSTaR is not a controlled study, it is not possible to show a causal association between B/F/TAF and these findings

References: 1. Desta F, et al. BMC Psychiatry 2022;22:557. **2.** Gonzalez JS, et al. J Acquir Immune Defic Syndr 2011;58:181-187. **3.** Pence BW, et al. JAMA Psychiatry 2018;75:379-385. **4.** Hoffman C, et al. Antivir Ther 2020;25:83-90. **5.** Pérez-Valero I, et al. Expert Rev Anti Infect Ther 2023;21:655-665. **6.** Suárez-Garcia I, et al. J Antimicrob Chemother 2023;78:1423-1432. **7.** Gandhi RT, et al. JAMA 2023;329:63-84. **8.** DHHS. https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv (accessed Aug. 7, 2023). **9.** EACS. https://www.eacsociety.org/guidelines/eacs-guidelines/ (accessed Aug. 7, 2023). **10.** Miralles C, et al. EACS 2023, Poster eP.A.081. **11.** Trottier B, et al. HIV Glasgow 2022, Poster P067.

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Abbreviations: AE, adverse event; ART, antiretroviral therapy; B, bictegravir; BICSTaR, BICtegravir Single Tablet Regimen; BL, baseline; c, copies; CD, cluster of differentiation; D/A/I, depression/anxiety and/or insomnia; D = F, discontinuation = failure; DOR, doravirine; DTG, dolutegravir; EACS, European AIDS Clinical Society; EVG, elvitegravir; F, emtricitabine; HIV-SI, HIV Symptom Index; HIVTSQ, HIV Treatment Satisfaction Questionnaire; INSTI, integrase strand-transfer inhibitor; max, maximum; MCS, mental component summary; M = E, missing = excluded; MedDRA, Medical Dictionary for Regulatory Activities; min, minimum; NA, not available; NNRTI, non-nucleoside reverse transcriptase inhibitor; PCS, physical component summary; PI, protease inhibitor; PRO, patient-reported outcome; PWH, people with HIV; Q, quartile; RAL, raltegravir; RPV, rilpivirine; SF-36, 36-Item Short Form Survey; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TE, treatment-experienced; TN, treatment-naïve.