

# 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



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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<sup>1-3</sup>
  - Limited published data are available on the effectiveness and safety of INSTIs in PWH who have neuropsychiatric comorbidities<sup>4-6</sup>
- The guideline-recommended single tablet regimen B/F/TAF<sup>7-9</sup> 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)<sup>10</sup>

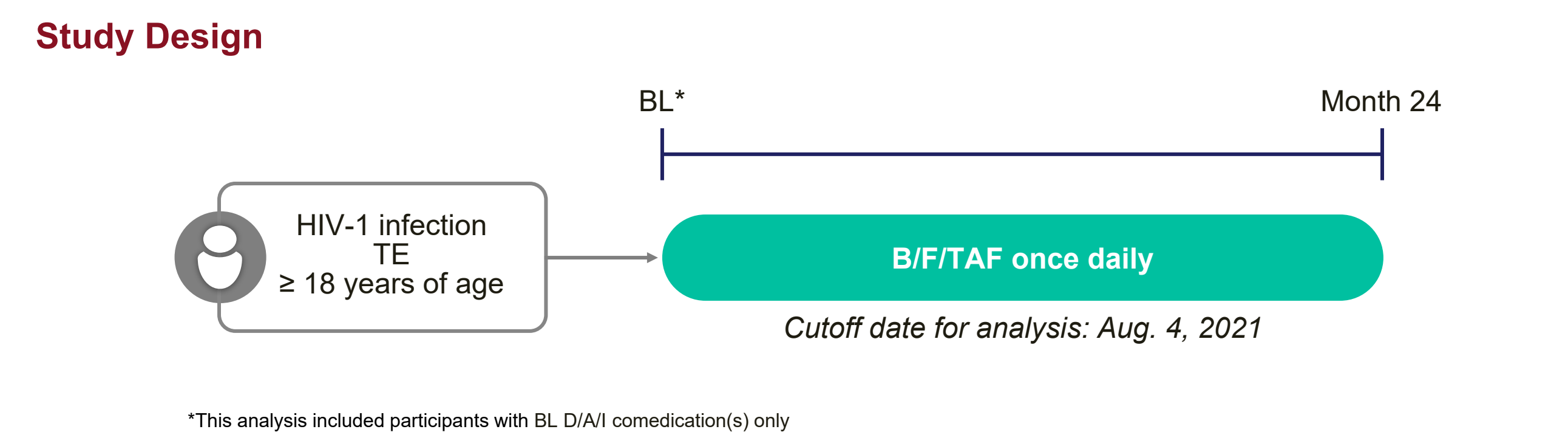
### Objective

- 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  $\geq 1$  comedication at BL were classified as having D/A/I according to the reported comedication indication
  - If participants had  $\geq 2$  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<sup>†</sup> regimen)
  - HIV-1 RNA < 50 c/mL
  - Participant-reported outcomes (PROs): changes in HIV-SI (mental health-related symptoms only), SF-36 PCS/MCS scores<sup>‡</sup> 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/MCS scores included participants with questionnaire data at BL and Month 12 or Month 24, respectively.



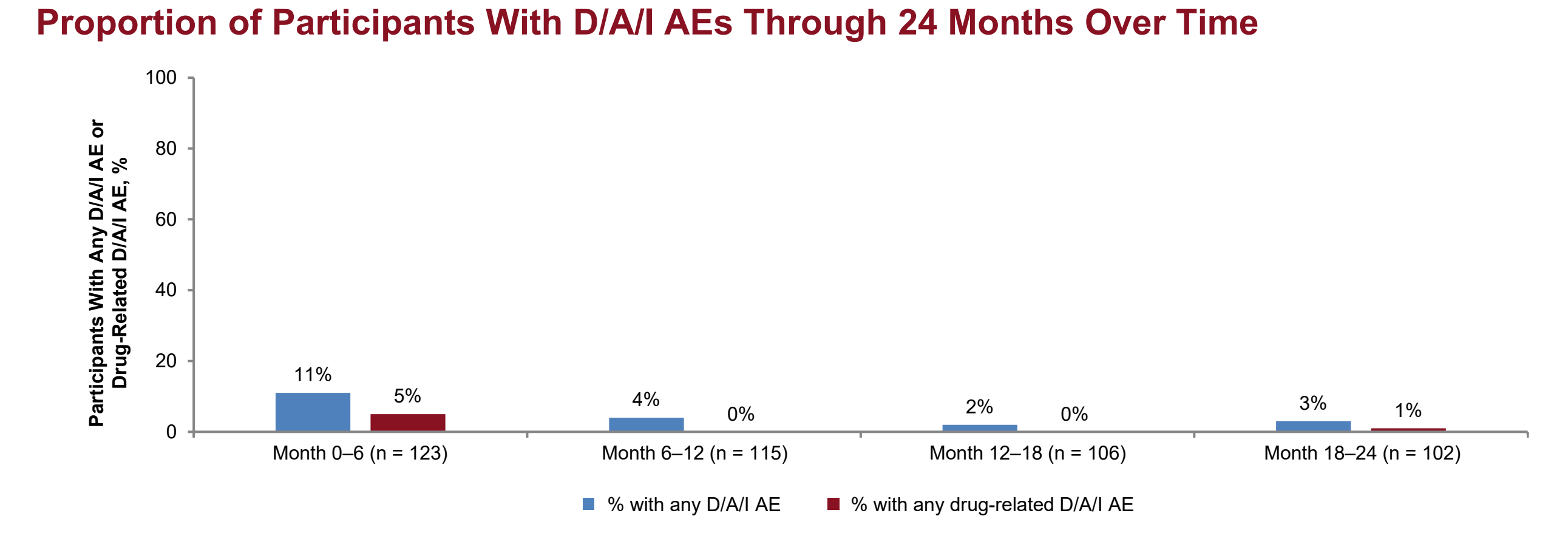
### Results

#### Baseline Characteristics

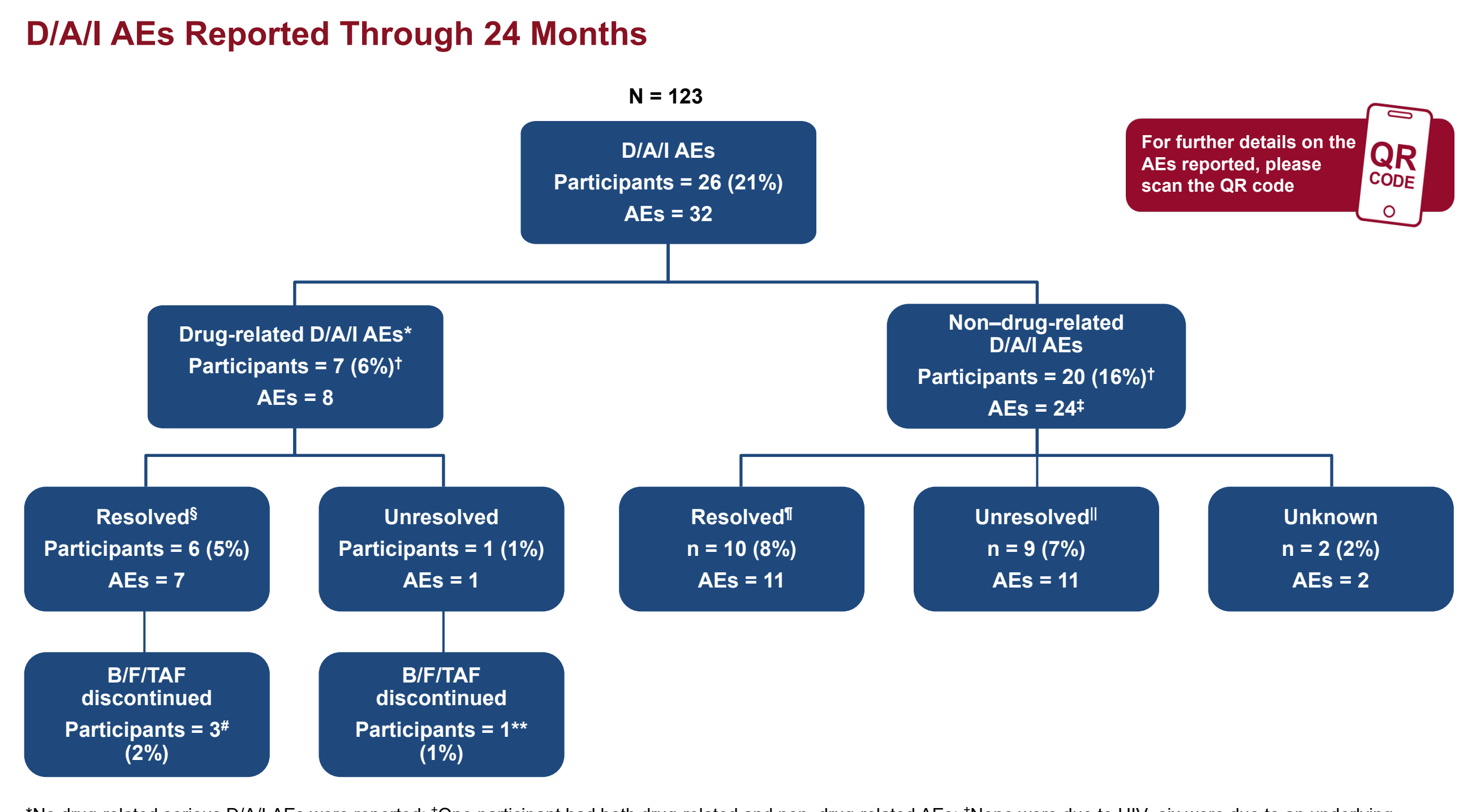
| Characteristic  | With D/A/I at BL (N = 123) |
|---|----------------------------|
| Sex, n (%)  |                            |
| Male  | 104 (85)                   |
| Female  | 19 (15)                    |
| Race, <sup>*</sup> n (%)  |                            |
| White   | 104 (85)                   |
| Black   | 7 (6)                      |
| Asian   | 4 (3)                      |
| Other   | 6 (5)                      |
| Age   |                            |
| Median (Q1, Q3), years  | 52 (43, 59)                |
| $\geq 50$ 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/ $\mu$ L                                       | 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/ $\mu$ L                                       | 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 (%)               |                            |
| 1   | 123 (99) <sup>†</sup>      |
| 2   | 83 (67)                    |
| $\geq 3$  | 30 (24)                    |
| 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<sup>11</sup>



\*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/MCS scores included participants with questionnaire data at BL and Month 12 or Month 24, respectively.



\*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 "resolved"; †††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/I AEs resolved while still receiving B/F/TAF

### Change in D/A/I Comedications in Participants

#### Overall Analysis Population

123 participants taking  $\geq 1$  medication for ongoing D/A/I at BL

24 months

123 participants taking  $\geq 1$  medication for D/A/I at 24 months

Medication stopped: Three participants stopped taking all D/A/I medications

Medication new or changed\*: 18 participants started new medications (in addition to existing D/A/I medication) and eight participants changed D/A/I medication

#### Participants Who Did Not Report Any D/A/I AEs\* Over 2 Years With B/F/TAF

97 participants Taking 135 medications at BL

24 months

94 participants Taking 135 medications at 24 months

Medication stopped: Three participants stopped taking all D/A/I medications†

Medication new or changed\*: Six participants started seven new medications for the same D/A/I condition that they had at BL†

#### Participants Who Reported D/A/I AEs\* Over 2 Years With B/F/TAF

26 participants Taking 42 medications at BL

24 months

26 participants Taking 45 medications at 24 months

Medication stopped: Two participants stopped  $\geq 1$  BL comedication but still had another D/A/I medication ongoing for the same indication

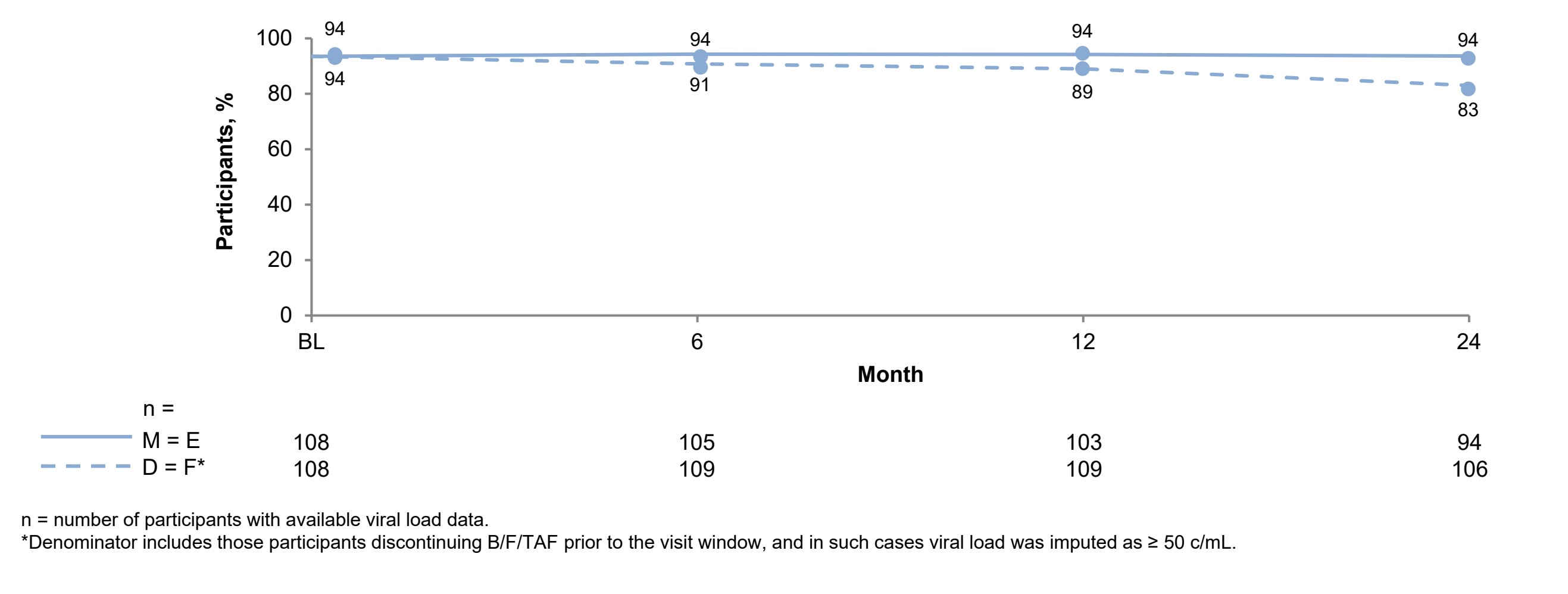
Medication new or changed\*: Six participants started eight new medications for the same D/A/I condition that they had at BL (depression/anxiety)

\*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 depression, 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

| Participant | 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)<br>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 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 <sup>†</sup>        | Change at 24 months <sup>†</sup> |
|--|------------------------|-----------------------|------------------------|----------------------------------|
| <b>HIV-SI score<sup>‡</sup></b>                        |                        |                       |                        |                                  |
| 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                        |
| <b>SF-36 score<sup>‡</sup></b>                         |                        |                       |                        |                                  |
| 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                      |
| <b>HIVTSQ score<sup>‡</sup></b>                        |                        |                       |                        |                                  |
| 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-García 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-art> (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, SF-36 Item Short Form Survey; TAF, tenofovir disoproxil fumarate; TE, treatment-experienced; TN, treatment-naïve.