THREE-YEAR B/F/TAF USE IN TREATMENT-NAÏVE AND TREATMENT-EXPERIENCED PEOPLE LIVING WITH HIV IN THE BICSTaR COHORT STUDY

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DÖAK 2023 DEUTSCH-ÖSTERREICHISCHER AIDS-KONGRESS

Poster 80874

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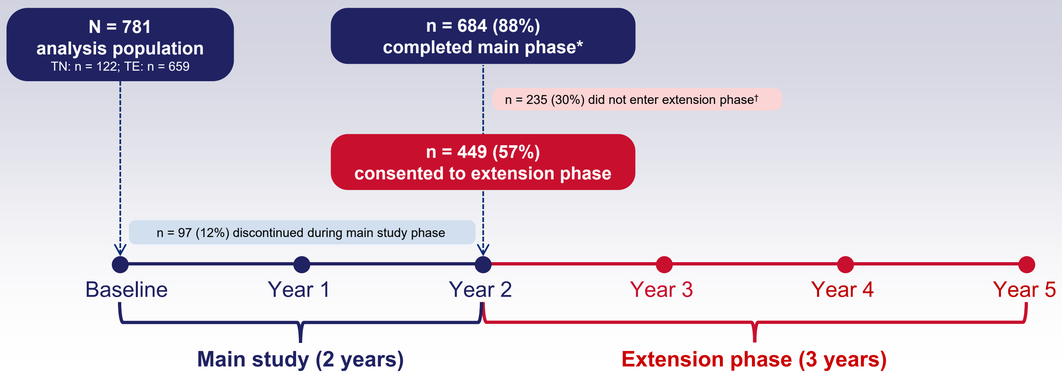
Background

- BICSTaR (BICtegravir Single Tablet Regimen) is an ongoing, multi-country, noninterventional, prospective cohort study evaluating the effectiveness and safety of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in clinical practice in antiretroviral treatment-naïve (TN) and antiretroviral treatment-experienced (TE) people living with HIV
- B/F/TAF demonstrated effectiveness and tolerability after 2 years in a pooled analysis of the large, real-world BICSTaR study cohort[1]
- All participants in Canada, France and Germany who completed the main study were given the opportunity to participate in an extension phase for an additional 3 years, thereby providing up to 5 years of real-world data on B/F/TAF use
- Here, we report pooled **effectiveness and safety** data through 3 years (2 years of main study plus 1 year of extension phase) in people receiving B/F/TAF in routine clinical care

Methods

- This interim analysis includes pooled data collected up to August 2022 in 781 participants (Canada: 177; France: 213; Germany: 391)
- The full analysis population includes participants who had a visit at 36 months and those who discontinued B/F/TAF having initiated treatment ≥ 30 months (lower bound of the 36 month visit window) prior to the data cutoff date
- **Virological and immunological outcomes**, **adverse events (AEs)** and **drug-related AEs (DRAEs), weight changes, metabolic assessments** and **patient-reported outcomes** (HIV–Symptom Index [HIV-SI] and 36-Item Short Form Survey [SF-36] physical component summary [PCS]/mental component summary [MCS] scores) were collected

Participant disposition



*Participants could complete the main phase either on B/F/TAF or on an alternative antiretroviral treatment regimen following discontinuation of B/F/TAF treatment; †Participants who were no longer on B/F/TAF after completing the main phase or who did not consent to the extension phase

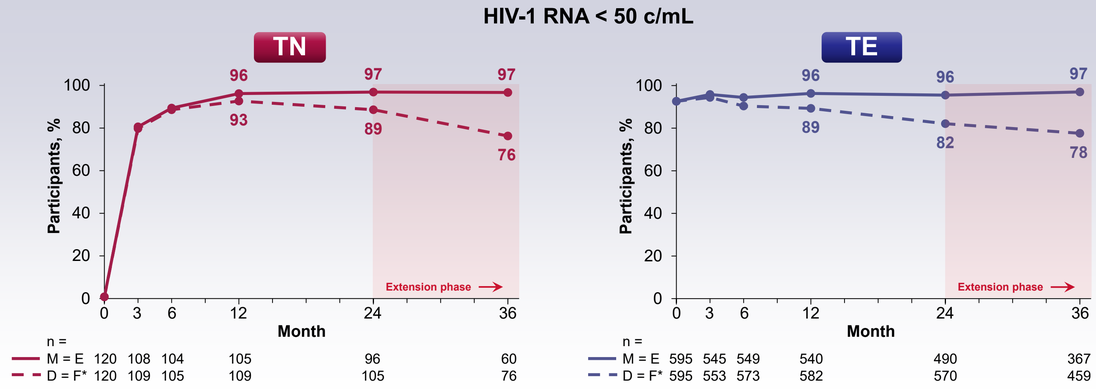
Results

Participant characteristics at baseline

TN n = 122		TE n = 659
90%	Male	87%
39 (30, 51)	Age,* years	49 (39, 56)
26% / 6%	≥ 50 years / ≥ 65 years	48% / 8%
71 (64, 82)	Weight,* kg	78 (67, 87)
23 (21, 26)	BMI,*,† kg/m²	25 (22, 28)
80% / 10% / 4%	White / Black / Asian	82% / 10% / 3%
53%	Ongoing comorbidity‡	76%
19%	Neuropsychiatric condition	32%
7%	Hyperlipidemia	21%
9%	Hypertension	20%
47%	Any concomitant medication	63%
1%	HIV-1 RNA < 50 c/mL§	93%
39%	HIV-1 RNA > 100,000 c/mL§	< 1%
425 (184, 543)	CD4 count,*,¶ cells/μL	657 (430, 870)
0.3 (0.2, 0.6)	CD4/CD8 ratio*,‖	0.9 (0.6, 1.2)
8%	≥ 1 primary mutation#	12%
4% / 2% / 2% / 0	NNRTI / PI / NRTI / INSTI primary mutation	6% / 2% / 6% / < 1%
28%	Late diagnosis: CD4 < 200 cells/μL and/or ≥ 1 AIDS-defining event**	NA

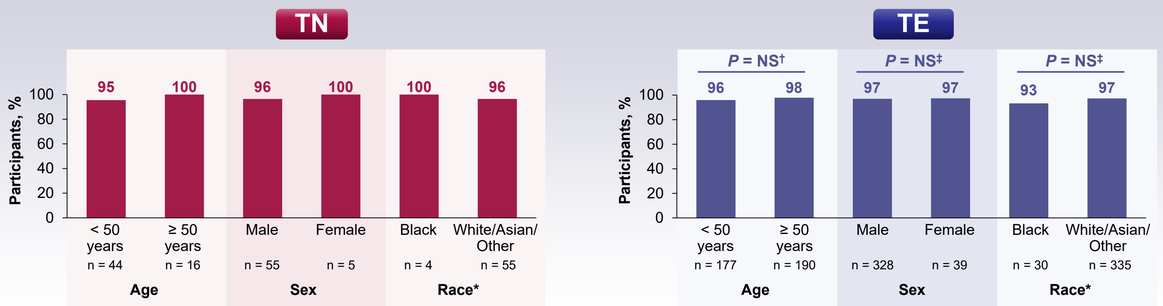
*Median (Q1, Q3); †n = 109 (TN), 574 (TE); ‡n = 120 (TN), 659 (TE); §n = 120 (TN), 595 (TE); ¶n = 115 (TN), 575 (TE); ‖n = 109 (TN), 525 (TE); #n = 118 (TN), 617 (TE); **n = 117 (TN), n = 0 (TE)
BMI, body mass index; c, copies; CD, cluster of differentiation; INSTI, integrase strand transfer inhibitor; NA, not applicable; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; Q, quartile

Virological effectiveness through 3 years: Overall (M = E and D = F analyses)



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
D = F, discontinuation = failure; M = E, missing = excluded

Virological effectiveness at 3 years: Key populations (M = E analysis)



Statistical tests were performed to compare subgroups containing > 20 participants. *Data were available at 3 years for three participants with missing race (TN: n = 1; TE: n = 2), all of whom had HIV-1 RNA < 50 c/mL; †Chi-square test (H_0: equal proportions in the key groups); ‡Fisher exact test (H_0: equal proportions in the key groups)
NS, not significant

No treatment-emergent resistance to the components of B/F/TAF was reported through 3 years

Treatment discontinuations through 3 years

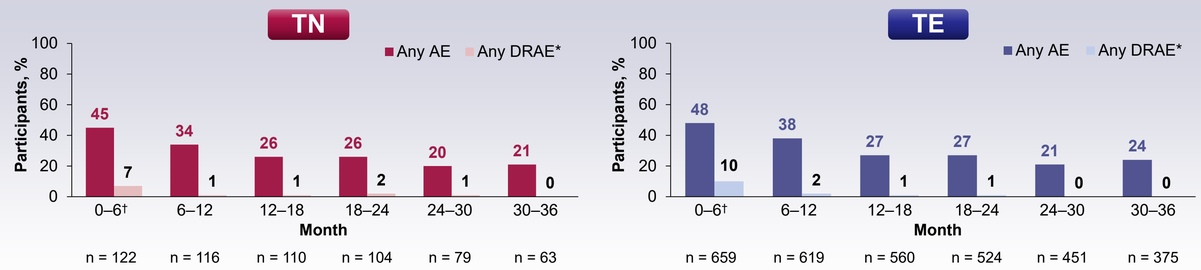
The most common reasons for B/F/TAF discontinuation in the overall population were AEs (8%), participant decision (2%) and investigator's discretion (2%)

Immunological outcomes at 3 years

	Median (Q1, Q3)	Baseline	TN n = 52*	Median change at 3 years	Baseline	TE n = 302*	Median change at 3 years
CD4 cell count, cells/μL		439 (302, 581)	→	+232 (118, 442) P < 0.001†	670 (464, 891)	→	+44 (-70, 150) P < 0.001†
CD4/CD8 ratio		0.42 (0.20, 0.59)	→	+0.50 (0.29, 0.75) P < 0.001‡	0.88 (0.60, 1.26)	→	+0.06 (-0.03, 0.20) P < 0.001‡

*Population with data available at baseline and 3 years; †Signed rank test (H_0 median = 0); ‡Sign test (H_0 median = 0). Median changes were calculated from the individual participant changes from baseline to 3 years

AEs through 3 years



n = the number of participants still in the study on B/F/TAF at the start of the visit window. *The most frequent DRAEs in the total population (n = 781) were weight increase (n = 31; 4%), depression (n = 12; 2%), fatigue (n = 8; 1%) and nausea (n = 8, 1%). Two TE participants experienced a serious DRAE (depression), which occurred in Months 0–6. There were no serious DRAEs at later timepoints or among TN participants. A total of 54 participants (7%) discontinued B/F/TAF due to a DRAE. The most common DRAEs leading to B/F/TAF discontinuation were weight increase (n = 19, 2%), depression (n = 7, 1%) and fatigue (n = 6, 1%); †33% of TN participants and 32% of TE participants experienced an AE within the first 3 months of starting B/F/TAF

Weight change at 3 years

	Median (Q1, Q3)	Baseline	TN n = 40*	Median change at 3 years	Baseline	TE n = 263*	Median change at 3 years
Weight, kg		72 (66, 82)	→	+4.3 (-0.5, 7.3) P = 0.003†	78 (67, 87)	→	+1.7 (-1.0, 4.3) P < 0.001†
BMI, kg/m²		23 (22, 27)	→	+1.5 (-0.1, 2.5) P = 0.003†	25 (22, 28)	→	+0.5 (-0.3, 1.5) P < 0.001†

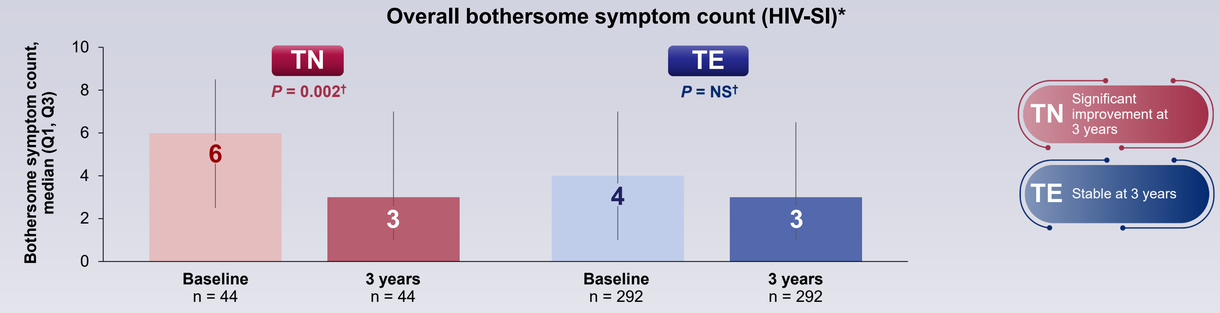
*Population with weight and BMI data available at baseline and 3 years; †Sign test (H_0 median = 0). Median changes were calculated from the individual participant changes from baseline to 3 years

Metabolic and renal assessment at 3 years

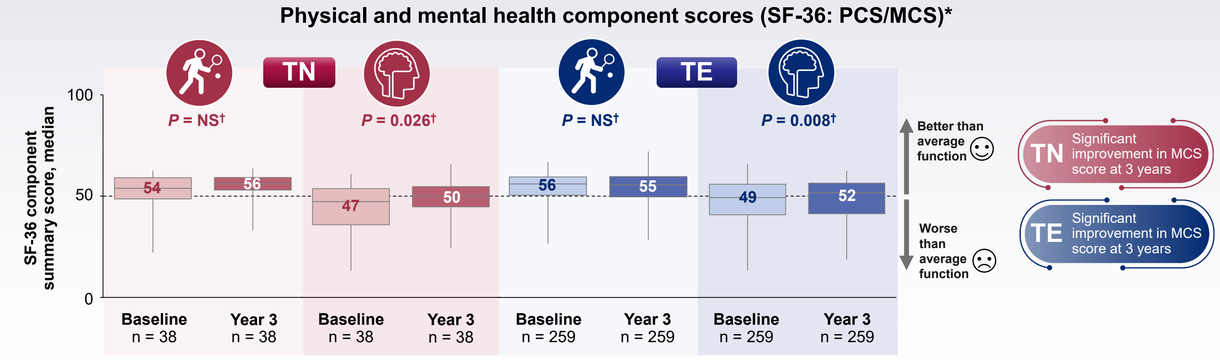
	TN		TE	
Median (Q1, Q3)	Baseline	Median change from baseline at 3 years	Baseline	Median change from baseline at 3 years
Total cholesterol, mg/dL	n = 37 84.69 (74.60, 96.22)	n = 37 2.88 (-2.52, 16.40)	n = 195 84.51 (72.79, 97.12)	n = 195 1.62 (-8.47, 11.17)
Low-density lipoprotein, mg/dL	n = 31 53.15 (46.67, 64.14)	n = 31 3.78 (-7.57, 13.15)	n = 167 53.15 (41.62, 64.32)	n = 167 2.16 (-9.37, 10.09)
High-density lipoprotein, mg/dL	n = 34 19.28 (16.76, 25.59)	n = 34 1.62 (-2.16, 5.05)	n = 171 20.54 (17.30, 26.67)	n = 171 0.00 (-2.52, 2.34)
Triglycerides, mg/dL	n = 36 24.87 (12.79, 35.50)	n = 36 0.54 (-11.71, 11.89)	n = 195 27.03 (17.84, 39.82)	n = 195 -0.18 (-8.83, 7.21)
Glucose, mg/dL	n = 34 96.58 (88.11, 102.70)	n = 34 3.60 (-9.01, 14.05)	n = 198 93.15 (84.69, 101.08)	n = 198 **2.70 (-7.21, 14.05)** P = 0.045
Creatinine, mg/dL	n = 53 0.91 (0.79, 1.00)	n = 53 **0.11 (0.04, 0.20)** P < 0.001	n = 320 1.00 (0.88, 1.14)	n = 320 **0.02 (-0.06, 0.10)** P = 0.001
eGFR, mL/min/1.73 m²	n = 36 114.82 (92.72, 127.95)	n = 36 -8.5 (-19.3, 4.2)	n = 235 94.18 (76.04, 114.90)	n = 235 -1.2 (-8.9, 7.2)

Population with data available at baseline and at 3 years. Only significant *P*-values are shown, calculated using the Sign test (H_0 median = 0). Median changes were calculated from the individual participant changes from baseline to 3 years. Changes in creatinine and eGFR are consistent with the known effect of bictegravir to inhibit the tubular secretion of creatinine.[2,3] eGFR, estimated glomerular filtration rate

Patient-reported outcomes at 3 years



Population with data available at baseline and at 3 years. *Overall bothersome symptom count indicates the number of bothersome symptoms and ranges from 0 to 20; †Signed rank test (H_0 median = 0)



Population with data available at baseline and at 3 years. Box plot represents minimum, Q1, median, Q3, and maximum values. *Scores are standardized: > 50 represents better than average function compared with the U.S. general population; †Signed rank test (H_0 median = 0)

Conclusions

- These real-world data through 3 years continue to support the use of B/F/TAF in TN and TE people living with HIV
  - The rate of virological effectiveness was high, with no treatment-emergent resistance
  - Significant improvements were seen in immunological outcomes (CD4 cell count and CD4/CD8 ratio)
  - Few DRAEs were identified, the majority of which occurred in the first 6 months
  - Weight changes were consistent with previous studies in TN and TE populations[4,5]
  - Significant improvements were observed in HIV-related bothersome symptoms (TN) and mental health scores (TN and TE)

References
1. Trottier B, et al. HIV Glasgow 2022, Poster 067; 2. Biktarvy® EU SmPC, Gilead Sciences, January 2023; 3. Biktarvy® U.S. Prescribing Information, Gilead Sciences, October 2022; 4. Erlandson KM, et al. Clin Infect Dis 2021;73:1440-1451; 5. Workowski K, et al. CROI 2021, Poster 2268

Abbreviations
AE, adverse event; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BICSTaR, Bictegravir Single Tablet Regimen; BMI, body mass index; c, copies; CD, cluster of differentiation; D = F, discontinuation = failure; DRAE, drug-related adverse event; eGFR, estimated glomerular filtration rate; HIV-SI, HIV-Symptom Index; INSTI, integrase strand transfer inhibitor; MCS, mental component summary; M = E, missing = excluded; NA, not applicable; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; NS, not significant; PCS, physical component summary; PI, protease inhibitor; Q, quartile; SF-36, 36-Item Short Form Survey; TE, treatment-experienced; TN, treatment-naive

Acknowledgments
We thank Andrea Marongiu for the analysis and interpretation of the data for this poster. We thank all study participants and participating study sites. The BICSTaR study is sponsored by Gilead Sciences. Medical writing support was provided by Anne Errichelli, DPhil (Aspire Scientific Ltd, U.K.), and was funded by Gilead.

Disclosures
BICSTaR is sponsored by Gilead (GS-EU-380-4472/GS-CA-380-4574/GS-IL-380-5335). S Schellberg: speaker/advisory fees/grants from AbbVie, Gilead, Janssen-Cilag, Pfizer, Sanofi, Theratechnologies and ViiV. PK: consulting fees/honoraria from AbbVie, Gilead, Johnson & Johnson, Sanofi and ViiV. CW: consulting fees/honoraria from AbbVie, AstraZeneca, Gilead, GSK, Janssen, MSD, Pfizer, Roche and ViiV. JDW: speaker/advisory board fees from Gilead, Merck and ViiV; study funding/study drug provision from Gilead for the BICSTaR study. AW: grants/honoraria from AbbVie, Gilead, Merck and ViiV. CD: consulting fees/speaker honoraria/travel grants from Gilead, MSD and ViiV. OR: personal fees from Gilead, MSD and ViiV. CDS: grants/personal fees from AbbVie, Janssen-Cilag, MSD and ViiV; grants/fees/non-financial support from Gilead; grants from Cepheid; personal fees from GSK during the conduct of the study; fees from AstraZeneca; other support from Apeiron; grants/personal fees/non-financial support from B. Braun Melsungen; grants/personal fees from BioNTech and Eli Lilly; personal fees from Formycon, Moderna, Molecular Partners, Novartis, Roche, SOBI, Shionogi and Pfizer. BA, S Schreiber, DT, MH, S Sahali, TS, TC: employees of, and own shares in, Gilead.