Four-Year Outcomes From the BICSTaR Study: Observational Analysis of B/F/TAF in Treatment-Naïve and Treatment-Experienced People With HIV in Canada, France, and Germany

P063

BICSTaR

Alexander Wong[1], Daniel Beer[2], Claudine Duvivier[3], Hugues Cordel[4], Anja Meurer[5], David Thorpe[6], Marion Heinzkill[7], Andrea Marongiu[6], Johanna Ramroth[6], Benoit Trottier[8]

[1]University of Saskatchewan, Regina, SK, Canada; [2]PZB Aachen, Praxis/Labor Dr. med. Heribert Knechten, Aachen, Germany; [3]AP-HP-Necker Hospital, Necker-Pasteur Infectiology Center, Paris, France; [4]Hopital Avicenne, Bobigny, France; [5]Zentrum für Innere Medizin und Infektiologie, Munich, Germany; [6]Gilead Sciences Europe Ltd, Stockley Park, Uxbridge, UK; [7]Gilead Sciences GmbH, Martinsried, Germany; [8]Clinique de Médecine Urbaine du Quartier Latin, Montréal, QC, Canada

Conclusions

- The virologic and immunologic benefits of B/F/TAF were maintained through 4 years of follow-up in TN and TE people with HIV in routine clinical care in Canada, France, and Germany
- B/F/TAF was well tolerated; no new safety signals were detected, and few participants discontinued B/F/TAF due to drug-related adverse events
- Measures of quality of life showed improvements in bothersome symptoms and mental health outcomes through 4 years in TN participants
- These longer-term, real-world data continue to support the selection of B/F/TAF as a guidelines-recommended treatment for people with HIV

Plain Language Summary

- B/F/TAF is a pill taken once a day to treat human immunodeficiency virus (HIV); the pill combines three medications: bictegravir (B), emtricitabine (F), and tenofovir alafenamide (TAF)
- In this study, researchers wanted to find out how well B/F/TAF worked and how safe it was in people who took it as part of their usual treatment
- The researchers looked at how well B/F/TAF worked in people from Canada, France, and Germany who had been taking B/F/TAF for 4 years
  - They found that B/F/TAF remained very effective at stopping HIV from showing in the blood
  - B/F/TAF had the same effect in people who were taking it as their first HIV medication and in people who started it after they had taken other HIV medicines
- Researchers found that few people stopped taking B/F/TAF because of side effects that were thought to be related to the medication
- At 4 years of treatment, people taking B/F/TAF as their first HIV medication said their mental health had improved
- This study shows that B/F/TAF is an effective and well-tolerated long-term treatment for people with HIV

Introduction

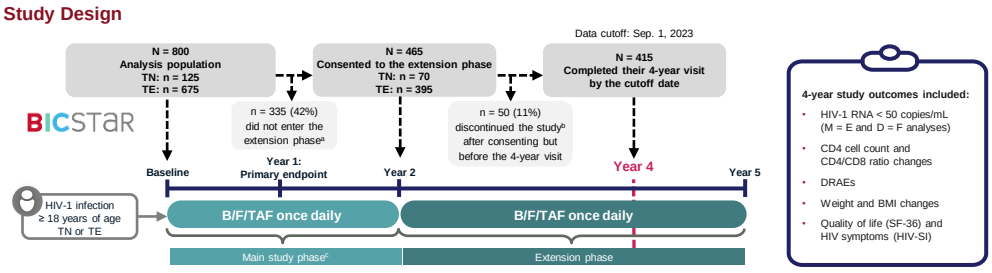
- Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is a guideline-recommended single tablet regimen for the treatment of HIV-1 infection[1-3]
- BICSTaR (BICtegravir Single Tablet Regimen) is a multinational, prospective, observational, 2-year cohort study evaluating the effectiveness and safety of B/F/TAF in treatment-naïve (TN) and treatment-experienced (TE) people with HIV in routine clinical practice[4]
- The study enrolled 2379 people with HIV across five observational cohorts (Asia, Canada, Europe, Israel, and Japan)
- B/F/TAF demonstrated effectiveness and tolerability in pooled analyses involving participants from all five observational cohorts through 2 years in the main phase of the BICSTaR study[5,6]
- Participants in Germany, France, and Canada were able to participate in a study extension phase for an additional 3 years

Objective

- To assess effectiveness and safety outcomes, quality of life, and HIV symptom measures in participants from Canada, France, and Germany who received B/F/TAF over 4 years of follow-up in the BICSTaR study (2 years of main study plus 2 years of extension phase)

Methods

Study Design



The analysis population includes participants who had a visit at 4 years and those who discontinued the study having initiated treatment ≥ 42 months (lower bound of the 4-year visit window) prior to the data cutoff date.
[a]102 participants (13%) discontinued during the main phase, 69 participants (9%) discontinued B/F/TAF but were still in the study at 24 months, and 164 (21%) were eligible for the extension phase but did not re-consent.
[b]Due to: study drug discontinuation (n = 20), loss to follow-up (n = 12), participant's decision (n = 7), death (n = 7), and investigator's discretion (n = 4).
[c]Participants could complete the main study phase either on B/F/TAF or on an alternative antiretroviral therapy regimen following discontinuation of B/F/TAF treatment.
B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BICSTaR, BICtegravir Single Tablet Regimen; BMI, body mass index; CD#, cluster of differentiation #; D = F, discontinuation = failure; DRAE, drug-related adverse event; HIV-SI, HIV Symptom Index; M = E, missing = excluded; SF-36, 36-Item Short Form Health Survey; TE, treatment experienced; TN, treatment naïve.

Results

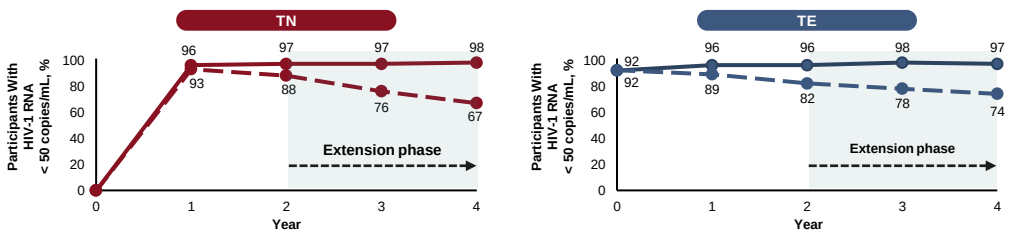
Baseline Characteristics at Entry to the Main Study

	TN (n = 125)	TE (n = 675)
Age, years, median (Q1, Q3)	40 (31, 51)	49 (39, 56)
≥ 50 years, n (%)	34 (27)	326 (48)
≥ 65 years, n (%)	7 (6)	53 (8)
Sex at birth, n (%)		
Male	112 (90)	585 (87)
Female	13 (10)	90 (13)
Race, n (%)[a]		
White	102 (82)	556 (82)
Black	14 (11)	67 (10)
Weight, kg, median (Q1, Q3)[b]	70.0 (65.0, 79.8) [n = 29]	77.0 (66.5, 86.5) [n = 269]
BMI, kg/m², median (Q1, Q3)[b]	23.0 (21.6, 25.2) [n = 29]	24.9 (22.3, 27.7) [n = 269]
Concomitant medication, n (%)	59 (50) [n = 119]	420 (64) [n = 659]
HIV-1 RNA, log_{10} copies/mL, median (Q1, Q3)	4.83 (4.02, 5.36) [n = 123]	1.28 (1.28, 1.28) [n = 608]
HIV viral load > 100,000 copies/mL, n (%)	48 (39) [n = 123]	3 (< 1) [n = 608]
Any medical history or ongoing comorbidity, n (%)[c]	76 (61)	552 (82)
Neuropsychiatric disorder	25 (20)	233 (35)
Hyperlipidemia	9 (7)	146 (22)
Hypertension	12 (10)	141 (21)
Late diagnosis		
CD4 count < 350 cells/µL and/or ≥ 1 AIDS-defining event	54 (45) [n = 121]	N/A
CD4 count < 200 cells/µL and/or ≥ 1 AIDS-defining event	35 (29) [n = 121]	N/A
≥ 1 primary resistance mutation, n (%)	8 (6)	81 (12)
Most common primary resistance mutations relevant to B/F/TAF, n (%)		
NRTI overall / K65R / T69ins / M184V/I	2 (2) / 1 (1) / 0 (0) / 0 (0)	47 (7) / 1 (< 1) / 1 (< 1) / 31 (5)
INSTI overall / T97A	0 (0) / 0 (0)	1 (< 1) / 1 (< 1)

[a]Data on race were missing for one TE participant. [b]Participants with values at baseline and 4 years. [c]Data on comorbidities were missing for one TN participant.
B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BMI, body mass index; CD4, cluster of differentiation 4; INSTI, integrase strand transfer inhibitor; N/A, not available; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; Q, quartile; TE, treatment-experienced; TN, treatment-naïve.

Baseline characteristics were similar in participants who were not eligible for the extension phase and in those who consented to the extension phase

Virologic Effectiveness Through 4 Years (M = E and D = F Analyses)



Number of participants with available viral load data

M = E	123	109	99	60	51
D = F	123	113	109	76	75

Number of participants with available viral load data

M = E	608	557	507	371	352
D = F	608	598	587	464	462

D = F, discontinuation = failure; M = E, missing = excluded; TE, treatment-experienced; TN, treatment-naïve.

Rates of virologic suppression with B/F/TAF were high through 4 years in both the TN and TE groups

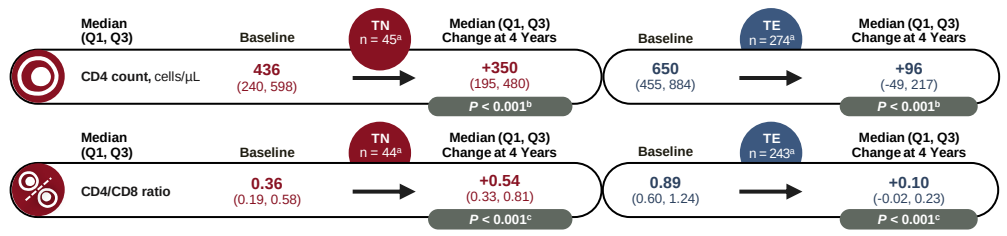
Discontinuations

	TN (n = 125)	TE (n = 675)	Overall (N = 800)
B/F/TAF discontinuations within 4 years, n (%)	23 (18)	120 (18)	143 (18)
Baseline to 2 years (main study phase)	14 (11)	91 (13)	118 (15)
2 to 4 years (extension phase)	9 (7)	29 (4)	25 (3)
Time to B/F/TAF discontinuation, months, median (Q1, Q3)	21.9 (12.6, 36.4)	13.5 (6.4, 28.1)	14.5 (7.5, 32.5)
Reasons for B/F/TAF discontinuation within 4 years, n (%)			
Any AE[a]	9 (7)	55 (8)	64 (8)
Participant's decision	5 (4)	20 (3)	25 (3)
Investigator's decision	5 (4)	15 (2)	20 (3)
Death	2 (2)	12 (2)	14 (2)
New treatment available	2 (2)	9 (1)	11 (1)
Lack of efficacy[b]	0	7 (1)	7 (1)
Pregnancy	0	2 (< 1)	2 (< 1)

[a]Not all AEs leading to discontinuation were considered drug related. [b]Last on-treatment HIV-1 RNA viral loads (copies/mL): 222 (231 days), 66 (1295 days), 131 (272 days), 740 (84 days), 214 (1458 days), 57 (267 days), and 148 (169 days).
AE, adverse event; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; Q, quartile; TE, treatment experienced; TN, treatment naïve.

No treatment-emergent resistance to the components of B/F/TAF was reported through 4 years

Immunologic Outcomes at 4 Years



Median changes were calculated from the individual participant changes from baseline to 4 years. [a]Population with data available at baseline and 4 years. [b]Signed rank test. [c]Sign test.
CD#, cluster of differentiation #; Q, quartile; TE, treatment experienced; TN, treatment naïve.

There were statistically significant increases in CD4 cell count and CD4/CD8 ratio from baseline to 4 years

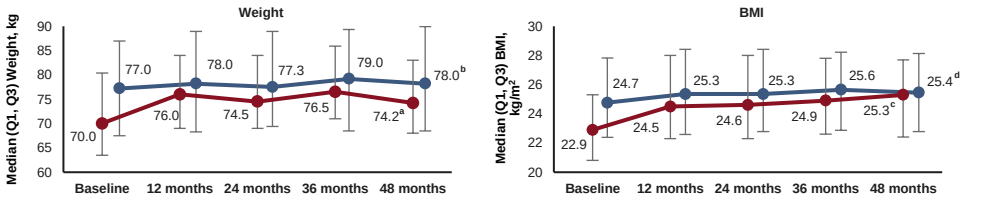
Safety Through 4 Years

n (%)	TN (n = 125)	TE (n = 675)	Overall (N = 800)
Any AE	98 (78)	513 (76)	611 (76)
DRAEs	21 (17)	96 (14)	117 (15)
Most common DRAEs (≥ 1)			
Weight increased	9 (7)	25 (4)	34 (4)
Depression	1 (1)	11 (2)	12 (2)
Fatigue	2 (2)	7 (1)	9 (1)
Nausea	1 (1)	8 (1)	9 (1)
Diarrhea	0	7 (1)	7 (1)
Flatulence	0	6 (1)	6 (1)
Sleep disorder	0	6 (1)	6 (1)
Arthralgia	0	5 (1)	5 (1)
Headache	0	5 (1)	5 (1)
Serious DRAEs	0	2 (< 1)	2 (< 1)
DRAEs leading to B/F/TAF discontinuation[a]	6 (5)	52 (8)	58 (7)

[a]Most common DRAEs leading to B/F/TAF discontinuation: weight increased (n = 21), depression (n = 7), fatigue (n = 6), and sleep disorder (n = 5).
AE, adverse event; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; DRAE, drug-related adverse event; TE, treatment experienced; TN, treatment naïve.

Additional safety data can be found in the supplement (by scanning the QR code)

Weight and BMI Through 4 Years



Number of participants

TN	113	77	74	43	30
TE	598	427	388	295	295

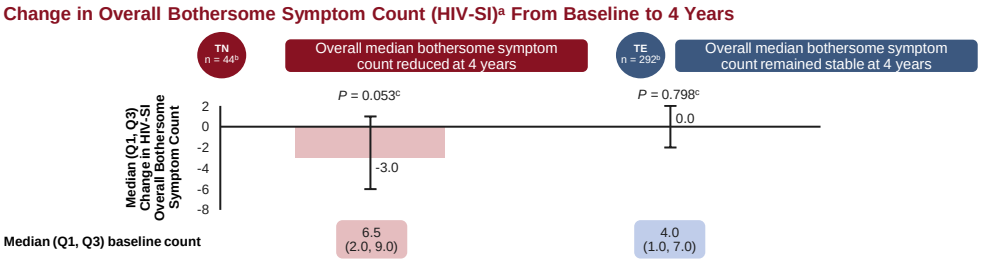
Number of participants

TN	111	73	69	42	29
TE	596	414	376	282	284

Median changes from baseline to 48 months in participants with data available at both timepoints: [a]4.4 kg (n = 29), $P = 0.019$; [b]1.6 kg (n = 269), $P < 0.001$; [c]1.6 kg/m² (n = 29), $P = 0.022$; [d]0.5 kg/m² (n = 269), $P < 0.001$;
P values calculated using sign test (weight) or signed rank test (BMI).
BMI, body mass index; Q, quartile; TE, treatment experienced; TN, treatment naïve.

Additional weight data can be found in the supplement (by scanning the QR code)

Change in Overall Bothersome Symptom Count (HIV-SI)[a] From Baseline to 4 Years

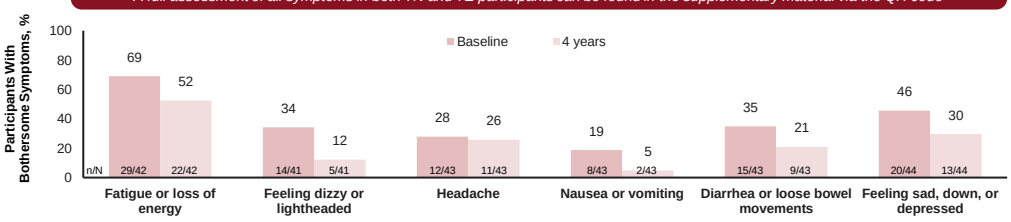


[a]Overall bothersome symptom count can range from 0 to 20, with higher values indicating more bothersome symptoms. [b]Participants with bothersome symptom count available at baseline and 4 years. [c]Sign test.
HIV-SI, HIV Symptom Index; Q, quartile; TE, treatment experienced; TN, treatment naïve.

Key Bothersome Symptoms (HIV-SI) at Baseline and 4 Years (TN participants)

TN

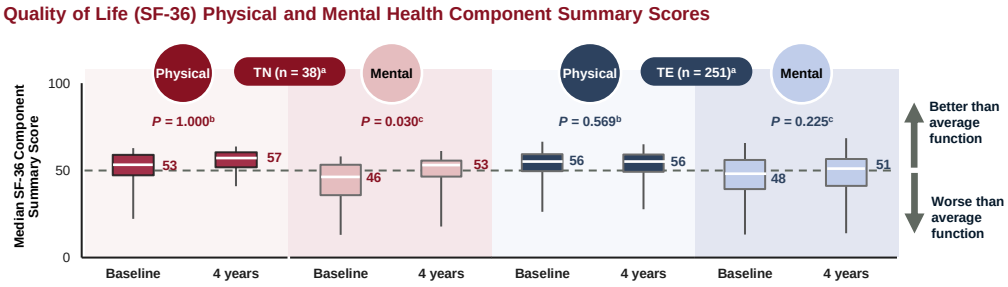
Participants reporting key symptoms as "bothersome" at baseline and 4 years after initiation of B/F/TAF (symptoms most relevant to the safety profile of B/F/TAF per Biktarvy© [B/F/TAF] SmPC are shown)
A full assessment of all symptoms in both TN and TE participants can be found in the supplementary material via the QR code



Differences in the key bothersome symptoms between baseline and 4 years shown were not statistically significant.
B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; HIV-SI, HIV Symptom Index; SmPC, Summary of Product Characteristics; TE, treatment experienced; TN treatment naïve.

The proportion of TN participants reporting key symptoms as "bothersome" decreased at 4 years

Quality of Life (SF-36) Physical and Mental Health Component Summary Scores



The summary component scores are standardized to have a mean score of 50; scores above or below 50 can be interpreted as indicating better or worse quality of life than in the general population. Bottom and top of boxes represent Q1 and Q3, respectively; horizontal lines within boxes represent medians; whiskers represent minimum and maximum values.
[a]Sample size restricted to participants with SF-36 scores available at baseline and 4 years. [b]Sign test. [c]Signed rank test.
Q, quartile; SF-36, 36-Item Short Form Health Survey; TE, treatment experienced; TN, treatment naïve.

Statistically significant increases in the mental component summary score were observed in TN participants

References: **1**. EACS. https://www.eacsociety.org/media/guidelines-12.0.pdf (accessed May 8, 2024). **2**. Gandhi RT, et al. *JAMA*. 2023;329:63-84. **3**. DHHS. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf (accessed May 8, 2024). **4.** Esser S, et al. *HIV Med*. 2024;25:440-53. **5.** Trottier B, et al. Poster P067 presented at: HIV Glasgow; November 10-13, 2022; Glasgow, UK. **6.** Garcia-Deltoro M, et al. Poster 180 presented at: GeSIDA; November 26-29, 2023; La Coruña, Spain.

Acknowledgments: We thank all study participants, investigators, and staff. BICSTaR (GS-EU-380-4472/GS-CA-380-4574/GS-IL-380-5335) is sponsored by Gilead Sciences, Inc. Medical writing support was provided by Josh Lilly, PhD, and Katy Beck, PhD (Aspire Scientific Ltd, Bollington, UK), and was funded by Gilead Sciences, Inc.

Disclosures: **AW** and **HC** report honoraria for advisory board consultation and as a speaker from Gilead Sciences, Inc., Merck, and ViiV Healthcare. **DB** reports honoraria as a speaker from Gilead Sciences, Inc., GSK/ViiV Healthcare, Johnson & Johnson, and MSD; institutional grant support from Gilead Sciences, Inc., Johnson & Johnson, and GSK/ViiV Healthcare; and travel expenses from Gilead Sciences, Inc. **CD** reports consultancy fees from Gilead Sciences, Inc., and Merck; and travel grants from Gilead Sciences, Inc., Merck, and ViiV Healthcare. **DT**, **MH**, and **AM** are employees of, and hold stock in, Gilead Sciences, Inc. **JR** is a contractor for Gilead Sciences, Inc. **BT** reports honoraria for consultation and as a speaker from Gilead Sciences, Inc., and ViiV Healthcare.

Correspondence: Alexander Wong, alexander.wong@usask.ca.