Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) in Antiretroviral Treatment-Naïve (TN) and -Experienced (TE) People With HIV (PWH): 3-Year Effectiveness and Safety Outcomes in the BICSTaR Observational Cohort

Poster eP.A.081

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Michael Sabranski,[1] Matteo Vassallo,[2,3] Joss de Wet,[4] Ansgar Rieke,[5] Alex Wong,[6] David Thorpe,[7] Tali Cassidy,[7] Andrea Marongiu,[7] Olivier Robineau[8,9]

[1]ICH Study Center, Hamburg, Germany; [2]Department of Infectious Diseases, Cannes General Hospital, Cannes, France; [3]Unité de Recherche Clinique Côte d'Azur (UR2CA), Côte d'Azur University, Nice, France; [4]Spectrum Health, Vancouver, BC, Canada; [5]Gemeinschaftsklinikum Mittelrhein, Kemperhof Koblenz, Koblenz, Germany; [6]Department of Medicine, University of Saskatchewan, Regina, SK, Canada; [7]Gilead Sciences Europe Ltd, Uxbridge, UK; [8]University of Lille, Lille, France; [9]Infectious Disease Department, Gustave Dron Hospital, Tourcoing, France

Key Findings

- In people with HIV (PWH) under routine clinical care, the virologic and immunologic benefits of B/F/TAF were maintained through 3 years of treatment
- Similar rates of virologic suppression were observed across key groups (participants with late diagnosis, reduced renal function and pre-existing resistance mutations) and regardless of reasons for switching to B/F/TAF or common prior ART regimens
- B/F/TAF was well tolerated, with most drug-related adverse events (DRAEs) occurring during the first 6 months
- Discontinuation of B/F/TAF due to DRAEs was infrequent
- No cases of proximal renal tubulopathy or disconinuations due to renal or bone AEs were observed
- For individuals who were treatment naïve (TN), most of the weight gain reported over the full 3 years was experienced in the first 6 months of B/F/TAF treatment
- Small lipid changes were observed, and median total cholesterol:HDL ratio remained stable across 3 years

Conclusion

- B/F/TAF was associated with high levels of effectiveness at 3 years across all groups, with no emergence of resistance and no new or unexpected safety findings. These real-world data continue to support the broad use of B/F/TAF in clinical practice

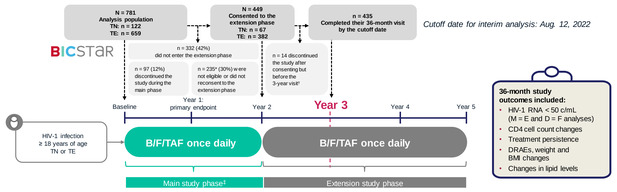
Introduction

- BICSTaR is a prospective, multinational, observational, 2-year cohort study evaluating the real-world effectiveness and safety of B/F/TAF in antiretroviral TN and treatment-experienced (TE) PWH
- The 2-year follow-up was recently completed for the main BICSTaR study
- Participants in Germany, France and Canada were given the opportunity to participate in an extension phase for an additional 3 years
- In planned interim analyses, BICSTaR has demonstrated the real-world effectiveness and tolerability of B/F/TAF through 2 years[1,2]
- As of July 11, 2023, approximately 5,164 participants have been enrolled in studies involving B/F/TAF, of whom approximately 4,442 have received B/F/TAF
  - Since first marketing approval, cumulative exposure to B/F/TAF is estimated to be 2,792,693 patient-years[3]

Objective

- This pooled, interim analysis assessed **effectiveness and safety** of B/F/TAF through 3 years (2 years of main study plus 1 year of extension phase) including **effectiveness in key groups** of PWH in Germany, France and Canada

Methods



Cutoff date for interim analysis: Aug. 12, 2022

The analysis population includes participants who had a visit at 36 months and those who discontinued the study having initiated treatment ≥ 30 months (lower bound of the 36-month visit window) prior to the data cutoff date.
*69 participants (9%) discontinued B/F/TAF but were still in the study at 24 months and 166 (21%) were eligible for the extension phase but did not reconsent; †Due to participant decision (n = 6), participant lost to follow-up (n = 5), study drug discontinuation (n = 2) and death (n = 1); ‡Participants could complete the main phase either on B/F/TAF or on an alternative ART regimen following discontinuation of B/F/TAF treatment.

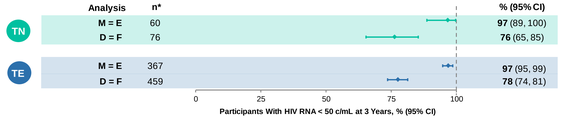
Results

Baseline Characteristics at Entry to the Main Study

Characteristic	TN (n = 122)		TE* (n = 659)	
	Not eligible for extension phase† (n = 55)	Consented to extension phase (n = 67)	Not eligible for extension phase† (n = 277)	Consented to extension phase (n = 382)
Demographics				
Sex: Male / female, n (%)	48 (87) / 7 (13)	62 (93) / 5 (7)	233 (84) / 44 (16)	338 (88) / 44 (12)
Race: White / Black, n (%)	39 (72) / 8 (15)	59 (91) / 4 (6)	219 (80) / 32 (12)	318 (84) / 34 (9)
Age, years, median (Q1, Q3)	37 (30, 51)	40 (32, 50)	48 (37, 55)	50 (41, 56)
Weight, kg, median (Q1, Q3)	69 (61, 79)	72 (67, 83)	77 (68, 88)	78 (67, 87)
BMI, kg/m², median (Q1, Q3)	22 (20, 25)	24 (22, 27)	25 (23, 28)	25 (22, 28)
Receiving ≥ 1 concomitant medication, n (%)	27 (49)	30 (45)	167 (60)	245 (64)
HIV viral load > 100,000 c/mL, n (%)	25 (46)	22 (33)	1 (< 1)	1 (< 1)
Any ongoing comorbidity, n (%)	29 (53)	36 (54)	153 (70)	310 (81)
Neuropsychiatric condition	7 (13)	16 (24)	86 (31)	128 (34)
Metabolic disorder	12 (22)	13 (19)	81 (29)	140 (37)
Hypertension	7 (13)	4 (6)	56 (20)	77 (20)
Late diagnosis, n (%)				
CD4 < 350 cells/µL and/or ≥ 1 AIDS-defining event	27 (51)	24 (38)	NA	NA
CD4 < 200 cells/µL and/or ≥ 1 AIDS-defining event	17 (32)	16 (25)	NA	NA
≥ 1 primary resistance mutation, n (%)	3 (9)	6 (13)	31 (23)	41 (23)
Most common primary resistance mutations relevant to B/F/TAF, n (%)				
NRTI overall / M184V/I	1 (3) / 0	1 (2) / 0	18 (12) / 9 (6)	23 (12) / 16 (8)
INSTI overall / T97A	0 / 0	0 / 0	0 / 0	1 (1) / 1 (1)
eGFR, n (%)‡				
< 60 mL/min/1.73 m²	3 (7)	0	5 (2)	21 (7)
≥ 60 mL/min/1.73 m²	43 (94)	59 (100)	214 (98)	284 (93)

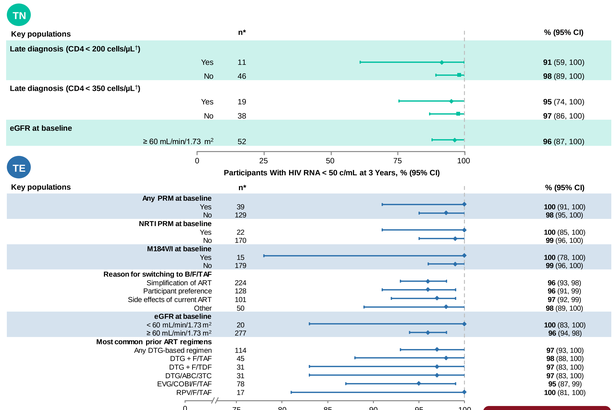
*Of the TE participants, 68% / 18% / 14% switched from INSTI- / NNRTI- / PI-based and 50% / 34% / 14% from TAF-based / TDF-based / ABC-based regimens, respectively; †Includes participants who did not consent, discontinued study or study drug, or were lost to follow-up; ‡In individuals with available eGFR data.

Virologic Effectiveness at 3 Years (M = E and D = F Analyses)



*Number of participants with available viral load data. For D = F, 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. Reasons for discontinuation before the 36-month window that resulted in D = F were, n-values for TN and TE, respectively: AEs, 8 and 52; death, 2 and 7; investigator decision, 1 and 11; lack of efficacy, 0 and 5; new treatment available, 0 and 2; pregnancy, 0 and 1; participant decision, 3 and 11.

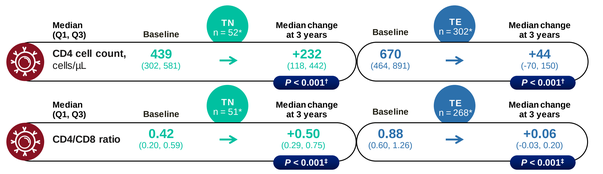
Virologic Effectiveness in TN and TE Key Populations at 3 Years (% HIV-1 RNA < 50 c/mL) (M = E Analysis)



There was no reported emergence of resistance to the components of B/F/TAF

*Number of participants with available viral load data; †And/or ≥ 1 AIDS-defining event at baseline.

Immunologic Outcomes at 3 Years

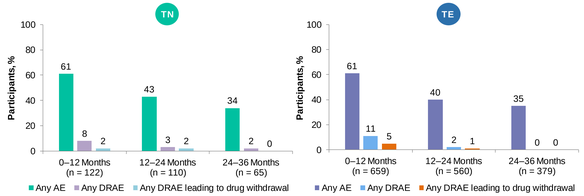


Median changes were calculated from the individual participant changes from baseline to 3 years.
*Population with data available at baseline and 3 years; †Signed-rank test (null hypothesis median = 0); ‡Sign test (null hypothesis median = 0).

Discontinuations

B/F/TAF discontinuations within 36 months of initiation, n (%)	All (N = 781)	TN (n = 122)	TE (n = 659)
Any discontinuations between baseline and 36 months	119 (15)	17 (14)	102 (16)
Reason for discontinuation			
AE	60 (8)	8 (7)	52 (8)
Participant decision	19 (2)	4 (3)	15 (2)
Investigator's discretion	16 (2)	2 (2)	14 (2)
Death	11 (1)	3 (2)	8 (1)
New treatment available	6 (1)	0	6 (1)
Lack of efficacy	5 (1)	0	5 (1)
Pregnancy	1 (< 1)	0	1 (< 1)
Missing	1 (< 1)	0	1 (< 1)

AEs Over 3 Years



n = the number of participants still in the study who were on B/F/TAF at the start of the time window.

- In total, 7% of TN participants and 10% of TE participants experienced a DRAE within the first 6 months of starting B/F/TAF

DRAEs Over 3 Years

DRAE type, n (%)	All (N = 781)	TN (n = 122)	TE (n = 659)
DRAEs	108 (14)	19 (16)	89 (14)
Frequently reported DRAEs (≥ 1% in any group)			
Weight increased*	31 (4)	9 (7)	22 (3)
Depression†	12 (2)	1 (1)	11 (2)
Nausea	8 (1)	1 (1)	7 (1)
Fatigue	8 (1)	1 (1)	7 (1)
Abdominal pain	3 (< 1)	2 (2)	1 (< 1)
Serious DRAEs	2 (< 1)	0	2 (< 1)
Depression	2 (< 1)	0	2 (< 1)
DRAEs leading to B/F/TAF discontinuation	54 (7)	6 (5)	48 (7)
Frequently reported DRAEs leading to B/F/TAF discontinuation (≥ 1% in any group)			
Weight increased	19 (2)	4 (3)	15 (2)
Depression	7 (1)	0	7 (1)
DRAEs between 24 and 36 months leading to BFTAF discontinuation	0	0	0

*Prior ARTs in TE individuals were: efavirenz/F/TDF (n = 1), EVG/COBI/F/TAF (n = 3), ABC + RAL (n = 1), atazanavir + F/TAF 200 mg/10 mg (n = 1), darunavir + COBI + F/TAF (n = 1), darunavir + F/TDF + ritonavir (n = 1), F/TAF 200/25 mg + nevirapine (n = 1), F/TAF 200/25 mg + RAL (n = 1), DTG + RPV + F/TDF (n = 1), DTG + F/TAF 200/25 mg (n = 4), DTG + F/TDF (n = 2), DTG + F/TAF (n = 1), stavudine + F/TDF + nevirapine (n = 1), F/TDF + lopinavir/ritonavir (n = 1). F/TDF + nevirapine (n = 1), F/TDF + RAL (n = 1); †Eight individuals with a DRAE of depression had an ongoing neuropsychiatric disorder at baseline.

DRAEs Over 3 Years in Key Groups

DRAE, n/N (%)	TN (n = 122)	TE (n = 659)
Late diagnosis CD4 (CD4 < 350 cells/µL*)	7/51 (14)	NA
Late diagnosis CD4 (CD4 < 200 cells/µL*)	4/33 (12)	NA
eGFR at baseline		
< 60 mL/min/1.73 m²	0/3 (0)	4/26 (15)
≥ 60 mL/min/1.73 m²	18/102 (18)	64/498 (13)

*And/or ≥ 1 AIDS-defining event at baseline.

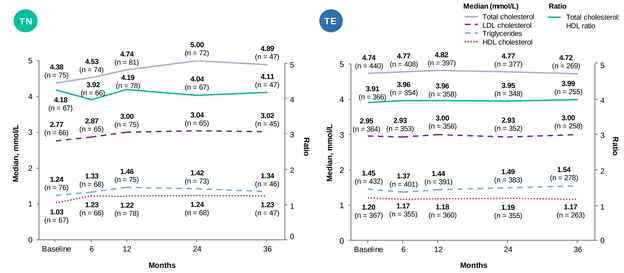
Weight Change at 3 Years

Change from baseline	n	TN (n = 122)	n	TE (n = 659)
Change from baseline in weight, kg, median (Q1, Q3)‡				
6 months	77	3.0 (0.4, 6.0)	430	0.7 (-1.0, 2.5)
12 months	69	4.0 (1.0, 7.6)	385	0.9 (-1.2, 3.0)
24 months	67	4.0 (0.0, 8.6)	343	1.0 (-1.0, 4.0)
36 months	40	4.3 (-0.5, 7.3), *P* = 0.003*	265	1.7 (-1.0, 4.3), *P* < 0.001*
People with a DRAE of weight increase, n	9		22	
Change from baseline in weight, kg, median (Q1, Q3) ‡				
12 months	8	8.8 (6.6, 14.2)	12	6.0 (3.7, 8.8)
24 months	5	16.2 (13.0, 19.0)	5	10.0 (2.0, 11.0)
36 months	3	8.0 (4.0, 24.2)	1	13.0 (13.0, 13.0)
Change from baseline in BMI, kg/m², median (Q1, Q3) ‡				
12 months	8	3.2 (2.0, 5.2)	12	2.0 (1.4, 2.9)
24 months	5	4.8 (3.7, 8.4)	5	3.2 (0.9, 3.9)
36 months	3	2.7 (1.1, 7.2)	1	4.6 (4.6, 4.6)

*P-value is for comparison with baseline and was calculated using the Sign test; †For participants with weight recorded at baseline and within the follow-up visit window; ‡For participants with weight recorded at baseline and at 3 years.

- For those participants with a DRAE of weight increase, 7/9 (78%) TN and 9/22 (41%) TE participants experienced weight gain ≥ 10% at any point up to 3 years
- At 3 years, TN (n = 40) and TE (n = 263) participants (with available baseline and 3-year data) experienced a median (Q1, Q3) change in BMI of 1.5 (-0.1, 2.5) kg/m² (*P* = 0.003) and 0.5 (-0.3, 1.5) kg/m² (*P* < 0.001), respectively, compared with baseline
  - Despite the increase in BMI, at 3 years, 48% of TN participants had a normal BMI (≥ 18.5 to < 25 kg/m²)

Lipid Levels Over 3 Years



Renal Assessment at 3 Years

Change from baseline in eGFR	TN participant consented to extension phase (n = 67)	TE participant consented to extension phase (n = 382)
n	36*	235*
Change in eGFR, mL/min/1.73 m², median (Q1, Q3), *P*-value	-11.4 (-21.9, 0.6), *P* = 0.011	-4.1 (-11.6, 3.9), *P* < 0.001

*For those participants with available data at baseline and 3 years.

- Changes in eGFR for TN participants are consistent with the known inhibitory effect of bictegravir on the tubular secretion of creatinine without affecting actual GFR[4]

References:
1. Trottier B, et al. HIV Glasgow 2022, Poster P067. **2.** Garcia-Deltoro M, et al. GeSIDA 2023, Poster 180. **3.** Data on file. Gilead Sciences, Inc. **4.** Biktarvy UK SmPC. Gilead Sciences Ltd, June 2023.

Acknowledgments: We thank all study participants and all participating study investigators and staff. BICSTaR is sponsored by Gilead (GS-EU-380-4472/GS-CA-380-4574/GS-IL-380-5335). Medical writing support was provided by Josh Lilly and Anna Chapman-Barnes (Aspire Scientific Ltd, U.K.), and was funded by Gilead.

Disclosures: **MS:** Honoraria for speaking at educational events or participation in advisory boards from AbbVie, Bristol Myers Squibb, Gilead, Janssen, MSD, ViiV Healthcare. **MV:** nothing to declare. **JdW:** speaker/advisory board fees from Gilead, Merck, ViiV Healthcare. **AR:** honoraria from Gilead, Janssen-Cilag, MSD, ViiV Healthcare; grant/research support from Gilead. **AW:** grants/honoraria from AbbVie, Gilead, Merck, ViiV Healthcare. **DT**, **TC** and **AM:** employed by, and own shares in, Gilead.

Disclosures (continued): **OR:** consultant/advisor for Gilead, MSD, ViiV Healthcare.

Abbreviations: 3TC, lamivudine; ABC, abacavir; AE, adverse event; AIDS, acquired immune deficiency syndrome; ART, antiretroviral therapy; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BICSTaR, BICtegravir Single Tablet Regimen; BMI, body mass index; c, copies; CD4, cluster of differentiation; CI, confidence interval; COBI, cobicistat; D = F, discontinuation = failure; DRAE, drug-related adverse event; DTG, dolutegravir; eGFR, estimated glomerular filtration rate; EVG, elvitegravir; F, emtricitabine; GFR, glomerular filtration rate; HDL, high-density lipoprotein; INSTI, integrase strand-transfer inhibitor; LDL, low-density lipoprotein; M = E, missing = excluded; NA, not applicable; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor; PRM, primary resistance mutation; PWH, people with HIV; Q, Quartile; RAL, raltegravir; RPV, rilpivirine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TE, treatment experienced; TN, treatment naïve.