NON-INTERVENTIONAL STUDY
ABBREVIATED FINAL CLINICAL STUDY REPORT

Study Title:	Multi-country, non-interventional, cohort study of the effectiveness, safety, adherence, and health-related quality of life in HIV-1 infected adult patients receiving Bictegravir/ Emtricitabine/Tenofovir alafenamide (B/F/TAF)
Active substances:	ATC Code: J05AR20, Antivirals for systemic use; antivirals for treatment of HIV infections, combinations. Bictegravir, Emtricitabine, Tenofovir Alafenamide
Medicinal product:	Bictegravir/ Emtricitabine/Tenofovir Alafenamide fixed dose combination
Product reference:	EU/1/18/1289/001-002 (EU); 06.03.2019 - 2019/135 (Turkey)
Indication:	HIV infections
Sponsor:	Gilead Sciences Europe Ltd 2 Roundwood Avenue, Stockley Park, Uxbridge UB11 1AF, United Kingdom
Study No.:	GS-EU-380-4472
EU PAS Register:	EUPAS22185
Research question and objectives:	To assess the effectiveness and safety of B/F/TAF in treatment naïve and treatment experienced HIV-1 infected adult participants, including adherence, resource utilization, quality of life, health status, and treatment satisfaction during its daily routine use.
Phase of Development:	Non-interventional cohort study
IND No.: **EudraCT No.:**	Not Applicable

ClinicalTrials.gov Identifier:	Not Applicable
Study Start Date:	27 June 2018 (first participant enrolled)
Study End Date:	12 June 2024 (last participant last visit for the primary end point) 24 June 2024 (last participant last visit for this report)
Country of study:	This study was carried out in France, Germany, Ireland, Italy, Netherlands, Spain, Turkey and United Kingdom.
Sponsor Authors:	Name: PPD Telephone: PPD Fax: PPD
Gilead EU Qualified Person Responsible for Pharmacovigilance:	Name: PPD Telephone: PPD
Marketing Authorization Holder (MAH):	**EU:** Gilead Sciences Ireland UC Carrigtohill T45 DP77 Country Cork, Ireland **Turkey:** Gilead Sciences Ilac. Tic. Ltd. Sti. İçerenköy Mahallesi, Umut Sokak. No: 10/12 Kat:21 Quick Tower 34752 Ataşehir, Istanbul, Turkey
Report Date:	Version 1.0 – 15 May 2025

This study was conducted in accordance with the guidelines of Good Pharmacoepidemiology Practices (GPP) and Heads of Medicines Agencies (HMA) and HC Good Pharmacovigilance Practices (GVP) Guidelines including archiving of essential documents.

STUDY SYNOPSIS

Study GS-EU-380-4472

Gilead Sciences Europe Ltd
2 Roundwood Avenue, Stockley
Park, Uxbridge UB11 1AF, United Kingdom

Title of Study: Multi-country, non-interventional, cohort study of the effectiveness, safety, adherence, and health-related quality of life in HIV-1 infected adult patients receiving Bictegravir/ Emtricitabine/Tenofovir alafenamide (B/F/TAF)
Investigators: The list of investigators is provided in Appendix 12.1.4.
Study Centers: 82 sites overall including 24 in France, 20 in Germany, 4 in Ireland, 10 in Italy, 5 in the Netherlands, 8 in Spain, 7 in Turkey, and 4 in the United Kingdom (UK).
Publications (published manuscripts using European [EU] data; the list of abstracts (123) using EU data is available upon request): Esser S, Brunetta J, Inciarte A, et al. Twelve-month effectiveness and safety of bictegravir/emtricitabine/tenofovir alafenamide in people with HIV: Real-world insights from BICSTaR cohorts. *HIV Med*. 2024;25(4):440-453. doi:10.1111/hiv.13593 Trottier B, Yang CJ, Watanabe D, et al. Bictegravir/emtricitabine/tenofovir alafenamide in clinical practice for people with HIV: final 24-month effectiveness and safety outcomes in key populations in the observational BICSTaR cohort. *HIV Res Clin Pract*. 2025;26(1):2456890. doi:10.1080/25787489.2025.2456890 Trottier B, Yang CJ, Watanabe D, et al. Bictegravir/emtricitabine/tenofovir alafenamide in clinical practice for people with HIV: final 24-month effectiveness and safety outcomes in key populations in the observational BICSTaR cohort. *HIV Res Clin Pract*. 2025;26(1):2456890. doi:10.1080/25787489.2025.2456890 Esser S, Inciarte A, Levy I, et al. Combined bictegravir, emtricitabine and tenofovir alafenamide for treating people with HIV: a plain language summary of the BICSTaR study up to 1 year. *Future Microbiol*. 2024;19(15):1273-1282. doi:10.1080/17460913.2024.2391190
Study Period: 27 June 2018 (first participant enrolled) 21 July 2022 (last participant last visit for the primary end point) 24 June 2024 (last participant last visit for this report)
Phase of Development: Non-interventional cohort study

Research Question and Objectives:

This non-interventional cohort study aimed to evaluate the effectiveness, safety, adherence, resource utilization and participants' health condition via patient reported outcome (PRO) questionnaires, during treatment with B/F/TAF in routine clinical care.

The primary objective of this study was as follows:

- To evaluate human immunodeficiency virus (HIV)-1 ribonucleic acid (RNA) suppression, defined as HIV-1 RNA <50 copies/mL, at 12 months after initiating or switching to B/F/TAF

The secondary objectives of this study were as follows:

- To evaluate HIV-1 RNA suppression (<50 copies/mL) at months 3, 6, and 24 after initiating or switching to B/F/TAF
- To evaluate changes in cluster determinant 4 (CD4) cell count and CD4 / cluster determinant 8 (CD8) ratio at months 3, 6, 12 and 24 after initiating or switching to B/F/TAF
- To assess rates of adverse events (AEs) and serious AEs (SAEs)
- To evaluate the long-term effectiveness and safety of B/F/TAF in an extension phase through Month 60 in a subgroup of participants recruited in France and Germany:
    - To evaluate HIV-1 RNA suppression (<50 copies/mL) at Months 36, 48, and 60 after initiating or switching to B/F/TAF
    - To evaluate changes in CD4 cell count and CD4/CD8 ratio at Months 36, 48, and 60 after initiating or switching to B/F/TAF

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Study Design: Prospective, non-interventional cohort study. Participant enrollment and data were collected using an electronic case report form (eCRF) by the participating sites. Each enrolled participant was followed up for up to 24 months or for 60 months for the participants entering the extension phase in France and Germany.

Number of Participants (Planned and Analyzed):

Planned: at least 1,500 participants starting treatment with B/F/TAF (ART-naïve or ART-experienced participants)

Analyzed: 1,435 participants

Diagnosis and Criteria for Inclusion:

Inclusion criteria:

1) HIV-1 infection

2) Signed informed consent

3) Age ≥18 years old

4) Initiating treatment with B/F/TAF in accordance with the summary of product characteristics (SmPC)

Exclusion criteria:

1) Participation in any interventional clinical trial without prior approval from the medical monitor

Duration of Treatment:

Participants were followed over a period of up to 24 months or 60 months for those participants consenting into the extension phase in France and Germany. B/F/TAF treatment duration was left to Investigators' discretion.

Reference Therapy, Dose, Mode of Administration:

B/F/TAF fixed dose combination was prescribed according to local treatment guidelines and/or routine clinical practice.

Criteria for Evaluation:

Effectiveness:

Primary outcome:

- HIV-1 RNA suppression (HIV-1 RNA viral load <50 copies/mL) at 12 months after initiating or switching to B/F/TAF

Secondary outcomes:

- HIV-1 RNA suppression (HIV-1 RNA viral load <50 copies/mL) at 3, 6, 24 months after initiating or switching to B/F/TAF, and at 36, 48, and 60 months after initiating or switching to B/F/TAF in participants in the extension phase in France and Germany.
- Changes in CD4 cell count and CD4/CD8 ratio at 3, 6, 12, 24 months after initiating or switching to B/F/TAF, and at 36, 48, and 60 months after initiating or switching to B/F/TAF in participants in the extension phase in France and Germany.

Pharmacokinetics:

No pharmacokinetic analyses were performed for this study.

Safety:

- All AEs, AEs related to B/F/TAF (as per investigator's judgment), SAEs, SAEs related to B/F/TAF (as per investigator's judgment) that occurred from the day of B/F/TAF initiation **to** the upper bound of the time window for 24 months for participants not in the extension phase and 60 months for participants in the extension phase **or to** 30 days after (a) the discontinuation of B/F/TAF or (b) temporary interruption >1 month (c) after the last visit for participants who did not discontinue B/F/TAF and without temporary interruption >1 month.
- Weight changes from baseline: weight increase >5% / weight decrease >5% and weight increase >10% / weight decrease >10%.

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Statistical Methods:

Continuous (quantitative) variables were described by the number of non-missing and missing observations, mean, standard deviation (SD), median, first and third quartiles and extreme values (minimum and maximum).

Categorical (qualitative) variables were described by the observed and relative (%) frequency of each class, and number of non-missing and missing observations. If 'Unknown' was a class of response, it was considered as a fully-fledged category.

Confidence intervals (CIs) for means and exact CIs (Clopper-Pearson) for percentages were calculated when appropriate and were 2-sided at the 95% level unless otherwise specified.

Demographics and baseline characteristics were summarized using descriptive statistics.

The questionnaires scores were calculated according to the algorithms elaborated for these questionnaires.

Visit windows were defined in the statistical analysis plan. Data (e.g., in PRO questionnaires, safety data, or CD4 cell count) were assigned to these defined visit windows in order to generate descriptive statistics across time and to assess potential trends. P-values and CIs (95% two-sided) were calculated when relevant.

Effectiveness:

HIV-1 RNA suppression was described using the missing-as-excluded analysis (main analysis) and the treatment discontinuation-as-failure analysis (sensitivity analysis).

Changes in CD4 cell count and CD4/CD8 ratio were analyzed descriptively.

Pharmacokinetics:

No pharmacokinetic analyses were performed for this study.

Safety:

Rates of AEs, AEs related to B/F/TAF, SAEs, SAEs related to B/F/TAF were described by system organ class (SOC) and preferred term (PT). Incidences in person-years were calculated. The number of deaths was reported. The number of pregnancies was reported.

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SUMMARY OF RESULTS:

Participant Disposition and Demographics:

The study was conducted on data collected from 27 June 2018 (first participant enrolled) to 12 September 2024 (database lock) by 82 physicians. A total of 1,492 participants were enrolled in the study (written informed consent obtained). Among them, 4 participants who had important protocol deviations were excluded from the dataset due to erroneous data collection after the important protocol deviation (3 participants no longer met the inclusion criteria as they were not treated with B/F/TAF in accordance with the SmPC, and 1 had been enrolled in an interventional trial, all since study enrollment). In total, 1,488 participants comprised the enrolled population included in this report. Among them, 1,435 were included in the Analysis population (enrolled participants who met all inclusion/exclusion criteria, received at least one dose of B/F/TAF and had at least one post-baseline visit completed): 381 participants (26.6%) were ART-naïve participants (never treated with ART before enrollment in the study and treated with B/F/TAF for the first time) and 1,054 participants

(73.4%) were ART-experienced participants (treated with ART before enrollment and switched to B/F/TAF).

A total of 628 participants were included in the Analysis population (enrolled participants who met all inclusion/exclusion criteria, received at least one dose of B/F/TAF and had at least one post-baseline visit completed) in France and Germany and 498 of them (79.3%) were eligible to the extension phase i.e., (no discontinuation of B/F/TAF and no premature study discontinuation during the main phase of the study). Of these, 366 (73.5%) reconsented to the extension phase (73 [70.2%] in the ART-naïve group and 293 [74.4%] in the ART-experienced group). Note that 368 participants are recorded as enrolled in the electronic data capture system, but one of these was subsequently excluded from the dataset due to erroneous data collection after an important protocol deviation, and another one did not meet the criteria to be included in the analysis population.

The median age at B/F/TAF initiation was 36.0 (Q1: 29.0, Q3: 45.0) years in the ART-naïve group and 49.0 (Q1: 39.0, Q3: 56.0) years in the ART-experienced group. The proportion of participants ≥50 years was 19.9% in the ART-naïve group and 47.2% in the ART-experienced group. The proportion of males was 90.0% in the ART-naïve group and 83.7% in the ART-experienced group.

Overall, participants were characterized by a high prevalence of comorbidities at baseline. Medical history or comorbidities/co-infections at B/F/TAF initiation were reported in 46.7% of participants in the ART-naïve group (most frequently reported conditions: neuropsychiatric disorders [8.7%], hypertension [6.1%], and cardiovascular disorders [5.3%]) and in 78.2% in the ART-experienced group (most frequently reported conditions: neuropsychiatric disorders [25.8%], hyperlipidemia [24.9%], and hypertension [18.6%]).

The median age at HIV diagnosis was 35.0 (Q1: 27.0, Q3: 45.0) years in the ART-naïve group and 34.0 (Q1: 28.0, Q3: 42.0) years in the ART-experienced group.

In the ART-experienced group, the most frequent combinations of ART taken immediately prior to B/F/TAF were EVG_COBI_FTC_TAF (Genvoya, 30.9%), DTG+FTC_TAF (Dolutegravir + Descovy, 8.8%), and ABC_DTG_3TC (Triumeq, 6.2%). History of virologic failure was reported in 11.8% of ART-experienced participants (unknown in 6.9% of participants). Current or prior resistance-associated mutations were reported in 281 participants (26.7% of participants). Mutations were associated with NNRTI (12.2%), PI (19.6%), NRTI (9.2%) and INI (1.7%). No information on resistance status was available in 49.6% of participants.

The majority of participants had a Centers for Disease Control and Prevention (CDC) stage A at B/F/TAF initiation (75.2% in the ART-naïve group and 66.8% in the ART-experienced group); 14.8% of participants in the ART-naïve group and 16.4% of participants in the ART-experienced group had a CDC stage B, and 10.0% of participants in the ART-naïve group and 16.7% of participants in the ART-Experienced group had a CDC stage C.

In the ART-naïve group, 111 participants (29.9%) were late presenters (CD4 <200 cells/µL and/or at least one AIDS defining event at baseline defined as any C stage).

At baseline, there were 3 participants with HIV-1 RNA viral load <50 copies/mL in the ART-naïve group, the median CD4 cell count was 344.9 (Q1: 169.0, Q3: 501.0) cells/µL and

median CD4/CD8 ratio was 0.33 (Q1: 0.20, Q3: 0.60). In the ART-experienced group, 80 participants (8.6 %) had a viral load ≥50 copies/mL, the median CD4 cell count was 701.0 (Q1: 480.0, Q3: 909.0) cells/µL and the median CD4/CD8 ratio at baseline was 0.89 (Q1: 0.60, Q3: 1.23).

Among French and German participants, demographics (age at B/F/TAF initiation, sex) and disease characteristics were comparable between participants who reconsented to the extension phase and participants who did not reconsent. However, the proportion of White participants was higher in participants who reconsented to the extension phase than in participants who did not reconsent (90.4% vs. 74.2%).

Effectiveness Results:

- Primary Outcome

The primary objective of this study was to evaluate HIV-1 RNA suppression, defined as HIV-1 RNA <50 copies/mL, at 12 months after initiating or switching to B/F/TAF.

At baseline, the median HIV-1 RNA viral load was 5.11 (Q1: 4.44, Q3: 5.64) log10 copies/mL in the ART-naïve group and 1.28 (Q1: 1.28, Q3: 1.28) log10 copies/mL in the ART-experienced group. Baseline viral load was >100,000 copies/mL in 196 participants (52.5%) in the ART-naïve group and 7 participants (0.8%) in the ART-experienced group. A total of 3 participants (0.8%) in the ART-naïve group and 845 participants (91.4%) in the ART-experienced group had a viral load <50 copies/mL. In France and Germany, the median HIV-1 RNA viral load at baseline was 4.78 (Q1: 4.00, Q3: 5.28) log10 copies/mL in the ART-naïve group and 1.28 (Q1: 1.28, Q3: 1.28) log10 copies/mL in the ART-experienced group. Baseline viral load was >100,000 copies/mL in 46 participants (38.7%) in the ART-naïve group and 4 participants (0.9%) in the ART-experienced group. No participants had a viral load <50 copies/mL in the ART-naïve group and 414 participants (90.8%) in the ART-experienced group had a viral load <50 copies/mL.

HIV-1 RNA suppression at 12 months after initiating or switching to B/F/TAF was achieved in 90.6% of participants (95% CI: 86.7%, 93.6%) in the ART-naïve group and was maintained in 96.8% of participants (95% CI: 95.4%, 97.9%) in the ART-experienced group. In France and Germany, HIV-1 RNA suppression at 12 months was achieved in 96.2% of participants (95% CI: 90.6%, 99.0%) in the ART-naïve group and in 95.9% of participants (95% CI: 93.5%, 97.6%) in the ART-experienced group.

The sensitivity analysis (treatment discontinuation/interruption >1 month considered as treatment failure) showed similar results: HIV-1 RNA suppression was achieved in 87.1% of participants (95% CI: 83.0%, 90.6%) in the ART-naïve group and was maintained in 90.5% of participants (95% CI: 88.4%, 92.3%) in the ART-experienced group. In France and Germany, HIV-1 RNA suppression was achieved in 92.7% of participants (95% CI: 86.2%, 96.8%) in the ART-naïve group and 88.5% of participants (95% CI: 85.2%, 91.3%) in the ART-experienced group.

- Secondary outcomes
    - HIV-1 RNA Suppression at 3, 6, 24, 36, 48, and 60 Months

Main phase (3, 6, and 24 months)

In the ART-naïve group, HIV-1 RNA suppression was achieved in 74.1% of participants (95% CI: 69.0%, 78.7%) at 3 months, 85.8% of participants (95% CI: 81.5%, 89.5%) at 6 months, and 94.3% of participants (95% CI: 91.0%, 96.7%) at 24 months.

In the ART-experienced group, HIV-1 RNA suppression was maintained in 96.0% of participants (95% CI: 94.4%, 97.3%) at 3 months, 94.6% of participants (95% CI: 92.8%, 96.0%) at 6 months, and 95.7% of participants (95% CI: 94.0%, 97.0%) at 24 months.

The sensitivity analysis (treatment discontinuation considered as treatment failure) showed comparable results. In the ART-naïve group, HIV-1 RNA suppression was achieved in 73.2% of participants (95% CI: 68.1%, 77.9%) at 3 months, 84.0% of participants (95% CI: 79.5%, 87.8%) at 6 months, and 88.1% of participants (95% CI: 83.9%, 91.5%) at 24 months. In the ART-experienced group, HIV-1 RNA suppression was achieved in 94.4% of participants (95% CI: 92.6%, 95.9%) at 3 months, 90.9% of participants (95% CI: 88.7%, 92.7%) at 6 months, and 84.1% of participants (95% CI: 81.5%, 86.4%) at 24 months.

France and Germany (3, 6, 24, 36, 48, and 60 months)

In the ART-naïve group in France and Germany, HIV-1 RNA suppression was achieved in 85.0% of participants (95% CI: 76.9%, 91.2%) at 3 months, 89.4% of participants (95% CI: 81.9%, 94.6%) at 6 months, 96.9% of participants (95% CI: 91.3%, 99.4%) at 24 months. During the extension phase, HIV-1 RNA suppression was maintained in 98.4% of participants (95% CI: 91.2%, 100%) at 36 months, 100% of participants (95% CI: 92.7%, 100%) at 48 months, and 100% of participants (95% CI: 92.0%, 100%) at 60 months.

In the ART-experienced group in France and Germany, HIV-1 RNA suppression was maintained in 95.8% of participants (95% CI: 93.3%, 97.5%) at 3 months, 94.0% of participants (95% CI: 91.3%, 96.1%) at 6 months, and in 94.2% of participants (95% CI: 91.4%, 96.3%) at 24 months. During the extension phase, HIV-1 RNA suppression was maintained in 97.1% of participants (95% CI: 94.4%, 98.7%) at 36 months, 97.3% of participants (95% CI: 94.5%, 98.9%) at 48 months, and in 97.4% of participants (95% CI: 94.4%, 99.0%) at 60 months.

The sensitivity analysis (treatment discontinuation considered as treatment failure) in France and German participants showed comparable results up to 24 months. After 24 months, results are less meaningful. Results are available in Table 19.

- CD4 Cell Count at 24 and 60 Months

Main phase (24 months)

In ART-naïve participants, the median CD4 cell count increased during the treatment period from 344.9 (Q1: 169.0, Q3: 501.0) cells/µL at baseline to 651.0 (Q1: 430.0, Q3: 890.0) cells/µL at 24 months. The median absolute change from baseline in CD4 cell count was +258.5 cells/µL (Q1: +106.0, Q3: +485.5, $p<0.001$) at 24 months.

In ART-experienced participants, the median CD4 cell count increased slightly during the treatment period from 701.0 (Q1: 480.0, Q3: 909.0) cells/µL at baseline to 734.0 (Q1: 533.0,

Q3: 960.5) cells/µL at 24 months. The median absolute change from baseline in CD4 cell count was +39.0 cells/µL (Q1: -75.0, +151.0; p<0.001) at 24 months.

France and Germany (24 and 60 months)

In ART-naïve participants in France and Germany, the median CD4 cell count increased during the treatment period from 424.5 (Q1: 220.0, Q3: 543.0) cells/µL at baseline, to 659.5 (Q1: 482.5, Q3: 865.0) cells/µL at 24 months, and to 830.5 (Q1: 661.0, Q3: 1113.0) cells/µL at 60 months in the extension phase. The median absolute change from baseline in CD4 cell count was +363.5 cells/µL (Q1: +229.0, Q3: +555.5, p<0.001) at 60 months.

In ART-experienced participants in France and Germany, the median CD4 cell count globally increased during the treatment period from 678.0 (Q1: 458.5, Q3: 914.5) cells/µL at baseline, to 723.5 (Q1: 532.0, Q3: 956.0) cells/µL at 24 months, and to 779.0 (Q1: 558.0, Q3: 1007.0) cells/µL at 60 months in the extension phase. The median absolute change from baseline in CD4 cell count was +87.0 cells/µL (Q1: -84.0, Q3: +220.0, p<0.001) at 60 months.

- CD4/CD8 Ratio at 24 and 60 Months

Main phase (24 months)

In the ART-naïve group, the median CD4/CD8 ratio increased during the treatment period from 0.33 (Q1: 0.20, Q3: 0.60) at baseline, to 0.84 (Q1: 0.57, Q3: 1.20) at 24 months. The median absolute change from baseline in CD4/CD8 ratio was +0.40 (Q1: +0.24, Q3: +0.65) at 24 months (p<0.001).

In the ART-experienced group, the median CD4/CD8 ratio increased during the treatment period from 0.89 (Q1: 0.60, Q3: 1.23) at baseline, to 0.99 (Q1: 0.68, Q3: 1.30) at 24 months. The median absolute change from baseline in CD4/CD8 ratio was +0.06 (Q1: -0.08, Q3: +0.20) at 24 months (p<0.001).

France and Germany (24 and 60 months)

In the ART-naïve participants in France and Germany, the median CD4/CD8 ratio increased during the treatment period from 0.32 (Q1: 0.20, Q3: 0.55) at baseline, to 0.86 (Q1: 0.58, Q3: 1.19) at 24 months, and 0.99 (Q1: 0.70, Q3: 1.33) at 60 months. The median absolute change from baseline in CD4/CD8 ratio was +0.51 (Q1: +0.26, Q3: +0.86) at 60 months (p<0.001).

In the ART-experienced participants in France and Germany, the median CD4/CD8 ratio increased during the treatment period from 0.84 (Q1: 0.59, Q3: 1.20) at baseline, to 1.00 (Q1: 0.69, Q3: 1.30) at 24 months, and 1.00 (Q1: 0.70, Q3: 1.31) at 60 months. The median absolute change from baseline in CD4/CD8 ratio was +0.10 (Q1: -0.03, Q3: +0.26) at 60 months (p<0.001).

Main phase

In the ART-naïve group, the median duration of B/F/TAF treatment was 23.8 (Q1: 21.9, Q3: 25.6) months. A total of 36 participants (9.5%) discontinued B/F/TAF treatment within 60 months following treatment initiation. The main reasons for B/F/TAF discontinuation were related AEs leading to drug withdrawn (n=14), participant decision (n=5), and investigator's discretion (n=9). Among the ART-naïve participants who discontinued B/F/TAF during the study, the median duration of B/F/TAF treatment was 19.9 (Q1: 8.5, Q3: 36.4) months. B/F/TAF persistence was 97.5% at 12 months and 95.4% at 24 months.

In the ART-experienced group, the median duration of B/F/TAF treatment was 24.0 (Q1: 22.1, Q3: 44.0) months. A total of 163 participants (15.5%) discontinued B/F/TAF treatment within 60 months following treatment initiation. The main reasons for B/F/TAF discontinuation were related adverse event leading to drug withdrawn (n=74), participant decision (n=23), and investigator's discretion (n=22). Among participants who discontinued B/F/TAF during the study, the median duration of B/F/TAF treatment was 12.5 (Q1: 5.8, Q3: 22.0) months. B/F/TAF persistence was 94.3% at 12 months and 89.1% at 24 months.

France and Germany

In ART-naïve participants in France and Germany, the median duration of B/F/TAF treatment was 36.0 (Q1: 23.3, Q3: 58.6) months. A total of 23 participants (19.0%) discontinued B/F/TAF treatment within 60 months following treatment initiation. The main reasons for B/F/TAF discontinuation were related AEs leading to drug withdrawn (n=7), investigator's discretion (n=6), and participant decision (n=4). Among participants who discontinued B/F/TAF during the study, the median duration of B/F/TAF treatment was 29.4 (Q1: 17.1, Q3: 41.2) months. B/F/TAF persistence was 98.3% at 12 months, 94.7% at 24 months, and 70.4% at 60 months.

In ART-experienced participants in France and Germany, the median duration of B/F/TAF treatment was 48.6 (Q1: 22.9, Q3: 59.1) months. A total of 109 participants (21.5 %) discontinued B/F/TAF treatment within 60 months following treatment initiation. The main reasons for B/F/TAF discontinuation was related adverse event leading to drug withdrawn (n=48), investigator's discretion (n=18) and participant decision (n=14). Among participants who discontinued B/F/TAF during the study, the median duration of B/F/TAF treatment was 14.5 (Q1: 6.4, Q3: 37.0) months. B/F/TAF persistence was 92.9% at 12 months, 86.2% at 24 months, and 70.1% at 60 months.

Pharmacokinetic Results:

No pharmacokinetic analyses were performed for this study.

Safety Results:

In the Analysis population, 873 participants (60.8%) experienced a total of 3,207 AEs; (incidence: 0.49 per patient-year [95% CI: 0.45, 0.52]; 0.61 per patient-year [95% CI: 0.55, 0.67] in France and Germany over the 60 month period). The median time from B/F/TAF initiation to the first AE was 96.0 (Q1: 6.0, Q3: 231.0) days in the ART-naïve group and 128.5 (Q1: 42.0, Q3: 320.0) days in the ART-experienced group. The most common AEs were

COVID-19 (101 participants [7.0%]), weight increased (85 participants [5.9%]), nasopharyngitis (67 participants [4.7%]), and syphilis (67 participants [4.7%]).

Overall, 188 participants (13.1%) experienced a total of 265 AEs considered by the investigators to be related to B/F/TAF; (incidence: 0.06 per patient-year [95% CI: 0.06, 0.08]; 0.05 per patient-year [95% CI: 0.04, 0.07] in France and Germany). The most common AEs related to B/F/TAF were weight increased (54 participants [3.8%]), nausea (14 participants [1.0%]), depression (14 participants [1.0%]), headache (12 participants [0.8%]), and fatigue (11 participants [0.8%]).

Overall, 126 participants (8.8%) experienced a total of 208 SAEs (incidence: 0.04 per patient-year [95% CI: 0.03, 0.05]; 0.05 per patient-year [95% CI: 0.04, 0.06] in France and Germany). In the ART-naïve group, 24 participants (6.3%) experienced a total of 34 SAEs (incidence: 0.03 per patient-year [95% CI: 0.02, 0.05]; 0.05 per patient-year (95% CI: 0.03, 0.08) in France and Germany). In the ART-experienced group, 102 participants (9.7%) experienced a total of 174 SAEs (incidence: 0.04 per patient-year [95% CI: 0.03, 0.05]; 0.04 per patient-year [95% CI: 0.03, 0.06] in France and Germany). Most SAEs were reported as 1 or 2 events in a single participant. The most frequent SAEs were depression (0.5%), acute kidney injury (0.3%), pneumonia (0.2%), metastases to central nervous system (0.2%), and cardiac failure (0.2%).

Overall, one participant (0.1%) from the ART-experienced group experienced one SAE of depression considered by the investigator to be related to B/F/TAF. Depression duration was 72 days and B/F/TAF was withdrawn as a result of the event. Other SAEs were considered unrelated to B/F/TAF.

A total of 14 deaths were reported during the study: 3 in the ART-naïve group and 11 in the ART-experienced group. No deaths were related to B/F/TAF.

Overall, 4 pregnancies were reported during the study in the ART-experienced group; for 2 of them, B/F/TAF was stopped during pregnancy.

Changes significantly different from zero were observed at 24 months for the following chemistry parameters:

- The median change from baseline in total cholesterol was +0.50 mmol/L (Q1: -0.03, Q3: +1.01; p<0.001) in the ART-naïve group, and -0.10 mmol/L (Q1: -0.67, Q3: +0.50; p=0.050) in the ART-experienced group.
- The median change from baseline in LDL was +0.36 mmol/L (Q1: -0.13, Q3: +0.67; p<0.001) in the ART-naïve group, and -0.06 mmol/L (Q1: -0.60, Q3: +0.39; p=0.001) in the ART-experienced group.
- The median change from baseline in eGFR was -9.79 mL/min (Q1: -21.75, Q3: +1.31; p<0.001) in the ART-naïve group and -4.94 mL/min (Q1: -14.23, Q3: +3.75; p<0.001) in the ART-experienced group.
- The median change from baseline in creatinine was +11.00 µmol/L (Q1: +4.00, Q3: +17.68; p<0.001) in the ART-naïve group and 3.00 µmol/L (Q1: -4.42, Q3: 10.61; p<0.001) in the ART-experienced group.

- The median change from baseline in total bilirubin was +1.20 µmol/L (Q1: -1.88, Q3: +3.80; p=0.021) in the ART-naïve group and +1.54 µmol/L (Q1: -1.54, Q3: +3.76; p<0.001) in the ART-experienced group.

Some changes significantly different from zero were observed at 24 months for the following chemistry parameters in ART-naïve participants only:

- The median change from baseline in HDL was +0.13 mmol/L (Q1: -0.03, Q3: +0.27; p<0.001).
- The median change from baseline in TC/HDL ratio was -0.16 (Q1: -0.72, Q3: +0.34; p=0.040).
- The median change from baseline in alanine aminotransferase was -3.00 U/L (Q1: -15.00, Q3: +5.99; p=0.023).
- The median change from baseline in aspartate aminotransferase was -1.75 U/L (Q1: -9.00, Q3: +3.00; p=0.001).
- The median change from baseline in albumin was +0.95 g/L (Q1: -1.00, Q3: +4.00; =0.039).
- The median change from baseline in phosphorus was +0.06 mmol/L (Q1: -0.05, Q3: +0.17; p=0.002).

Changes significantly different from zero were observed at 24 months for the following parameters in ART-experienced participants only:

- The median change from baseline in triglycerides was -0.07 mmol/L (Q1: -0.50, Q3: +0.32; p=0.005).
- The median change from baseline in glucose was +0.11 mmol/L (Q1: -0.44, Q3: +0.67; p=0.005).
- The median change from baseline in direct bilirubin was +0.17 µmol/L (Q1: -0.68, Q3: +1.03; p=0.043).

In France and Germany, some changes were significantly different from zero at 60 months for the following chemistry parameters:

- The median change from baseline in creatinine was +11.00 µmol/L (Q1: +1.77, Q3: +17.68 ; p<0.001) in the ART-naïve group and +3.54 µmol/L (Q1: -6.19, Q3: +10.61 ; p=0.001) in the ART-experienced group.

In France and Germany, some changes were significantly different from zero at 60 months for the following chemistry parameters in the ART-experienced group only:

- The median change from baseline in eGFR was -4.89 mL/min (Q1: -13.79, Q3: +4.04; p<0.001).
- The median change from baseline in glucose was +0.30 mmol/L (Q1: -0.22, Q3: +0.78; <0.001).

- The median change from baseline in aspartate aminotransferase was +2.00 U/L (Q1: -3.00, Q3: +7.00; p=0.006).
- The median change from baseline in total bilirubin was +0.90 µmol/L (Q1: -1.80, Q3: +3.65; p=0.013).

For urinary parameters, the median change from baseline to 24 months in UPCR was -4.17 mg/mmol (Q1: -8.70, Q3: -0.11) in the ART-naïve group and was statically different from zero (p=0.008). No major findings were observed in France and Germany.

In addition, weight increased during the treatment period: at 24 months the median change in weight from baseline was +4.0 kg (Q1: +0.2, Q3: +8.6; p<0.001) in the ART-naïve group and was +1.0 kg (Q1: -1.4, Q3: +4.0; p<0.001) in the ART-experienced group; at 60 months in France and Germany (extension phase), the median change in weight from baseline was +5.5 kg (Q1: +2.0, Q3: +12.0; p=0.001) in the ART-naïve group and +2.0 kg (Q1: -1.0, Q3: +5.0; p<0.001) in the ART-experienced group.

Overall, the safety results were consistent with the known safety profile of B/F/TAF. No new safety concerns associated with B/F/TAF were identified for the treatment of HIV-1 infected participants in Europe.

DISCUSSION:

In the ART-naïve group, HIV-1 RNA suppression was achieved in 90.6% of participants at 12 months, and 94.3% of participants at 24 months. In France and Germany, HIV-1 RNA suppression was achieved in 96.2% of participants at 12 months, 96.9% of participants at 24 months and 100% of participants at 60 months (participants in the extension phase).

In the ART-experienced group, switching to B/F/TAF was associated with maintenance of HIV-1 RNA suppression in 96.8% of participants at 12 months, and 95.7% of participants at 24 months. In France and Germany, HIV-1 RNA suppression was maintained in 95.9% of participants at 12 months, 94.2% of participants at 24 months, and 97.4% of participants at 60 months (participants in the extension phase).

Overall, these results are consistent with results from previous phase 3 studies. Study GS-US-380-1489 and study GS-US-380-1490 conducted in ART-naïve participants showed that HIV-1 RNA suppression at week 48 was achieved in 92% and 89% of participants, respectively. Study GS-US-380-1878 was conducted in virologically suppressed participants switching to B/F/TAF (median age: 48 years) and showed that HIV-1 RNA suppression was achieved in 92.1% of participants at Week 48. Similarly, Molina et al. reported that in virologically suppressed participants switching to B/F/TAF (median age: 47 years), 94% achieved virologic suppression at week 48. Results are also consistent with multicountry results from the pooled BICSTaR cohort.

Consistent with viral suppression, a significant increase in CD4 cell count was observed during the study. The median CD4 cell count change was +258.5 cells/µL (Q1: +106.0, Q3: +485.5, p<0.001) at 24 months in ART-naïve participants and was +39.0 cells/µL (Q1: -75.0, +151.0; p<0.001) at 24 months in ART-experienced participants. A significant increase in CD4 cell count was also observed in France and Germany at 60 months in the extension phase: the median absolute change from baseline in CD4 cell count was

+363.5 cells/µL (Q1: +229.0, Q3: +555.5, p<0.001) in ART-naïve participants, and +87.0 cells/µL (Q1: -84.0, Q3: +220.0, p<0.001) in ART-experienced participants.

The study did not raise any new safety concerns regarding the use of B/F/TAF in the treatment of participants living with HIV-1 in Europe. The safety data were in line with the known safety profile of B/F/TAF in this indication.

CONCLUSIONS:

In conclusion, this study provided insights into the effectiveness and safety, as well as patterns of use of B/F/TAF in HIV-1 infected participants in routine clinical care in Europe over a period of 24 months and up to 60 months in France and Germany. The results of this study confirmed that treatment with B/F/TAF used in a real-world cohort, including ART-naïve and ART-experienced participants, is associated with rapid achievement and maintenance of high rates of virologic suppression. This study also confirmed that the safety of B/F/TAF in real-world settings in participants with HIV-1 in Europe does not differ from the previously established B/F/TAF safety profile. No new safety concerns were identified.