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ORIGINAL RESEARCH

Bictegravir/emtricitabine/tenofovir alafenamide in older individuals with HIV: Results of a 96-week, phase 3b, open-label, switch trial in virologically suppressed people ≥65 years of age

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Abstract

Objectives: Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is an effective treatment for HIV-1 infection; however, clinical trial data in older people living with HIV (PLWH) are lacking. The primary 24-week and secondary 48-week analyses of study GS-US-380-4449 (NCT03405935), which assessed the efficacy and safety of switching to B/F/TAF in older PLWH, have been published. Here we report the results of the final 96-week analyses from the study.

Methods: In this 96-week, phase 3b, open-label, single-arm trial, virologically suppressed PLWH aged ≥65 years switched from elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide or a tenofovir disoproxil fumarate-based regimen to B/F/TAF. Viral suppression, resistance, immune response, safety, tolerability and adherence were evaluated through week 96.

Susan K. Chuck was employed by Gilead at the time of writing the manuscript.

Results: Of 90 participants screened, 86 were enrolled and switched to B/F/TAF. No participants had HIV-1 RNA ≥50 copies/ml (by FDA Snapshot algorithm) at weeks 72 or 96; virologic suppression rates were 94.2% (81/86; 95% CI 87.0–98.1) and 74.4% (64/86; 95% CI 63.9–83.2), respectively. No treatment-emergent resistance was observed, and CD4 counts remained stable. There were no study drug-related serious adverse events. Three participants experienced drug-related treatment-emergent adverse events that led to premature drug discontinuation. There were no clinically relevant changes from baseline to week 96 in fasting lipid parameters, and the median change in body weight at week 96 was 0.0 kg (IQR −2.3, 2.0). Median self-reported adherence was 100% (IQR 100–100%).

Conclusions: Switching to B/F/TAF is an effective long-term option for virologically suppressed adults ≥65 years of age, with favourable safety and tolerability profiles in this population.

KEYWORDS

age, bictegravir, clinical trial, emtricitabine, tenofovir alafenamide

INTRODUCTION

Older people living with HIV (PLWH) represent an important and growing population around the world. In the USA in 2018, 51% of the HIV-diagnosed population were ≥50 years of age, with 10% aged ≥65 years.[1] By 2030, the median age of PLWH in the USA is projected to increase from 50 to 53 years.[2] Furthermore, overall life expectancy among 20-year-old PLWH has greatly increased, with one study reporting improvement from 11.8 years (1988–1991) to 54.9 years (2006–2013).[3]

Older PLWH experience specific medical challenges not faced by younger PLWH. By 2030, it is predicted that 36% of PLWH will have two or more comorbidities,[2] and the likelihood of non-HIV illness increases with age.[4] One US study found that PLWH have rates of non-HIV conditions and non-antiretroviral therapy (ART) use that are comparable to those of people without HIV who are 5–10 years their senior.[5] Polypharmacy is common in PLWH ≥50 years of age, with one study finding that this population was prescribed an average of 11.6 concomitant non-ART medications and that over one-third received 16 or more medications.[6] As a result of these increased levels of comorbidities and polypharmacy, drug–drug interactions (DDIs) tend to be more common in older PLWH,[7] and additional scrutiny may be necessary to limit the risk of ART-related DDIs in this population. It is critical that the efficacy, safety and adherence of ART regimens are investigated in older PLWH; however, clinical trial data in this population are notably lacking.

Two- and three-drug ART regimens are recommended for the initial treatment of HIV infection.[8,9] Three-drug regimens usually consist of two nucleoside reverse transcriptase inhibitors (NRTIs) plus an integrase strand transfer inhibitor (INSTI).[8,9] Individuals may switch ART for a number of reasons, including to reduce pill burden or to simplify the dosing regimen, as well as to avoid side effects or decrease the risk of drug–food interactions or DDIs.[8] Switching ART regimens may occur more frequently in older PLWH, who have a higher prevalence of comorbidities and polypharmacy.

B/F/TAF, a coformulation of bictegravir (B), emtricitabine (F) and tenofovir alafenamide (TAF), is indicated as a complete regimen for the treatment of HIV-1 infection in individuals without present or past evidence of viral resistance to the INSTI class or to the individual components of the regimen.[10,11] Bictegravir is a potent, unboosted, once-daily INSTI with a favourable pharmacokinetic profile.[12] The combination of emtricitabine and either TAF or tenofovir disoproxil fumarate (TDF) is commonly recommended as an NRTI backbone.[8,9] TAF is a newer alternative to TDF with a more favourable bone and renal safety profile,[13] and is an effective treatment for hepatitis B.[14] B/F/TAF has been shown to have an acceptable safety profile and to be well tolerated and effective in treatment-naïve PLWH, virologically suppressed PLWH, and suppressed PLWH with pre-existing NRTI resistance.[15–21] Additionally, switching to B/F/TAF has been demonstrated to reduce the risk of DDIs in treatment-experienced individuals.[22]

The present 96-week phase 3b study evaluates the efficacy and safety of switching to B/F/TAF from an

elvitegravir (E)/cobicistat (C)/F/TAF fixed-dose or TDF-containing regimen in virologically suppressed PLWH ≥65 years of age. To our knowledge, this is the first European trial investigating the efficacy and safety of B/F/TAF in older PLWH. Previously published data from this study indicated that switching to B/F/TAF was effective and well tolerated through 48 weeks.[18] Here, we report the final 96-week analysis performed at trial completion.

METHODS

The full methods of this phase 3b, open-label, multicentre, single-arm trial (GS-US-380-4449; NCT03405935), including inclusion and exclusion criteria, have been reported in detail, along with data from the 48-week analysis[18]; the methods are summarized here in brief. Additional methods used for the 96-week analyses are described below.

Study design and participants

Participants were PLWH ≥65 years of age who were receiving a stable ART regimen (i.e., ≥3 months without changes); permitted regimens were E/C/F/TAF, or F/TDF plus a third agent in the case of participants who were/had previously enrolled in another trial that studied a switch from a TDF-based regimen to E/C/F/TAF (GS-US-292-1826; NCT02616783). Participants were required to have plasma HIV-1 RNA levels <50 copies/ml for the last two visits prior to screening.

Participants switched to B/F/TAF (50/200/25 mg), which was administered as an oral, fixed-dose combination, given once daily for 96 weeks without regard to food intake. Clinical visits were carried out at day 1 (baseline) and weeks 4, 12, 24, 36, 48, 60, 72, 84 and 96. A follow-up visit was carried out 30 days after the 96-week visit. The trial was conducted in Belgium, France, Italy, Spain and the UK and was approved by institutional review boards and independent ethics committees at each participating site. The trial was performed in accordance with Good Clinical Practice and the Declaration of Helsinki. All participants provided written informed consent.

Efficacy endpoints

The primary endpoint was the proportion of participants with HIV-1 RNA <50 copies/ml at week 24, defined using the US Food and Drug Administration (FDA)'s Snapshot algorithm.[23] Secondary endpoints included the proportion of participants with HIV-1 RNA <50 copies/ml at weeks 48, 72 and 96; the proportion of participants with HIV-1 RNA <50 copies/ml where missing data were treated as HIV-1 RNA ≥50 copies/ml (missing = failure); the proportion of participants with HIV-1 RNA <50 copies/ml where missing data were excluded from percentage calculations (missing = excluded); the change from baseline in CD4 cell count and percentage at weeks 24, 48, 72 and 96; and the safety and tolerability of B/F/TAF. Additional supportive endpoints included the proportion of participants with HIV-1 RNA <20 copies/ml and medication adherence assessed using a visual analogue scale (VAS) adherence questionnaire at day 1 and weeks 4, 12, 24, 36, 48, 60, 72, 84 and 96. The findings of other patient-reported outcomes have been reported elsewhere.[18]

Viral blips

Participants with at least one on-treatment, post-baseline HIV-1 RNA measurement were also included in a post hoc viral blip analysis. Viral blips were defined as a transient episode of viremia with HIV-1 RNA level ≥50 copies/ml, which was both preceded and followed by HIV-1 RNA levels <50 copies/ml.

Virologic resistance

Pre-existing resistance-associated mutations (RAMs) in reverse transcriptase (RT), protease and integrase were assessed via historical plasma RNA and proviral DNA genotypes (GenoSure Archive®, Monogram Biosciences, San Francisco, CA, USA), where available, and by retrospective proviral DNA genotype testing performed on baseline samples. Additional resistance testing was conducted for participants with virologic failure (VF), as defined by either a rebound in HIV-1 RNA to ≥50 copies/ml at any visit and ≥200 copies/ml at the following visit, or any participant with HIV-1 RNA ≥200 copies/ml at week 96 or study discontinuation. Genotype and phenotype testing were performed at the time of VF on HIV-1 RT, protease and integrase using PhenoSense® GT, GeneSeq® Integrase and PhenoSense® Integrase (Monogram Biosciences). Sequences obtained at the time of VF were compared with baseline and/or historic sequences to determine whether RAMs had developed during treatment. Where pretreatment sequences were unavailable and a RAM was present following treatment, the RAM would be considered treatment emergent.

Safety

Safety was assessed throughout the study and at follow-up. Assessments included monitoring of adverse events

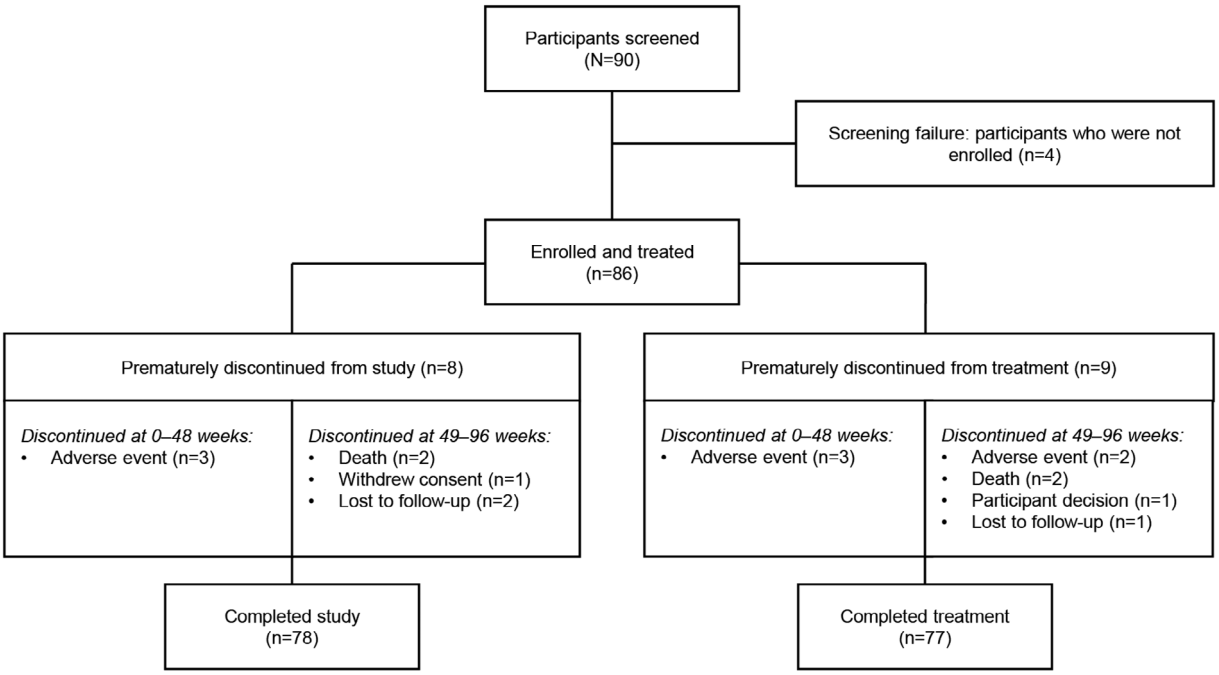

FIGURE 1 Participant disposition

(AEs; coded using the Medical Dictionary for Regulatory Activities, version 23.0), as well as of concomitant medications, clinical laboratory analyses, vital signs and electrocardiograms. Clinical laboratory analyses included urine retinol-binding protein to creatinine ratio (RBP:Cr), urine β_2-microglobulin to creatinine ratio (β_2m:Cr), estimated glomerular filtration rate as calculated by the Cockcroft–Gault equation ($eGFR_{CG}$), urine protein to creatinine ratio (UPCR), and lipid and glucose levels. Changes in UPCR were analysed using three classifications: urine protein <4.0 mg/dl, UPCR ≤200 mg/g and UPCR >200 mg/g.

Statistical analyses

Methods for statistical analyses and sample size calculation were reported in detail previously.[18] In brief, efficacy was evaluated using the full analysis set, which included all participants who had received at least one dose of study drug and had no major protocol violations. The safety analysis set included all enrolled participants who had received study drug. The Clopper–Pearson exact method was used to calculate 95% confidence intervals (CIs) for virologic data. Descriptive statistics were used to summarize changes from baseline in CD4 cell counts and percentage CD4, VAS adherence questionnaire results, AEs and clinical laboratory data. Changes from baseline in laboratory data were analysed using the two-sided Wilcoxon signed-rank test. Statistical analyses were performed using SAS® version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Participants

Ninety participants were screened, of whom 86 were enrolled and received study drug. Of these, 77 (89.5%) completed treatment and nine (10.5%) prematurely discontinued study drug (5 [5.8%] due to AEs, 2 [2.3%] due to death, 1 [1.2%] due to participant decision and 1 [1.2%] lost to follow-up; Figure 1). Due to the COVID-19 pandemic, 44 participants missed or had virtual visits for at least one of their 96-week or 30-day follow-up clinical assessments.

Full baseline demographics were previously reported (Table S1).[18] In brief, the majority of participants were male (75/86 [87.2%]) and White (82/86 [95.3%]). The median age of participants was 69 years (IQR 67–72; range 65–80) and the median body mass index was 26.6 kg/m^2 (IQR 24.0–28.7). The median number of chronic non-ART medications per participant at baseline was 3 (IQR 2–5); these were most commonly used for treating conditions related to the cardiovascular system and gastrointestinal tract (used by 55/86 participants [64.0%] and 54/86 [62.8%], respectively). The proportion of participants with a medical history of other conditions was high, with 44 (51.2%), 23 (26.7%) and 19 (22.1%)

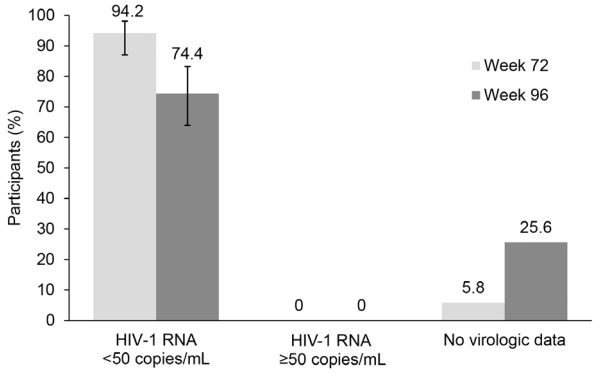

FIGURE 2 Virologic suppression at weeks 72 and 96 (FDA Snapshot analysis; full analysis set, $N = 86$). Values shown as percentage of participants (95% CI). FDA, Food and Drug Administration

participants having a record of hypertension, cardiovascular disease and diabetes, respectively (Figure S1).

Efficacy

Efficacy data for weeks 24 and 48 have been reported.[18] For the primary endpoint at week 24, the rate of virologic suppression (HIV-1 RNA <50 copies/ml; FDA Snapshot algorithm) was 97.7% (84/86; 95% CI 91.9–99.7).[18]

In the present analysis, the rates of virologic suppression determined by FDA Snapshot algorithm at weeks 72 and 96 were 94.2% (81/86; 95% CI 87.0–98.1%) and 74.4% (64/86; 95% CI 63.9–83.2%), respectively. No participants had HIV-1 RNA ≥50 copies/ml for either time point; virologic data were missing for 5 and 22 participants at weeks 72 and 96, respectively (Figure 2). The relatively high number of missing records at week 96 was largely due to the impact of the COVID-19 pandemic.

The results of the Snapshot analysis were consistent with the results of the missing = failure and missing = excluded analyses. When missing data were treated as failures, the proportions of participants with HIV-1 RNA <50 copies/ml were 94.2% (81/86; 95% CI 87.0–98.1%) and 79.1% (68/86; 95% CI 69.0–87.1%) at weeks 72 and 96, respectively. When missing data were excluded, the proportions of participants with <50 copies/ml at weeks 72 and 96 were 100.0% (81/81; 95% CI 95.5–100.0%) and 100.0% (68/68; 95% CI 94.7–100.0%), respectively.

The proportion of participants with HIV-1 RNA <20 copies/ml was 93.0% (80/86; 95% CI 85.4–97.4%) at week 72. One (1.2%) participant had HIV-1 RNA ≥20 copies/ml, and data were missing for five (5.8%) participants. At week 96, the proportion of participants with HIV-1 RNA <20 copies/ml was 68.6% (59/86; 57.7–78.2%). Six (7.0%) participants had HIV-1 RNA ≥20 copies/ml and 21 (24.4%) were missing data.

CD4 cell count and percentage remained stable throughout the study (Table S2). Median overall self-reported adherence was 100% (IQR 100–100%) at each time point (Table S3).

Viral blips

Of the 86 enrolled participants, 85 were included in the viral blip analysis. No viral blips occurred. One participant was viraemic at baseline (HIV-1 RNA 200 copies/ml) and another participant had HIV-1 RNA ≥50 copies/ml at two visits (125 and 60 copies/ml at baseline and week 4, respectively). Both participants subsequently achieved viral suppression, with HIV-1 RNA remaining <50 copies/ml throughout the remainder of the study.

Virologic resistance

At baseline, three participants had M184V mutations and nine had thymidine analogue mutations (TAMs) (Table S4). No participants met the criteria for additional resistance testing during the study; therefore, no treatment-emergent resistance was observed. All participants with pre-existing resistance maintained HIV-1 RNA <50 copies/ml at week 96 (or their last study visit, if earlier).

Safety

Median exposure to B/F/TAF was 96 weeks (IQR 95–96). Eighty-two (95.3%) participants experienced a treatment-emergent AE (TEAE). Eleven (12.8%) participants experienced a TEAE considered to be related to study drug; these included abdominal discomfort, abnormal faeces, constipation, dizziness, increased gamma-glutamyl transferase (GGT), headache, insomnia, irritability, myalgia, pruritus, sleep disorder, tendonitis and weight gain ($n = 1$ for each event; a participant could have had more than one event). The most commonly reported TEAEs, occurring in ≥3% of participants, are detailed in Table 1. There was a low rate of study drug-related TEAEs.

The majority of TEAEs were grade 1 or 2. Fifteen (17.4%) participants experienced a grade 3 or 4 TEAE. Two (2.3%) had a grade 3 TEAE considered to be related to study drug (Table 1); these were weight gain, irritability and sleep disorder ($n = 1$ for each event). Nine (10.5%) participants experienced at least one serious TEAE; none were considered related to study drug (Table 1).

TABLE 1 Treatment-emergent adverse events

TEAE	Safety analysis set ($N = 86$)
Any	82 (95.3)
Grade 3 or 4	15 (17.4)
Study drug-related	11 (12.8)
Grade 3 study drug-related	2 (2.3)
Serious	9 (10.5)
Study drug-related, serious	0
Leading to study drug discontinuation	5 (5.8)
Death	2 (2.3)
TEAEs reported in ≥3% of participants	
Bronchitis	10 (11.6)
Arthralgia	8 (9.3)
Hypertension	8 (9.3)
Nasopharyngitis	7 (8.1)
Diarrhoea	6 (7.0)
Sciatica	5 (5.8)
Urinary tract infection	5 (5.8)
Asthenia	4 (4.7)
Depression	4 (4.7)
Dizziness	4 (4.7)
Muscle spasms	4 (4.7)
Back pain	3 (3.5)
Dyspepsia	3 (3.5)
Haematuria	3 (3.5)
Headache	3 (3.5)
Hypercholesterolaemia	3 (3.5)
Hypotension	3 (3.5)
Myalgia	3 (3.5)
Onychomycosis	3 (3.5)
Radius fracture	3 (3.5)
Respiratory tract infection	3 (3.5)
Syncope	3 (3.5)
Syphilis	3 (3.5)
Upper respiratory tract infection	3 (3.5)
Visual impairment	3 (3.5)
Vitamin D deficiency	3 (3.5)
TEAEs considered study drug-related	
Abdominal discomfort	1 (1.2)
Abnormal faeces	1 (1.2)
Constipation	1 (1.2)
Dizziness	1 (1.2)
Headache	1 (1.2)
Increased gamma-glutamyl transferase	1 (1.2)
Increased weight	1 (1.2)
Insomnia	1 (1.2)
Irritability	1 (1.2)
Myalgia	1 (1.2)
Pruritus	1 (1.2)
Sleep disorder	1 (1.2)
Tendonitis	1 (1.2)

Note: Data reported as *n* (%).
Abbreviation: TEAE, treatment-emergent adverse event.

Drug discontinuations related to TEAEs were uncommon. Five (5.8%) participants reported TEAEs that led to study drug discontinuation (Table 1); these included TEAEs attributed to the study drug in three participants (3.5%; abdominal discomfort, weight gain, irritability and sleep disorder), as well as those not attributed to the study drug (drug withdrawal syndrome and alcohol withdrawal syndrome). One (1.2%) participant died from suicide (participant had a medical history of ongoing depressive disorder) and one (1.2%) died from COVID-19 pneumonia during the study; these deaths were not considered related to the study drug.

Three (3.5%) participants experienced grade 1 or 2 hepatic TEAEs (abnormal faeces, increased GGT and hepatocellular injury). While the events of abnormal faeces and increased GGT were considered related to the study drug, hepatocellular injury was not; none led to study drug discontinuation. No participants discontinued the study because of renal or urinary TEAEs, and no participants had proximal tubulopathy, including Fanconi syndrome.

Small initial variations from baseline in median values for urine RBP:Cr, urine β_2m:Cr and $eGFR_{CG}$ were previously reported,[18] but these values remained stable between weeks 48 and 96 (Figures S1 and 3a). Of the eight participants with clinically significant proteinuria (UPCR >200 mg/g) at baseline, data were obtained from five participants at week 96. Of these, one shifted to the classification of urine protein <4.0 mg/dl; the rest remained unchanged. Of the 39 participants with UPCR ≤200 mg/g at baseline, 28 had data after 96 weeks. One of these participants shifted to the classification of UPCR >200 mg/g, 13 were unchanged in classification and 14 shifted to urine protein <4.0 mg/dl. Thirty-two of the 39 participants with urine protein <4.0 mg/dl at baseline had data at week 96, with one shifting to the classification of UPCR >200 mg/g, five to that of UPCR ≤200 mg/g and the remainder unchanged.

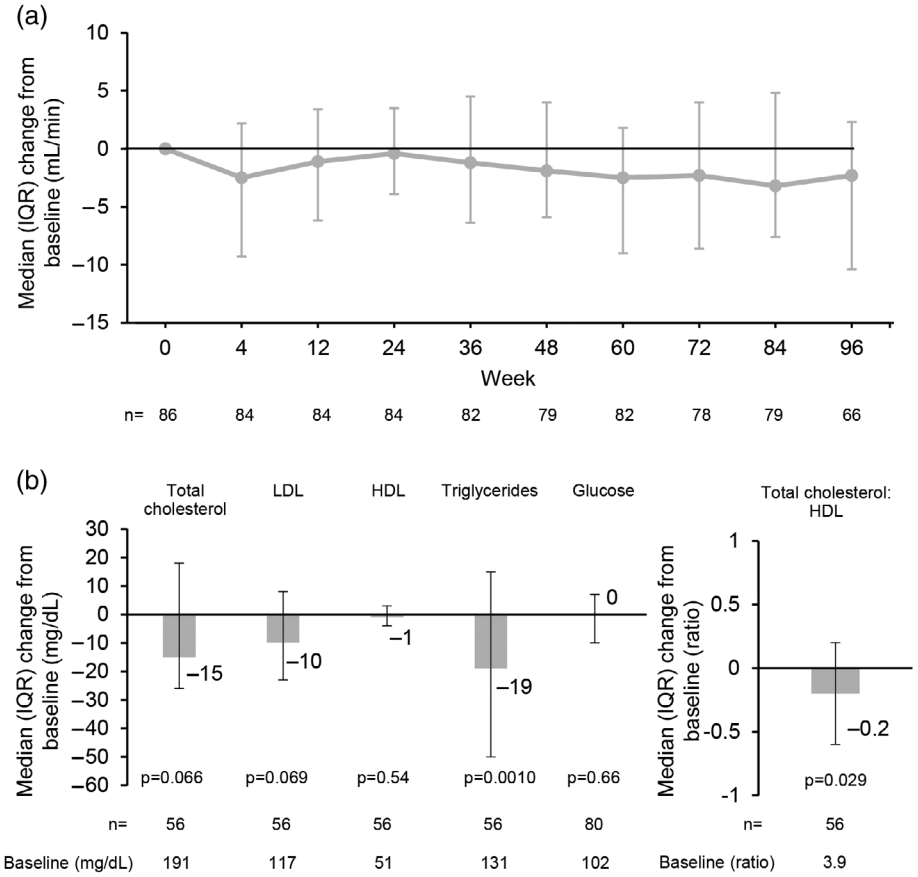

FIGURE 3 Changes in (a) estimated glomerular filtration rate calculated by the Cockcroft–Gault equation* and (b) fasting lipids and glucose at week 96 (safety analysis set). *Creatinine samples analysed on or after 1 July 2018 were from a new calibrator; the corrected values are summarized. HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein

There were no clinically relevant changes from baseline in haematological or clinical chemistry parameters, including metabolic parameters (Figure 3b), or in vital signs or electrocardiograms throughout the study. The median change in body weight from baseline at week 96 was 0.0 kg (IQR −2.3, 2.0) (Figure S2).

DISCUSSION

We previously reported that older, virologically suppressed PLWH who switched to B/F/TAF maintained viral suppression at 48 weeks, with no treatment-emergent resistance. The 48-week analyses identified no grade 3 or 4 drug-related TEAEs; no serious drug-related TEAEs; no discontinuations due to renal, hepatic or bone-related AEs; and no deaths.[18] The final 96-week analyses from this study demonstrate that B/F/TAF maintains these effects, with no participants experiencing HIV-1 RNA ≥50 copies/ml at 96 weeks. There were again no serious TEAEs or deaths related to study drug, and no study discontinuations related to renal or hepatic TEAEs. The number of study drug discontinuations was limited, with five (5.8%) participants experiencing TEAEs leading to discontinuation; in three (3.5%) of these participants, the TEAE leading to discontinuation was considered related to study drug. The observed B/F/TAF discontinuation rates due to TEAEs were similar to those found in previous studies that included younger adults (≥18 years of age), which reported rates of up to approximately 2%.[15–17,19–21] While the numbers discontinuing due to TEAEs were too low in all studies to allow comparisons, discontinuation rates are likely to be slightly higher in older PLWH as this population has a higher frequency of comorbidities and polypharmacy.[2,4–6] There were no bone-related AEs in the current analysis. Low rates of bone toxicity have been reported with TAF-based regimens.[13]

The study results are consistent with those of previous studies in younger individuals switching to B/F/TAF. Other studies in participants with median ages between 39 and 51 years showed that switching to B/F/TAF was non-inferior to comparator regimens.[15,16,19] Furthermore, a retrospective cohort analysis found that 94% (287/306) of participants ≥50 years of age maintained HIV-1 RNA <50 copies/ml 48 weeks after switching to B/F/TAF.[24] Other ART regimens have also been shown to have

similar virologic outcomes in older and younger participants.[25] In contrast, immunologic responses tend to be blunted in older PLWH initiating ART.[26] In the present 96-week analysis of participants with prolonged prior viral suppression, CD4 counts remained stable.

While adherence is generally better in older PLWH,[27] it remains important to consider adherence when switching regimens, as pill burden is likely to increase with age.[28] Self-reported adherence to B/F/TAF, a single, once-daily oral tablet, was high in the present study.

The study found no treatment-emergent resistance, including in participants with M184V or TAMs at baseline. This is aligned with the findings of other studies in patients with pre-existing resistance substitutions, which showed maintenance of viral suppression without emergent resistance on B/F/TAF.[15,29,30] Viral blip findings from the current analysis were also consistent with other data on switches to B/F/TAF in which blips were rare.[29]

There were no significant changes in body weight over the 96-week study period and no clinically relevant changes in metabolic parameters. This finding is consistent with a recent post hoc analysis of metabolic health parameters in participants from the phase 3 TANGO study; PLWH (primarily White males) who continued a TAF-based regimen experienced a small increase in weight from baseline to 48 weeks similar to that experienced by participants who had switched to a dolutegravir/lamivudine regimen (0.76 and 0.81 kg, respectively).[31] Weight gain is generally seen more often in Black, Hispanic and female PLWH[32]; as in TANGO, our trial participants were primarily White males. However, in the phase 3b BRAAVE study, which enrolled virologically suppressed Black PLWH, no significant difference in weight change was observed in participants switching to B/F/TAF compared with those who remained on their baseline regimen at 24 weeks.[33] The median weight gain in the B/F/TAF and comparator groups at 24 weeks was 0.9 and 0.2 kg, respectively.[33] In patients who initially switched to B/F/TAF, the median weight change remained at 0.9 kg 48 weeks after switching.[33] The association between INSTI treatment and weight gain may not apply in older populations, as one other study reported no weight gain in PLWH ≥65 years of age when switching to an INSTI-based regimen.[34] Notably, switching from weight-suppressant drugs such as efavirenz and TDF may increase the risk of weight gain.[35] In this study, the majority of participants were not taking weight-suppressant drugs at baseline (92% switched from E/C/F/TAF), so this effect was not observed.

A key strength of the present study is that the population, PLWH ≥65 years of age, is largely underrepresented in clinical trials, and the study provides much-needed data in this group. However, there are limitations – most importantly those inherent to open-label, single-arm and non-comparative studies. The impact of the COVID-19 pandemic also meant that data were missing for some participants at 96 weeks and at follow-up; overall, 44 participants missed or had virtual visits for at least one of their 96-week or 30-day follow-up clinical assessments because of the pandemic. These missing data affected the Snapshot and missing = failure analyses at week 96: of the participants with missing data at week 96 who were still on study drug, all had HIV-1 RNA <50 copies/ml at their last visit (either at week 84 or after week 96). Another limitation of this study is that 95% of participants were White, and the results may not be generalizable to non-White PLWH.

In conclusion, in this first European trial of B/F/TAF in older PLWH recruited from Belgium, France, Italy, Spain and the UK, switching to B/F/TAF was shown to be effective, with favourable safety and tolerability profiles through 96 weeks in virologically suppressed adults ≥65 years of age who had a high burden of baseline comorbidities and comedications. High rates of virologic suppression were observed, even when accounting for COVID-19-related study challenges, and adherence was high. Additionally, there was no development of resistance to B/F/TAF, including in participants with M184V mutations or TAMs at baseline. Switching to B/F/TAF is an effective long-term option for virologically suppressed adults ≥65 years of age.

AUTHOR CONTRIBUTIONS

MLD'A, SKC, DP, HM, RH, IRM and JG conceived and designed the study. FM, GR, J-MM, FP, SDW, LV and JB acquired the study data. MLD'A, CB, RH, IRM and JG verified and analysed the data. All authors interpreted the data, were involved with drafting or critical revisions of the manuscript, provided approval of the final manuscript for submission, and agree to be accountable for all aspects of the work.

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CONFLICTS OF INTEREST

FM reports advisory board fees from Gilead, ViiV, MSD and Janssen, and institutional grant support from Janssen, MSD and ViiV, outside the submitted work. GR reports

personal fees from ViiV, Gilead and MSD, outside the submitted work. J-MM reports grants from Gilead and personal fees from Gilead, Sanofi, Merck, ViiV and Aelix, outside the submitted work. FP reports payment to his institution from Gilead during the conduct of the study, personal fees and non-financial support from Gilead, grants and personal fees from Janssen, personal fees from MSD, and personal fees and non-financial support from ViiV, outside the submitted work. SDW reports grants from Gilead during the conduct of the study, and grants from Gilead, Janssen, MSD and ViiV, outside the submitted work. LV has nothing to disclose. JB reports personal fees from Janssen, and grants and personal fees from Gilead, MSD and ViiV, outside the submitted work. MLD'A, CB, SKC, DP, HM, RH, IRM and JG are employed by Gilead and hold stocks in Gilead.

ETHICS STATEMENT

The study was approved by the institutional review boards or independent ethics committees at each participating site and was performed in accordance with Good Clinical Practice and the Declaration of Helsinki. Study-related procedures were conducted with the understanding and informed consent of each participant.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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