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Descovy® (FTC/TAF) TAF-Based Regimens and Bone Safety

This document is in response to your request for information on data from key trials on the bone safety profile of Descovy® (emtricitabine/tenofovir alafenamide [FTC/TAF])-based regimens, including Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]), Genvoya® (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide [E/C/F/TAF]) and Odefsey® (emtricitabine/rilpivirine/tenofovir alafenamide [FTC/RPV/TAF]) in people with HIV-1 (PWH).

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Summary

Gilead Clinical Data on TAF-Based Regimens and Bone Safety

Pooled analysis: In a pooled analysis of five phase 3, randomized, clinical trials, participants who switched from a TDF- to a TAF-based regimen showed improvements in BMD at Week 48, independent of the use of a third agent.[1]

TAF vs TDF Studies: Multiple analyses showed changes in BMD that favored the TAF-based regimens when compared to the TDF-based regimens, including in participants with low BMD at baseline.[2-16]

TAF vs Other NRTI Studies: Changes in BMD from baseline were similar and did not differ significantly between FTC/TAF-based regimens and ABC/3TC-based regimens through Week 48 or Week 144.[17-25]

Non-Gilead Data on TAF-Based Regimens and Bone Safety

In the BFTAF Elderly Switch Study, the impact on BMD of switching to BIC/FTC/TAF from another ARV regimen in virologically suppressed, PWH aged ≥60 years was assessed. At enrollment, the prevalence of osteoporosis and osteopenia was 37.5% and 47.3%, respectively. Compared with participants with normal BMD, those with osteoporosis or osteopenia were more likely to be female, older, and have lower BMI and CrCl.[26]

In a randomized pilot study in which participants switched to BIC/FTC/TAF or continued their TDF-based regimen, bone quality (via BMSi) significantly improved from baseline to Week 24 in the BIC/FTC/TAF group (P=0.041) and did not significantly change in the TDF-based group.[27]

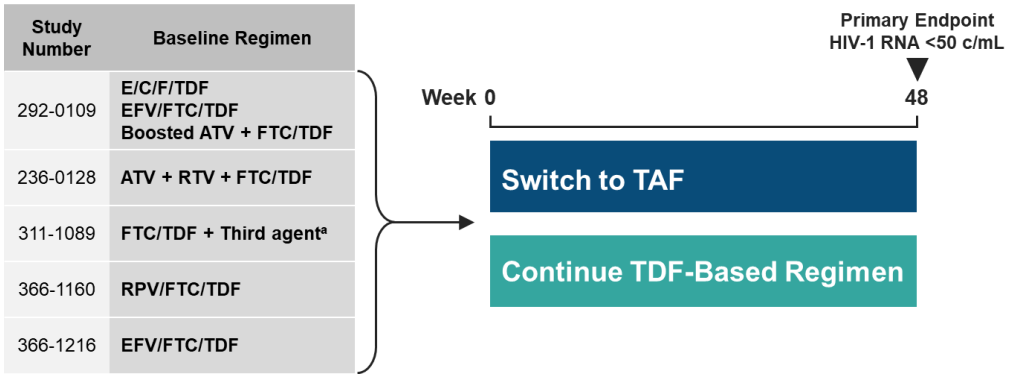
Gilead Clinical Data on TAF-Based Regimens and Bone Safety

Pooled Analysis[1]

Study design and demographics

Results were pooled from five phase 3, randomized, international, multicenter clinical studies of virologically suppressed participants who switched to a TAF-based regimen (n=2205). Key inclusion criteria were HIV-1 RNA <50 c/mL with stable renal function ($eGFR_{CG}$ ≥50 mL/min). Study design and baseline characteristics are presented in Figure 1 and Table 1.

Figure 1. Pooled Analysis: Study Design[1]



[a]Included RTV-boosted ATV, RTV-boosted DRV, DTG, EFV, RTV-boosted LPV, maraviroc, NVP, RAL, and RPV.

Table 1. Pooled Analysis: Baseline Demographics and Disease Characteristics[1]

Key Demographics and Characteristics		TAF-Based Regimen (n=2205)	TDF-Based Regimen (n=1611)	Total (N=3816)
Age, median, years		44	45	45
Male, %		81	86	83
Race/ethnicity, n (%)	White	68	69	68
	Black or African descent	22	23	23
	Latinx	20	18	19
BMI, mean ± SD, kg/m^2		26.8±5.3	26.7±5.1	26.7±5.3
HIV-1 RNA <50 c/mL, %		98	99	98
CD4 count, median, cells/mcL		665	659	662
$eGFR_{CG}$, median (Q1, Q3), mL/min		105.3 (88.7, 124.8)	105.1 (87.6, 125.7)	105.2 (88.2, 125.2)

Abbreviation: Q=quartile
Note: No participants had Grade 3 proteinuria at baseline.

Bone safety results

In the overall population, switching from a TDF-based regimen to a TAF-based regimen was associated with improvements in BMD for both the hip (1.4 vs -0.2, respectively; Δ1.5; *P*<0.001) and spine (1.6 vs -0.2; Δ1.8; *P*<0.001) at Week 48, independent of the third agent

used. Among the subpopulation of women, a TAF-based regimen compared with a TDF-based regimen was associated with higher BMD scores for both the hip (1.4 vs 0.1, respectively; Δ1.3; *P*<0.001) and spine (2.3 vs -0.4; Δ2.7; *P*<0.001). Similarly, among the subpopulation of participants aged ≥50 years, switching from a TDF-based regimen to a TAF-based regimen was associated with improvements in BMD for both the hip (1.1 vs -0.3, respectively; Δ1.4; *P*<0.001) and spine (1.9 vs -0.1; Δ2; *P*<0.001).

Bone Safety Data in Specific Populations

Analyses in women

Pooled analysis of seven clinical trials[13]

An analysis of five double-blind and two open-label randomized studies evaluated the efficacy and safety of TAF vs TDF in women. The integrated analysis in women included two studies in ARV-naive participants (n=260) and five studies in virologically suppressed participants (n=519). In ARV-naive women, participants initiating TAF showed less decline in hip and spine BMD at Week 96 than did participants initiating TDF. At Week 96, virologically suppressed women switching from a TDF-based regimen to a TAF-based regimen showed improvements in BMD for both the hip and spine. These BMD results in women were similar to those reported in men.

Pooled analysis of five clinical trials[25]

The efficacy and safety of BIC/FTC/TAF in female participants were assessed in a pooled analysis of five clinical studies through 48 weeks. In Study 1489, participants received either BIC/FTC/TAF or DTG/ABC/3TC. Mean decreases in BMD in the BIC/FTC/TAF vs DTG/ABC/3TC treatment arms at Week 48 were 0.5% vs 1.1%, respectively (*P*=0.52) for spine and 0.7% vs 1.7% (*P*=0.16) for hip. At Week 144, slight increases in BMD were observed, with no significant differences between study arms (spine, *P*=0.91; hip, *P*=0.29). In the overall pooled population, no discontinuations related to bone, renal, or hepatic AEs were observed.

Randomized trial in women[16]

A randomized clinical trial assessed whether switching to BIC/FTC/TAF (n=111) or staying on a TDF-based ARV regimen (n=110) would lead to bone mass recovery in women with HIV who were also receiving DMPA-IM. A third group included women who switched to BIC/FTC/TAF from a TDF ARV regimen and were using a non-hormonal contraception method (n=125). BMD assessments were determined by DXA scans.

In both groups that switched to BIC/FTC/TAF, there was improvement in the mean percent change in BMD at 6 and 12 months after switching. After switching, participants receiving non-hormonal contraception had a significantly greater increase in lumbar spine BMD than did participants receiving DMPA-IM (*P*=0.029); differences were not significant at the total hip (*P*=0.516) or femoral neck (*P*=0.615). Participants receiving non-hormonal contraception had higher BMD Z-scores at baseline and throughout treatment than did both groups receiving DMPA-IM (*P*≤0.021).

Pooled analysis in Latinx and Black participants[14]

An integrated analysis included Latinx and Black participants from two studies in ARV-naive participants (n=770) and five studies in virologically suppressed participants (n=1692). The analysis compared efficacy and safety outcomes in these subgroups with those in the

overall study populations. At Week 96, there were no significant differences in the median change from baseline in hip BMD or spine BMD in the Hispanic/Latinx and Black participants compared with the overall study population. Hispanic/Latinx and Black participants who initiated TAF had fewer BMD declines than those who initiated TDF, and participants who switched from TDF to TAF had improvements in BMD compared with participants remaining on TDF.

Analyses in participants aged ≥50 years

Pooled analysis of five studies[19]

An analysis of five studies evaluating the efficacy and safety of switching from TDF-containing regimens to TAF-containing regimens in study participants aged ≥50 years was conducted. At Week 96, participants who switched to TAF had significant increases from baseline in hip and spine BMD compared with those who remained on TDF, and BMD improvements after switching to TAF were observed both in participants aged ≥50 years and in those aged <50 years.

Post hoc analysis of Study 1489[28]

A post hoc analysis of participants in Study 1489 who were randomly assigned to receive BIC/FTC/TAF for 144 weeks and continued on BIC/FTC/TAF in the open-label extension phase for an additional 96 weeks evaluated the efficacy and safety of BIC/FTC/TAF in treatment-naive participants aged ≥50 years compared with those aged <50 years. Mean changes in hip and spine BMD from baseline to Week 240 were minimal, with no significant differences between participants aged ≥50 years and those aged <50 years: 0.3% vs -0.4%, respectively, for hip (*P*=0.38) and 1.3% and -0.9% for spine (*P*=0.1).

Integrated Data Through Week 144: GS-US-292-0104 and GS-US-292-0111

Study design and demographics

An integrated analysis of two phase 3, prospective, randomized, double-blind, active-controlled clinical trials that compared E/C/F/TAF (n=866) to E/C/F/TDF (n=867) in HIV-1 infected ARV-naive adults was performed. Key inclusion criteria were HIV-1 RNA ≥1000 c/mL, $eGFR_{CG}$ ≥50 mL/min, and genotypic sensitivity to study drugs. The primary endpoint was the percentage of participants with HIV-1 RNA <50 c/mL at Week 48 by the FDA Snapshot analysis. The secondary endpoints were efficacy and safety through Week 96 and Week 144. The prespecified key safety endpoints included spine and hip BMD. The predefined criterion for non-inferiority was the lower bound of a two-sided 95% CI >-12%. Baseline demographics and disease characteristics were similar between treatment arms. Most participants (85%) were male, and the median age was 34 years.[2,29]

Bone safety results through Week 144

Effects on markers of bone safety (changes in spine and hip BMD) significantly favored E/C/F/TAF through Week 144 (Table 2). Through Week 144, the percentage change from baseline in PTH levels was lower in the E/C/F/TAF group than in the E/C/F/TDF group. Median values were within the normal range in both treatment groups. At Week 144, recovery of osteopenia or osteoporosis at the hip was observed in 14 participants in the E/C/F/TAF group and 10 participants in the E/C/F/TDF group (*P*<0.001). Similar results were

observed in recovery of osteopenia or osteoporosis of the spine (24 participants vs 10 participants; *P*<0.001).[2]

Table 2. Changes in Bone Safety Parameters From Baseline Through Week 144 (Arribas et al)[2]

Parameters, %	E/C/F/TAF			E/C/F/TDF			*P*-Value[a]
	Week 48	Week 96	Week 144	Week 48	Week 96	Week 144	
Spine BMD, mean	-1.3	-1	-0.9	-2.8	-2.8	-3	<0.001
Hip BMD, mean	-0.7	-0.6	-0.8	-2.9	-3.3	-3.4	<0.001
Serum PTH, median	+23.1	+38.4	+47.3	+42.1	+61.7	+71.8	<0.001

[a]*P*-values for all parameters at all time points.

All bone-related AEs that led to discontinuation occurred in the E/C/F/TDF group and included bone density decrease, bone loss, osteopenia, and osteoporosis. Six participants in the E/C/F/TDF group discontinued study drug due to decreases in BMD. Fractures were rare and were not related to study drug (E/C/F/TAF group, 0.7% of participants; E/C/F/TDF group, 1.8% of participants; *P*=0.051). Favorable changes in hip and spine BMD scores in the E/C/F/TAF arm vs the E/C/F/TDF arm were also observed in subanalyses of participants aged ≥50 years, women, and Black vs non-Black participants.[30-32]

GS-US-292-0109

Study design and demographics[33,34]

A phase 3, randomized, open-label, active-controlled clinical trial evaluated the efficacy and safety of switching to E/C/F/TAF (n=959) vs continuing an FTC/TDF plus a third agent regimen (n=477) in virologically suppressed participants. Eligible participants had an HIV-1 RNA <50 c/mL for ≥96 weeks on a stable TDF-containing regimen and eGFR ≥50 mL/min. The primary endpoint was the proportion of participants with HIV-1 RNA <50 c/mL at Week 48 (FDA Snapshot analysis). Secondary endpoints included safety through Week 96. The following baseline demographics were similar between the E/C/F/TAF and FTC/TDF arms: median age, 41 vs 40 years, respectively; female, 11% (both arms); White/Black or African descent/Latinx, 68/18/26% vs 66/21/17%; and median CD4 cell count, 675 vs 662 cells/mcL.

Bone safety results through Week 96

Spine and hip BMD increased from baseline through Week 96 in participants who switched to E/C/F/TAF and decreased in those who remained on their TDF-based regimen (median percentage change: spine BMD, +2.1% vs -0.1%; hip BMD, +2.4% vs -0.5%, respectively; *P*<0.001 for each). Through Week 96, improvements (*P*<0.001) in BMD categorical outcomes (normal, osteopenia, and osteoporosis, as defined by T-score) at both the spine and the hip were observed in participants treated with E/C/F/TAF compared to those remaining on TDF-based regimens.[3,35]

Participants who switched to E/C/F/TAF, compared with those who continued a TDF-based regimen, had a smaller increase from baseline in PTH at Week 96 (median percentage change: +7% vs +20.4%, respectively; *P*<0.001) and a decrease from baseline in the bone turnover biomarkers CTx and P1NP at Week 48 (median percentage change: -3% vs +2.9% and -30% vs +2.9%, respectively; *P*<0.001 for each comparison). Subgroup analyses by pre-switch regimen demonstrated that changes in PTH and bone turnover biomarkers

trended in the same direction and magnitude as observed in the overall study population, except for in those who continued EFV/FTC/TDF. Changes in CTx and P1NP for participants taking EFV/FTC/TDF and those who switched to E/C/F/TAF were similar.[36]

Integrated Analysis in Low BMD Subgroup: GS-US-292-109 and GS-US-292-0112[4]

Analyses of pooled data were performed on two phase 3, prospective clinical trials in virologically suppressed adult PWH who switched to E/C/F/TAF (Study GS-US-292-109 and GS-US-292-0112) and met two criteria at study entry: 1) on a TDF-containing regimen and switched to E/C/F/TAF, and 2) presence of clinically significant low BMD (as defined by a T-score ≤-2 at either the lumbar spine, total hip, or femoral neck) at baseline. Of the 1117 enrolled patients who switched from TDF to TAF, 214 (19%) had clinically significant low BMD at baseline. In patients with a baseline T-score ≤-2, significant BMD increases from baseline to Week 96 were observed at both the spine and hip (median increase: +2.53% and +2.39%, respectively; *P*<0.001). Twenty-seven percent and 16% of patients with low BMD had clinically significant (≥5%) BMD increases at the lumbar spine and total hip, respectively. Of the 86 patients with low BMD and osteoporosis (T-score ≤-2.5) at baseline, 23% improved to osteopenia by Week 96.

In multivariate analyses, baseline factors associated with ≥5% BMD increase at Week 96 included higher $FEPO_4$ (≥10%) for the hip, higher BMI (≥30 kg/m^2), and higher P1NP levels (>1.85 log_{10} ng/mL) levels for the lumbar spine.

Study GS-US-311-1089

Study design and demographics

Study 1089 was a phase 3, randomized, double-blind, multicenter, active-controlled clinical trial in virologically suppressed adult participants (N=663) that evaluated the efficacy and safety of switching to FTC/TAF vs continuing FTC/TDF while remaining on the same third agent. Participants were virologically stable (HIV-1 RNA <50 c/mL) on FTC/TDF plus a third agent for ≥6 months and had an $eGFR_{CG}$ ≥50 mL/min prior to switch. The primary endpoint was the percentage of participants maintaining virologic suppression (HIV-1 RNA <50 c/mL) by FDA Snapshot analysis at Week 48, with a prespecified non-inferiority margin of 10%.[5] Baseline demographics and disease characteristics for the FTC/TAF and FTC/TDF arms were well balanced: mean age, 48 vs 49 years, respectively; female, 14% vs 16%; Black, 21% vs 20%; median CD4 count, 663 vs 624 cells/mcL; median eGFR, 99.4 vs 100.2 mL/min; median duration on FTC/TDF before enrollment, 5.2 vs 5 years. In the FTC/TAF and FTC/TDF arms baseline third agents consisted of the following: DRV + RTV, 25% for both arms; ATV + RTV, 16% vs 15%, respectively; LPV + RTV, 5% for both arms; NVP, 22% vs 20%; RAL, 20% vs 22%; DTG, 8% vs 7%.[7,37]

Bone safety results through Week 96[5]

At Week 48, switching to FTC/TAF vs staying on FTC/TDF was associated with significant increases in both spine (1.7 vs -0.1) and hip (1.2 vs -0.1) mean BMD scores, as measured by DXA scans. At Week 96, additional increases in mean BMD scores in both spine (2.2 vs -0.2; *P*<0.001) and hip (1.9 vs -0.3; *P*<0.001) were observed.

In subgroup analyses, significant improvements in renal and bone safety were observed after switching from FTC/TDF to FTC/TAF, regardless of the third agent.

Study GS-US-366-1216 and Study GS-US-366-1160

Study design and demographics

Two phase 3, randomized, double-blind, active-controlled non-inferiority studies evaluated the efficacy, safety, and tolerability of switching to FTC/RPV/TAF vs continuing on a TDF-based regimen in virologically suppressed (HIV-1 RNA <50 c/mL) PWH through Week 96.[11,12]

The primary endpoint for both studies was to evaluate the efficacy of switching from FTC/RPV/TDF or EFV/FTC/TDF to FTC/RPV/TAF, measured by the proportion of participants who maintained virologic suppression at Week 48 by FDA Snapshot Analysis.[11,12] The secondary endpoints included change from baseline in hip and spine BMD at Weeks 48 and 96.[11,12,38]

Table 3. Studies 1216 and 1160: Baseline Demographics and Disease Characteristics[11,12]

Key Demographics and Characteristics		Study 1216		Study 1160	
		FTC/RPV/TAF (n=316)	FTC/RPV/TDF (n=314)	FTC/RPV/TAF (n=438)	EFV/FTC/TDF (n=437)
Age, median, years		46	44	49	48
Male, n (%)		275 (87)	289 (92)	373 (85)	390 (89)
Race, n (%)	White	238 (75)	235 (75)	291 (66)	292 (67)
	Black or African descent	65 (21)	54 (17)	118 (27)	120 (27)
Duration of current regimen, median, years		2.3	2.5	6.5	6.6
CD4 count, median, cells/mcL		673	668	673	666
$eGFR_{CG}$, median, mL/min		104	100	110	108

Bone safety results through Week 96[12]

For both studies, switching to FTC/RPV/TAF was associated with statistically significant increases in hip and spine BMD at Week 96, compared to minimal changes in BMD with continuation of the baseline regimen (Table 4). Fractures were infrequent, and rates were similar in both studies.

Table 4. Studies 1216 and 1160: Changes in BMD From Baseline to Week 96[12]

Mean % Change	Study 1216			Study 1160		
	FTC/RPV/TAF	FTC/RPV/TDF	*P*-Value[a]	FTC/RPV/TAF	EFV/FTC/TDF	*P*-Value[a]
Hip BMD	+1.62	-0.61	<0.001	+1.83	-0.62	<0.001
Spine BMD	+2.04	-0.25	<0.001	+1.7	+0.13	<0.001

[a]*P*-values from analysis of variance including treatment as fixed effect.

Study GS-US-380-1489

Study design and demographics[17,18,39,19]

A phase 3, prospective, randomized, double-blind, active-control clinical trial compared BIC/FTC/TAF (n=314) to DTG/ABC/3TC (n=315) in HIV-1 infected, ARV-naive adults. Key inclusion criteria were HIV-1 RNA ≥500 c/mL at screening, $eGFR_{CG}$ ≥50 mL/min, and genotypic sensitivity to the NRTI components of the study regimen. The primary endpoint

was the proportion of participants with plasma HIV-1 RNA <50 c/mL at Week 48 by the FDA Snapshot analysis, with a prespecified non-inferiority margin of 12%. Secondary endpoints were efficacy and safety through Week 96 and Week 144, including the mean percentage changes from baseline in hip and lumbar spine BMD. BMD assessments were determined by DXA scans. The following baseline demographics were similar between the BIC/FTC/TAF and DTG/ABC/3TC groups: median (range) age, 31 (18–71) vs 32 (18–68) years, respectively; male, 91% vs 90%; White/Black or African descent/Latinx, 58/36/23% vs 57/36/21%; and median CD4 cell count, 443 vs 450 cells/mcL.

Week 144 data[24]

At Week 144, the mean percentage change from baseline in both hip and lumbar spine BMD were statistically nonsignificant between the two groups (spine, *P*=0.26; hip, *P*=0.39).

Open-label extension – bone safety[40]

At the Week 144, all participants were offered enrollment in the open-label extension phase with BIC/FTC/TAF. A total of 254 participants receiving DTG/ABC/3TC switched to BIC/FTC/TAF, and 252 participants continued BIC/FTC/TAF from Study 1489.

At Week 240, participants initially randomized to receive BIC/FTC/TAF had small declines in spine and hip BMD from baseline, with a mean change of -0.2% in spine BMD and -0.3% in hip BMD.

Study GS-US-311-1717[20]

Study design and demographics

Study 1717 was a phase 3b, randomized, double-blind, multicenter, active-control clinical trial in virologically suppressed PWH evaluating the efficacy and safety of switching to FTC/TAF (n=280) or continuing 3TC/ABC (n=276) while remaining on the same third agent. Eligible participants had HIV-1 RNA <50 c/mL on 3TC/ABC plus a third agent for ≥6 months and had $eGFR_{CG}$ ≥50 mL/min prior to switch. The primary endpoint was the proportion of participants who maintained virologic suppression (HIV-1 RNA <50 c/mL) by FDA Snapshot analysis at Week 48. Baseline demographics and disease characteristics for the FTC/TAF and 3TC/ABC arms were well balanced.

Bone safety results through Week 48

Switching to FTC/TAF was associated with small increases in BMD vs remaining on 3TC/ABC at the spine (mean change from baseline, +0.1 vs +0.03, respectively; *P*=0.78) and hip (mean change from baseline, +0.27 vs +0.16; *P*=0.55).

Study GS-US-380-1844

Study design and demographics

A phase 3, randomized, double-blind study evaluated the safety and efficacy of switching to BIC/FTC/TAF (n=282) vs staying on a baseline regimen of DTG + ABC/3TC or DTG/ABC/3TC (n=281) in virologically suppressed PWH. Key inclusion criteria were HIV-1 RNA <50 c/mL at screening for ≥3 months with no history of treatment failure, $eGFR_{CG}$ ≥50 mL/min, and no documented or suspected resistance to study drugs. The primary endpoint was the proportion of participants with plasma HIV-1 RNA ≥50 c/mL at

Week 48 by the FDA Snapshot analysis, with a prespecified non-inferiority margin of 4%.[23,41] Secondary endpoints included the change from baseline in hip and spine BMD at Week 48.[41] Baseline demographics and disease characteristics were similar between groups.[23]

Bone safety results through Week 48

Changes in BMD from baseline to Week 48 were similar between the BIC/FTC/TAF and DTG/ABC/3TC groups, with mean percentage changes of 0.69% and 0.42%, respectively, in lumbar spine BMD (*P*=0.33) and 0.3% and 0.16% in hip BMD (*P*=0.47).[23]

Non-Gilead Data on TAF-Based Regimens and Bone Safety

BFTAF Elderly Switch Study[26]

Study design and demographics

A randomized, open-label, active-controlled, multicenter, non-inferiority trial conducted in Kenya evaluated the impact on BMD of switching to BIC/FTC/TAF from another ARV regimen in virologically suppressed (HIV-1 RNA <50 c/mL) PWH aged ≥60 years with no history of virologic failure. Exclusion criteria included those with a history of fragility fracture, lytic or blastic metastases, hip arthroplasty, and lumbar spine internal fixation. At enrollment, participants in the BMD monitoring population (N=296) underwent DXA scans of the lumbar spine, total hip, and femoral neck. The prevalence of osteoporosis (T-score ≥-2.5) and osteopenia (T-score between -1 and -2.5) in this population at baseline was reported. At baseline, the median age was 64 years, 49.7% were female, all participants were Black, the median BMI was 27.5 kg/m^2, 35.5% had CrCl <60 mL/min, and the median time on ARV was 9.5 years.

Results

At enrollment, the median (IQR) BMDs of the lumbar spine, total hip, and femoral neck were 0.87 (0.78–0.99) g/cm^2, 0.89 (0.79–1.01) g/cm^2, and 0.75 (0.67–0.84) g/cm^2, respectively. The corresponding median (IQR) T-scores were -1.85 (-2.77 to -0.71), -1.03 (-1.89 to -0.27), and -1.54 (-2.19 to -0.85), respectively. Based on the lowest T-score in any area at baseline, 37.5% of participants had osteoporosis, and 47.3% had osteopenia. A bivariate analysis found a significant association between osteoporosis and female sex (*P*<0.001), lower BMI (*P*=0.02), and lower CrCl (*P*=0.02). Compared with participants with normal BMD, those with osteoporosis or osteopenia were more likely to be female, older, and have lower BMI and CrCl.

Open-Label, Randomized Pilot Study in Spain[27]

An open-label, randomized, single-center pilot study in Spain evaluated the changes in bone quality and BMD in virologically suppressed PWH who switched from a TDF-based regimen (a three-drug regimen including FTC) to BIC/FTC/TAF (n=12) or continued their previous TDF-based regimen (n=12). BMSi (correlated with bone quality using a minimally invasive bone microindentation procedure) and BMD at the lumbar spine and femoral neck were assessed at baseline and at Week 24. The primary endpoint was the mean percentage

change in BMSi at Week 24, and secondary endpoints included changes from baseline to Week 24 in spine and hip BMD and bone turnover markers. Most participants were male, and the median age at enrollment was 45 years.

A significant increase from baseline to Week 24 in bone quality (BMSi) was observed for the BIC/FTC/TAF group (mean change, +5.1%; *P*=0.041); the change in the TDF-based group was not significant (-0.05%; *P*=0.812). The difference in bone quality at Week 24 between the BIC/FTC/TAF and TDF-based groups was significant (*P*=0.049). No significant changes from baseline or differences between treatment groups in BMD values at Week 24 were observed. In both treatment groups, significant decreases at Week 24 in P1NP (bone formation marker) were observed (*P*≤0.032); significant decreases in CTx (bone resorption marker) were only observed in the BIC/FTC/TAF group (*P*=0.028).

References

1. Rockstroh J, Orkin C, Yazdanpanah Y, et al. Switching From TDF to TAF Improves Bone and Renal Safety Independent of Age, Sex, Race, or 3rd Agent: Results From Pooled Analysis (N=3816) of Virologically Suppressed HIV-1 Infected Adults [Presentation MOPEB0289]. Paper presented at: 9th IAS Conference on HIV Science; 23–26 July 2017; Paris, France.
2. Arribas JR, Thompson M, Sax PE, et al. A Randomized, Double-Blind Comparison of Tenofovir Alafenamide (TAF) vs. Tenofovir Disoproxil fumarate (TDF), Each Coformulated with Elvitegravir, Cobicistat, and Emtricitabine (E/C/F) for Initial HIV-1 Treatment: Week 144 Results [Accepted]. *J Acquir Immune Defic Syndr.* 2017:1-20. http://www.ncbi.nlm.nih.gov/pubmed/28282300
3. DeJesus E, Haas B, Segal-Maurer S, et al. Superior Efficacy and Improved Renal and Bone Safety After Switching From a Tenofovir Disoproxil Fumarate Regimen to a Tenofovir Alafenamide-Based Regimen Through 96 Weeks of Treatment [Poster LB-087]. Paper presented at: ASM Microbe; 16-20 June, 2016; Boston, MA.
4. Brown TT, Yin MT, Gupta S, et al. Switching from TDF To TAF in HIV-Infected Adults With Low BMD: A Pooled Analysis [Poster 683]. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); 13-16 February, 2017; Seattle, WA.
5. Raffi F, Orkin C, Clarke A, et al. Long-term (96-week) Efficacy and Safety After Switching from Tenofovir Disoproxil Fumarate (TDF) to Tenofovir Alafenamide (TAF) in HIV-infected, Virologically Suppressed Adults [Accepted]. *Journal of Acquired Immune Deficiency Syndromes (JAIDS).* 2017.
6. Gallant J, Daar E, Raffi F, et al. Switching to F/TAF (Tenofovir Alafenamide) from F/TDF (Tenofovir DF) based Regimen Study 311-1089: 48-Week Data [Presentation]. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); 22-25 February, 2016; Boston, MA.
7. Gallant JE, Daar ES, F. R, et al. Efficacy and safety of tenofovir alafenamide versus tenofovir disoproxil fumarate given as fixed-dose combinations containing emtricitabine as backbones for treatment of HIV-1 infection in virologically suppressed adults: a randomised, double-blind, active-controlled phase 3 trial *Lancet HIV.* 2016;3:e158-e165.
8. Custodio JM, Ting LS, Zack JZ, et al. Tenofovir Alafenamide Has Wide Efficacious Range for Treatment of HIV-1 Infection: Pharmacokinetic-Pharmacodynamic Relationship From a Phase 3 Study [Poster SUNDAY-407]. Paper presented at: ASM Microbe; 16-20 June, 2016; Boston, MA.
9. Custodio JM, Ting LS, Zack JZ, et al. Pharmacokinetics–Pharmacodynamics of Emtricitabine/Tenofovir Alafenamide Demonstrated Wide Exposure Range Associated With Clinical Safety [Poster SUNDAY-410]. Paper presented at: ASM Microbe; 16-20 June, 2016; Boston, MA.
10. Custodio JM, Ting LS, Zack JZ, et al. Enhanced Exposure of Tenofovir-Diphosphate in Peripheral Blood Mononuclear Cells by Tenofovir Alafenamide Compared With Tenofovir Disoproxil Fumarate [Poster SUNDAY-409]. Paper presented at: ASM Microbe; 16-20 June, 2016; Boston, MA.

11. Orkin C, DeJesus E, Ramgopal M, et al. 48 Week Results from two studies: Switching to RPV/FTC/TAF from EFV/FTC/TDF (Study 1160) or RPV/FTC/TDF (Study 1216) [Presentation]. Paper presented at: HIV Glasgow; 23-26 October, 2016; Glasgow, United Kingdom.
12. Hagins D, Orkin C, et al. Switching to coformulated rilpivirine (RPV), emtricitabine (FTC) and tenofovir alafenamide from either RPV, FTC and tenofovir disoproxil fumarate (TDF) or efavirenz, FTC and TDF: 96-week results from two randomized clinical trials. *HIV Med.* 2018. https://www.ncbi.nlm.nih.gov/pubmed/30101539
13. Thompson MA, Brar I, Brinson C, et al. Tenofovir Alafenamide vs Tenofovir DF in Women: Pooled Analysis of 7 Clinical Trials [Presentation]. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); 04-07 March, 2019; Seattle, WA.
14. DeJesus E, Villanueva J, Lopez J, et al. Tenofovir Alafenamide vs Tenofovir Disoproxil Fumarate in Hispanic/Latinx and Black Participants: Efficacy, Bone and Renal Safety Results From a Pooled Analysis of 7 Clinical Trials [Poster 318]. Paper presented at: IDWeek; 2-6 October, 2019; Washington, DC.
15. Stellbrink HJ, Post FA, Podzamczer D, et al. Safety and Efficacy of Switching From Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide in People With HIV Aged 50 Years and Older [Poster]. Paper presented at: 17th European AIDS Conference (EACS); 06-09 November, 2019; Basel, Switzerland.
16. Kiweewa F, Beksinska ME, Nabwana M, et al. Recovery of Bone Mass in Women on Depo-Provera and TDF based ART Switched to B/F/TAF [Poster 0685] Paper presented at: CROI; February 19-22, 2023; Washington, USA.
17. Gallant J, Lazzarin A, Mills A, et al. A Phase 3 Randomized Controlled Clinical Trial of Bictegravir in a Fixed Dose Combination, B/F/TAF, vs DTG/ABC/3TC in Treatment-Naïve Adults at Week 48 [Presentation W48]. Paper presented at: 9th IAS Conference on HIV Science; 23–26 July, 2017; Paris, France.
18. Gallant J, Lazzarin A, Mills A, et al. Bictegravir, Emtricitabine, and Tenofovir Alafenamide Versus Dolutegravir, Abacavir, and Lamivudine for Initial Treatment of HIV-1 Infection (GS-US-380-1489): A Double-Blind, Multicentre, Phase 3, Randomised Controlled Non-Inferiority Trial. *Lancet.* 2017;390:2063-2072. http://www.ncbi.nlm.nih.gov/pubmed/28867497
19. ClinicalTrials.gov. *Safety and Efficacy of Bictegravir/Emtricitabine/Tenofovir Alafenamide Versus Abacavir/Dolutegravir/Lamivudine in HIV-1 Infected, Antiretroviral Treatment-Naïve Adults. ClinicalTrials.gov Identifier: NCT02607930. Last Updated: 05 December.* 2017.
20. Winston A, Post FA, DeJesus E, et al. Randomized Double-blind Trial Comparing Switching to TAF/FTC- versus Continuing ABC/3TC-based Regimens in Virologically Suppressed Adults (Study 1717): 48 Week Results [Presentation]. Paper presented at: 16th European AIDS Conference; 25-27 October, 2017; Milan, Italy.
21. Mallon PW, Maughan RT, Garcia AA, et al. Change in Soluble Glycoprotein VI When Switching From ABC/3TC to TAF/FTC [Poster 677LB]. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); 04-07 March, 2018; Boston, MA.
22. Mallon PW, Winston A, Post F, et al. Platelet Function Upon Switching To TAF vs Continuing ABC: a Randomized Substudy [Presentation 80]. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); 04-07 March, 2018; Boston, MA.
23. Molina JM, Ward D, Brar I, et al. Switch to Bictegravir/F/TAF From DTG and ABC/3TC [Presentation 022]. Paper presented at: Conference on Retroviruses and Opportunisitc Infections (CROI); 04-07 March, 2018; Boston, MA.
24. Orkin C, DeJesus E, Sax PE, et al. Three-Year Outcomes of the Fixed-Dose Combination Bictegravir, Emtricitabine, and Tenofovir Alafenamide vs Dolutegravir-Containing Regimens for Initial Treatment of HIV-1 Infection: Week 144 Results from Two Randomised, Double-Blind, Multicentre, Phase 3, Non-Inferiority Trials. *The Lancet HIV.* 2020;7:e389–400.
25. Orkin C, Ajana F, Kityo C, et al. Brief Report: Efficacy and Safety of Bictegravir/Emtricitabine/Tenofovir Alafenamide in Females Living With HIV: An Integrated Analysis of 5 Trials. *J Acquir Immune Defic Syndr.* 2021;88(4):393-398.
26. Penner J, Ombajo LA, Nkuranga J, et al. High prevalence of osteoporosis among virally suppressed older people (>/=60 years) living with HIV. *HIV Med.* 2025;26(3):382-389.
27. Soldado-Folgado J, Rins-Lozano O, Arrieta-Aldea I, et al. Changes in bone quality after switching from a TDF to a TAF based ART: A pilot randomized study. *Front Endocrinol.* 2023;14:1076739.

28. Kityo CM, Gupta SK, Kumar PN, et al. Efficacy and Safety of B/F/TAF in Treatment-Naïve People With HIV Aged ≥ 50 Years: 5-Year Follow-Up From Two Phase 3 Studies [Poster P-547]. Paper presented at: IDWeek; October 16-19, 2024; Los Angeles, CA.
29. Sax PE, Wohl D, Yin MT, et al. Tenofovir alafenamide versus tenofovir disoproxil fumarate, coformulated with elvitegravir, cobicistat, and emtricitabine, for initial treatment of HIV-1 infection: two randomised, double-blind, phase 3, non-inferiority trials *Lancet.* 2015;385:2606-2615. http://www.ncbi.nlm.nih.gov/pubmed/25890673
30. Ward D, Thompson M, Goldstein D, et al. Week 96 Efficacy and Safety of Tenofovir Alafenamide (TAF) vs Tenofovir Disoproxil Fumarate (TDF) in Older, HIV-Infected Treatment-Naïve Adults [Poster 33]. Paper presented at: 7th International Workshop on HIV & Aging; 26-27 September, 2016; Washington, DC.
31. Wohl D, Gathe J, Thompson M, et al. Safety and Efficacy of TAF vs TDF Single-Tablet Regimen in HIV-1 Treatment-Naïve Black and Nonblack Patients Through Week 48 [Poster 1073]. Paper presented at: IDWeek™; 07-11 October, 2015; San Diego, CA.
32. Orkin C, Koenig E, Clarke A, et al. Improved Safety and Efficacy of TAF vs TDF Single-Tablet Regimen in HIV-1 Treatment-Naïve Women Through Week 48 [Poster PE7/13]. Paper presented at: 15th European, AIDS Conference (EACS); 21-24 October, 2015; Barcelona, Spain.
33. Mills A, Andrade-Villanueva J, DiPerri G, et al. Switching From a Tenofovir Disoproxil Fumarate (TDF)-Based Regimen to a Tenofovir Alafenamide (TAF)-Based Regimen: Data in Virologically Suppressed Adults Through 48 Weeks of Treatment [Presentation]. Paper presented at: International AIDS Society (IAS) Conference on HIV Pathogenesis, Treatment and Prevention2015; Vancouver, Canada.
34. Mills A, Arribas JR, Andrade-Villanueva J, et al. Switching from tenofovir disoproxil fumarate to tenofovir alafenamide in antiretroviral regimens for virologically suppressed adults with HIV-1 infection: a randomised, active-controlled, multicentre, open-label, phase 3, non-inferiority study. *Lancet Infect Dis.* 2016;16(1):43-52. http://www.ncbi.nlm.nih.gov/pubmed/26538525
35. DeJesus E, Haas B, et al. Superior Efficacy and Improved Renal and Bone Safety After Switching From a Tenofovir Disoproxil Fumarate (TDF) to a Tenofovir Alafenamide (TAF) based Regimen Through 96 Weeks of Treatment. *AIDS Research & Human Retroviruses.* 2018. https://doi.org/10.1089/AID.2017.0203
36. Overton ET, Shalit P, Crofoot G, et al. Switch From TDF Regimens to E/C/F/TAF Is Associated With Improved Bone Mineral Density, Decreased Serum PTH, and Decreased Bone Turnover Biomarkers [Poster 3537]. Paper presented at: ASM Microbe; 16-20 June, 2016; Boston, MA.
37. DeJesus E, Ellion R, Ramgopal M, et al. Efficacy and Safety of Tenofovir Alafenamide in HIV-Infected Black Adults: Subgroup Analysis of a Randomized, Double-blind Switch Study [Poster 1508]. Paper presented at: IDWeek; 26-30 October, 2016; New Orleans, LA.
38. Clinicaltrials.gov. *Study to Evaluate Switching From a Regimen Consisting of Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate (EFV/FTC/TDF) Fixed Dose Combination (FDC) to Emtricitabine/Rilpivirine/Tenofovir Alafenamide (FTC/RPV/TAF) FDC in Virologically-Suppressed, HIV-1 Infected Adults. ClinicalTrials.gov Identifier: NCT02345226. Available at: https://clinicaltrials.gov/ct2/show/NCT02345226. Last updated: 14 July.* 2016.
39. Wohl D, Yazdanpanah Y, Baumgarten A, et al. A Phase 3, Randomized, Controlled Clinical Trial of Bictegravir in A Fixed-Dose Combination, B/F/TAF, vs DTG/ABC/3TC in Treatment-Naive Adults at Week 96 [Presentation 74246]. Paper presented at: IDWeek; 03-07 October, 2018; San Francisco, CA.
40. Wohl DA, Pozniak A, Workowski K, et al. B/F/TAF Five-Year Outcomes in Treatment-Naïve Adults [Poster 494]. Paper presented at: Virtual Conference on Retroviruses and Opportunistic Infections (CROI) 2022; 12-16 February, 2022.
41. U.S. National Institutes of Health. *Safety and Efficacy of Switching From Dolutegravir and ABC/3TC or ABC/DTG/3TC to B/F/TAF in HIV-1 Infected Adults Who Are Virologically Suppressed. ClinicalTrials.gov Identifier: NCT02603120. Available at: https://www.clinicaltrials.gov/ct2/show/record/NCT02603120. Last Update Posted: 21 November* 2017.

Abbreviations

3TC=lamivudine
ABC=abacavir
AE=adverse event
ARV=antiretroviral
ATV=atazanavir
BIC=bictegravir
BMD=bone mineral density
BMSi=Bone Material Strength index
c/mL=copies/mL
CG=Cockcroft-Gault
CTx=C-terminal telopeptide
DMPA-IM=intramuscular depot medroxyprogesterone acetate
DRV=darunavir
DTG=dolutegravir
DXA=dual energy X-ray absorptiometry
E/C/F/TAF=elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide
E/C/F/TDF=elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate
EFV=efavirenz
$FEPO_4$=fractional excretion of phosphate
FTC=emtricitabine
LPV=lopinavir
NRTI=nucleos(t)ide reverse transcriptase inhibitor
NVP=nevirapine
P1NP=procollagen N-terminal propeptide of type-1 collagen
PTH=parathyroid hormone
PWH=people with HIV-1
RAL=raltegravir
RPV=rilpivirine
RTV=ritonavir
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate

Product Label

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