Weight Changes in Antiretroviral–Treatment-Naïve and -Experienced Patients Receiving *Tivicay*-Based Regimens

Summary

- An increase in weight ranging from 0.8 to 8 kgs (Week 48 or Week 96 or Week 144) has been observed in participants receiving a Tivicay (dolutegravir [DTG]) based regimen in 1 Phase 2b, 7 Phase 3 treatment naïve clinical trials (SPRING-1, GS-US-380–1489, GS-US-380–1490, GEMINI 1&2, ARIA, NAMSAL, and ADVANCE) and 2 Phase 3 treatment experienced clinical trials (TANGO and SALSA).[1-13]
- Adverse drug reactions (ADRs) associated with changes in participant weight are available from 10 Phase 3 clinical trials (SPRING-2, SINGLE, FLAMINGO, GEMINI-1 and -2, SAILING, SWORD-1 and -2, ARIA, and STRIIVING) evaluating DTG-based regimens compared to various treatments for HIV-1. ADRs associated with increases in weight were mostly Grade 1 to 2 in intensity.[4,5,13-22]
- In the NEAT 022 study, participants switched to DTG-based regimens from regimens containing a protease inhibitor (PI) with ritonavir (RTV).[23] Through 48 weeks, there was a small but significant increase in the median change from baseline in weight (0.82 kg vs 0.25 kg) in a post hoc analysis, when participants switched to a DTG-based regimen.
- ViiV Healthcare acknowledges that lower levels of evidence (ie, retrospective cohort studies and case reports) have reported data on the use of DTG-based regimens and changes in weight in patients with a range of treatment experience.[24-56]
- Important safety information can be found in the Prescribing Information link and can also be accessed at Our HIV Medicines.

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In post-marketing experiences, increased weight has been identified as a common (may affect up to 1 in 10 people) ADR in patients receiving a regimen containing DTG.[57]

CHANGE FROM BASELINE IN WEIGHT IN TREATMENT NAÏVE CLINICAL TRIALS FOR DTG-BASED REGIMENS

The change from baseline in participant weight (measured in kg) as a vital signs parameter is available from the 96-week, Phase 2b, SPRING-1 dose-ranging study in HIV-1 infected ART-naïve adults, designed to select a once daily oral dose of DTG for further evaluation in Phase 3 clinical trials are provided in Table 1.[1]

Table 1. SPRING-1: Mean (SD) Change From Baseline in Weight (kg) in Treatment-Naïve Participants[1]

	DTG 10 mg + 2 NRTIs	DTG 25 mg + 2 NRTIs	DTG 50 mg + 2 NRTIs	EFV 600 mg + 2 NRTIs
Week 24	0.8 (3) (n = 52)	2 (3.9) (n = 49)	1 (2.8) (n = 48)	0.5 (3.4) (n = 45)
Week 48	1.1 (4.3) (n = 51)	0.9 (5.5) (n = 48)	0.7 (3.4) (n = 47)	0 (5.1) (n = 44)
Week 96	1.3 (5.4) (n = 48)	1.6 (4.5) (n = 44)	2.1 (4.5) (n = 46)	0 (4.4) (n = 39)

DTG = dolutegravir; EFV = efavirenz; NRTIs = nucleoside reverse transcriptase inhibitors.

The change from baseline in participant weight (measured in kg) is available for Week 96 and 144 in Phase 3 studies in HIV-1 infected ART-naïve adults are provided below in Table 2.[2-5]

Table 2. Phase 3 Clinical Trials: Median (IQR) Change From Baseline in Weight (kg) in Treatment-Naïve Participants[2-5,9]

	GS-US-380–1489		GS-US-380–1490		GEMINI 1&2 Pooled Data	
	DTG/ABC/3TC (N = 315)	BIC/FTC/TAF (N = 314)	DTG + FTC/TAF (N = 325)	BIC/FTC/TAF (N = 320)	DTG + 3TC (N=716)	DTG + FTC/TDF (N=717)
Week 96	2.4 (-0.4-5.8)	3.6 (0-8.5)	3.9 (0.8-7.4)	3.5 (0.1-8.2)	3 (0-6)	1 (-1.4-4.5)
Week 144	3.5 (0-7.7)	4.1 (0.3-8.7)	5 (0.5-9.7)	4.4 (1-9)	3.5 (0-7.4)	1.6 (-1.3-5.5)

3TC = lamivudine; ABC = abacavir; BIC = bictegravir; DTG = dolutegravir; EFV = efavirenz; FTC = emtricitabine; RAL = raltegravir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate.

ARIA[7]

A retrospective analysis of weight change in women with HIV-1 taking DTG/ABC/3TC was conducted in a Phase 3 study. Only baseline weight data were prospectively captured within the case report form; however, weight data at study visits were submitted to the central laboratory for calculation of eGFR via the Cockcroft-Gault equation.

Adjusted mean change in weight from baseline to Week 48 for the DTG (n =248) vs ATV/r (n = 247) group was 2.61 vs 1.41 kg (difference, 1.20 kg [95% CI, 0.10-2.30]; P=0.0328). In a subgroup of 99 patients who continued on DTG/ABC/3TC through Week 96, mean (SD) change in weight was 1.3 (4.65) kg at Week 48 and 1.99 (5.73) kg at Week 96.

NAMSAL[8]

The NAMSAL study was a Phase 3, randomized, open-label trial conducted in 613 treatment-naïve participants in Cameroon who received DTG + lamivudine/tenofovir disoproxil fumarate (3TC/TDF) or efavirenz (EFV) + 3TC/TDF.

Table 3. NAMSAL: Mean Change From Baseline in Weight (kg) in Treatment-Naïve Participants[8,58]

	DTG + 3TC/TDF (n=293)	EFV + 3TC/TDF (n=278)	P-value for difference
Week 48	+5.5	+3.8	<0.001
Week 96	+6.7	+4.2	<0.001
Week 192	-	-	-
Women	+8.0	+5.0	0.010
Men	+6.0	+4.0	0.024

3TC/FTC = lamivudine/emtricitabine; DTG = dolutegravir; EFV = efavirenz

More women and men receiving DTG experienced weight gain of 10% or more compared to EFV; however, this was only statistically significant among women.

ADVANCE[6]

The ADVANCE study was a Phase 3, randomized, open-label trial conducted in 1053 treatment naïve participants in South Africa who received DTG + emtricitabine/tenofovir alafenamide (FTC/TAF), DTG + FTC/TDF, or EFV/FTC/TDF. Please see table 4.

Table 4. ADVANCE: Mean Change From Baseline in Weight (kg) in Treatment-Naïve Participants[6,59]

	DTG + FTC/TAF (n=351)	DTG + FTC/TDF (n=351)	EFV/FTC/TDF (n=351)
Week 48	+6	+3	+1
Week 96	+8	+5	+2
Men	+5	+4	+1
Women	+10	+5	+3
Week 144	-	-	-
Men	+7.2	+5.5	+2.6
Women	+12.3	+7.4	+5.5

DTG = dolutegravir; EFV/FTC/TDF = efavirenz/emtricitabine/tenofovir disoproxil fumarate; FTC/TAF = emtricitabine/tenofovir alafenamide; FTC/TDF = emtricitabine/tenofovir disoproxil fumarate.

Sax et al[60]

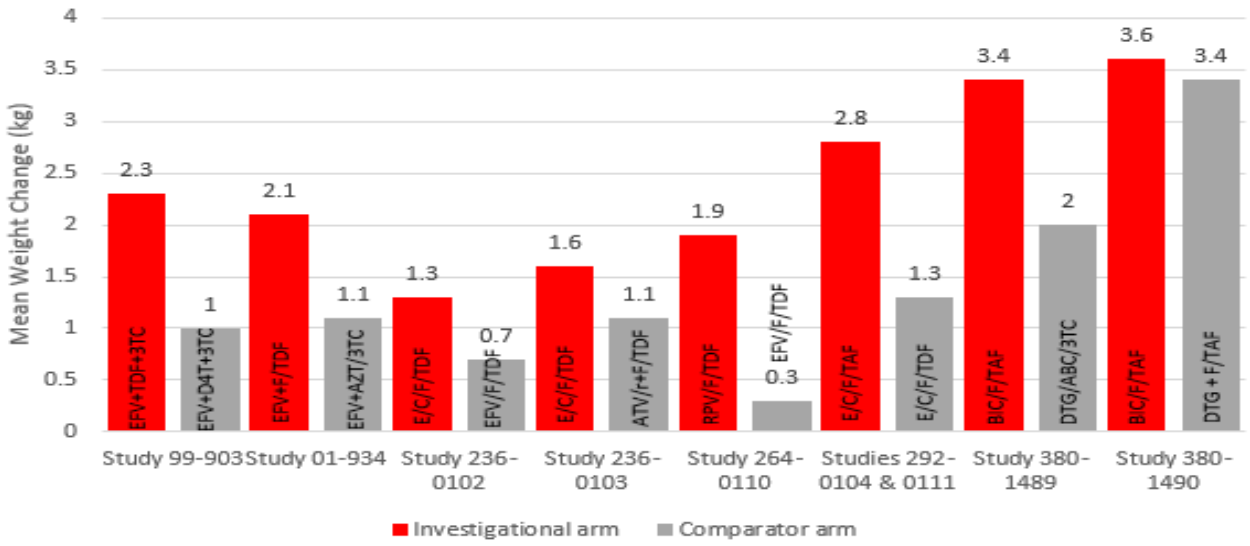
Pooled data from 8 randomized clinical trials was assessed in over 5,000 treatment-naïve patients to identify risk factors for weight gain after the initiation of ART. INSTIs were associated with more mean weight gain than PIs or NNRTIs, with DTG and BIC being associated with more mean weight gain than elvitegravir/cobicistat (EVG/c). Among the NNRTIs, rilpivirine (RPV) was associated with more weight gain than EFV. Among NRTIs, TAF was associated with more weight gain than TDF, ABC, or zidovudine (AZT). Please see table 5 and figure 1.

Table 5. Initiating ART with ≥ 10% Weight gain[60]

Variable	Odds Ratio	95% CI	*P* value
Third agent (DTG/BIC vs. EFV)	1.82	1.24, 2.66	0.002
Third agent (EVG/c vs. EFV)	1.36	1.04, 1.78	0.026
Third agent (RPV vs. EFV)	1.51	1.03, 2.2	0.035
Third agent (ATV/r vs. EFV)	0.92	0.59, 1.45	0.73
NRTI (TAF vs. AZT)	1.75	1.04, 2.95	0.034
NRTI (TDF vs. AZT)	1.19	0.76, 1.87	0.44
NRTI (ABC vs. AZT)	0.93	0.47, 1.8	0.82
NRTI (TAF vs. ABC)	1.9	1.25, 2.88	0.003
NRTI (TDF vs. ABC)	1.29	0.79, 2.11	0.31
NRTI (TAF vs. TDF)	1.47	1.14, 1.9	0.003

ABC = abacavir; ATV/r = atazanavir/ritonavir; AZT = zidovudine; BIC = bictegravir; DTG = dolutegravir; EFV = efavirenz; EVG/c = elvitegravir/cobicistat; NRTIs = nucleoside reverse transcriptase inhibitors; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate.

Figure 1. Mean Weight Change at Week 48 from 8 Clinical Trials[60]



CHANGE FROM BASELINE IN WEIGHT IN TREATMENT EXPERIENCED CLINICAL TRIALS FOR DTG-BASED REGIMENS

TANGO[12]

TANGO (NCT03446573) is an ongoing, randomized, open-label, phase 3 non-inferiority trial evaluating the efficacy and safety of a switch to DTG/3TC FDC in HIV-1–infected adults with virologic suppression on a 3- or 4-drug tenofovir alafenamide (TAF)-based regimen.[12]

The adjusted mean weight increase from baseline to week 48 was 0.8 kg in both groups (P = 0.863).[18] The adjusted mean weight increase from baseline to week 144 was 2.2 kg in the DTG/3TC arm and 1.7 kg in the TAF-based regimen arm (treatment difference, 0.49 kg; 95% CI: -0.46kg, 1.44kg, P = 0.314).[11]

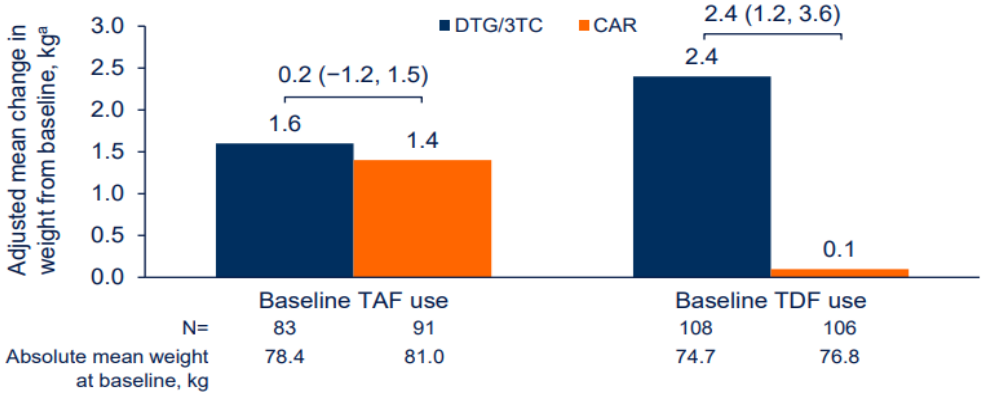
The proportion of participants with ≥ 10% weight gain was 13% (42/316) and 12% (37/303) in the DTG/3TC vs TBR groups, respectively.

SALSA[10]

SALSA is a randomized, open-label phase 3 non-inferiority trial evaluating the efficacy and safety of a switch to DTG/3TC FDC in HIV-1–infected adults with virologic suppression on a 3- or 4-drug regimen (2 NRTIs + INSTI, NNRTI, or PI).[10]

The adjusted mean change in weight increase from baseline to week 48 was 2.1 vs 0.6 kg in the DTG/3TC vs CAR groups (treatment difference, 1.49 kg; 95% CI, 0.70-2.28, P < 0.001)).[10] Weight change was similar between groups in participants with baseline TAF use and was greater in the DTG/3TC group for those with baseline TDF use, as shown in Figure 2.

Figure 2. Adjusted Mean Change in Weight from Baseline to Week 48 by Baseline TAF or TDF Use[10]



[a]Calculated from MMRM adjusting for treatment, visit, baseline third agent class, CD4+ cell count, age, sex, race, baseline value, prior TDF/EFV, subgroup, treatment-by-visit interaction, baseline value-by-visit interaction, treatment-by-subgroup interaction, subgroup-by-visit interaction, and subgroup-by-treatment-by-visit interaction, with visit as the repeated factor.

In the overall analysis, the proportion of participants with ≥ 10% weight gain was 12% (27/230) vs 4% (9/224) in the DTG/3TC vs CAR groups, respectively.[10] Proportions of participants with ≥ 10% weight gain were similar in the baseline TAF use subgroup (DTG/3TC, 8% [6/79] vs CAR, 7% [6/86]) and higher with DTG/3TC vs CAR (14% [14/98] vs 3% [3/95]) in the baseline TDF use subgroup.

Erlandson et al[61]

Pooled data from 12 Gilead Sciences-sponsored trials was assessed in over 7,000 PWH on ART and virologically suppressed for a minimum of 3 months.[61] Body weight was measured at least every 12 weeks, and follow-up duration was at least 48 weeks after ART switch. A switch from 1st generation ART (EFV and EVG) to a 2nd generation ART (RPV, BIC, and DTG), as well as switch from TDF or ABC to TAF, was associated with greater mean weight gain vs remaining on the respective regimens. In a logistic regression model also including ART switch categories, there was increased risk for ≥ 10% weight gain with switch from EFV to RPV or to EVG/c but not with other third agent switches.

ADRS RELATED TO WEIGHT IN THE VIIV DTG PHASE 3 CLINICAL TRIALS

DTG Trials in HIV-1-Infected Treatment-Naïve Participants

The safety assessment of DTG in HIV-1-infected treatment naïve participants was based on the analyses of data from four international, multicenter, double-blind trials - SPRING-2, SINGLE, GEMINI-1 and GEMINI-2, and data from the international, multicenter, open-label FLAMINGO trial.[62,63] SPRING-2 randomized 822 HIV-1 infected, treatment-naive participants to receive DTG 50 mg once daily or 400 mg raltegravir (RAL) twice daily with 2 NRTIs for 96 weeks. FLAMINGO randomized 484 HIV-1 infected, treatment-naive patients to receive DTG 50 mg once daily or darunavir/ritonavir (DRV/r) 800 mg/100 mg once daily with 2 NRTIs for 96 weeks.[14,15,64,65] SINGLE compared the efficacy and safety of DTG 50 mg + ABC/3TC 600/300 mg with that of EFV/TDF/FTC 600/200/300 mg in treatment-naïve HIV patients for 144 weeks.[16,66] GEMINI-1 and-2 (pooled analysis) randomized 1433 patients to receive DTG 50 mg once daily plus 3TC 300 mg once daily or DTG 50 mg once daily plus TDF/FTC; data are available through Week 48.[4,5,67] Please see table 6.

Table 6. Weight-Related ADRs from SPRING-2, SINGLE, FLAMINGO and GEMINI-1 and -2. [2-6]

	SPRING-2 (96 Weeks)		SINGLE (144 Weeks)		FLAMINGO (96 Weeks)		GEMINI 1&2 (144 Weeks, Pooled)
	DTG + 2NRTIs[a] (N=411) n (%)	RAL + 2NRTIs[a] (N=411) n (%)	DTG + ABC/3TC (N=414) n (%)	EFV/ TDF/FTC (N=419) n (%)	DTG + 2NRTIs[a] (N=242) n (%)	DRV/r + 2NRTIs[a] (N=242) n (%)	DTG + (3TC or TDF/FTC) (N=1433) n (%)
Weight increase							
Grade 1 to 2	1 (< 1)	4 (< 1)	2 (< 1)	1 (< 1)	1 (< 1)	2 (< 1)	9 (< 1)
Grade 3 to 4	0	0	0	0	0	0	0
Weight decrease							
Grade 1 to 2	0	1 (< 1)	0	0	0	0	1 (< 1)
Grade 3 to 4	0	0	0	0	0	0	0

[a]ABC/3TC or TDF/FTC.; 3TC = lamivudine; ABC = abacavir; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; FTC = emtricitabine; RAL = raltegravir; TDF = tenofovir disoproxil fumarate.

DTG Trials in HIV-1 Treatment-Experienced Participants

The safety assessment of DTG in 719 HIV-1-infected treatment experienced, INSTI-naïve participants with resistance to ≥ 2 antiretroviral drug classes was evaluated in SAILING which compared DTG 50 mg once daily or raltegravir 400 mg twice daily with investigator-selected background regimen (BR) consisting of up to 2 agents, including at least one fully active agent.[17,68] VIKING-3 was a 48-week open-label, single arm trial of 183 HIV-1-infected, INSTI-experienced participants with virological failure and

current or historical evidence of RAL and/or elvitegravir (EVG) resistance and received DTG 50 mg twice daily with their current failing background regimen for 7 days and with OBR from Day 8.[19,69] The primary endpoints were the mean change from baseline in plasma HIV-1 RNA at day 8 and the percentage of participants with HIV-1 RNA < 50 copies/mL at Week 24.SWORD-1 and SWORD-2 were identically designed, phase 3, open-label studies of 1024 HIV-1-infected virologically-suppressed adults (confirmed HIV-1 RNA < 50 copies/mL for at least 6 months) randomized to receive DTG 50 mg once daily + rilpivirine (RPV) 25 mg once daily or remain on their current antiretroviral regimens (CAR).[13,18] The primary endpoint for all three trials was the percentage of participants with HIV-1 RNA <50 copies/mL at 48 weeks using an Intent-to-Treat exposed (ITT-E), MSDF or FDA "snapshot" analysis.

ADRs related to weight gain or weight loss from SAILING, VIKING-3, SWORD-1 and -2, TANGO, and SALSA are provided below in Table 7.[13,17-19,22,70]

Table 7. Weight-Related ADRs from SAILING, VIKING-3, SWORD-1 and -2, TANGO, and SALSA Trials[13,17-19,22,70]

	SAILING (48 Weeks)		VIKING-3 (48 Weeks)	SWORD-1 and -2 (48 Weeks, Pooled)		TANGO (48 Weeks)		SALSA (48 Weeks)	
	DTG + BR (N=357) n (%)	RAL + BR (N=362) n (%)	DTG + OBR (N=183) n (%)	DTG + OBR (N=183) n (%)	DTG + BR (N=357) n (%)	DTG/ 3TC (N=369) n (%)	TAF-based regimen (N=372) n (%)	DTG/ 3TC (N=246) n (%)	CAR (N=247) n (%)
Weight increase									
Grade 1 to 2	1 (< 1)	1 (< 1)	2 (< 1)	2 (< 1)	1 (< 1)	3 (0.8)	6 (1.6)	20 (8)	5 (2)
Grade 3 to 4	0	0	0	0	0	0	0	0	0
Weight decrease									
Grade 1 to 2	1 (< 1)	0	0	1 (< 1)	0	0	0	1 (< 1)	1 (< 1)
Grade 3 to 4	0	0	0	0	0	0	0	0	0

3TC = lamivudine; BR = background regimen; CAR = current antiretroviral regimen; DTG = dolutegravir; OBR = optimized background regimen; RAL = raltegravir.

ABC/DTG/3TC Trials in HIV-1 Treatment-Naïve and -Experienced Participants

ABC/DTG/3TC as a fixed dose combination (FDC) tablet was evaluated in ARIA and STRIIVING.[20,21,71,72] ARIA was a Phase 3b, randomized, open-label study that evaluated the safety and efficacy of ABC/DTG/3TC 600/50/300 mg once daily compared to atazanavir/ritonavir (ATV/r) 300/100 mg + TDF/FTC 300/200 mg FDC tablet once daily in 499 HIV-1 infected ART-naive women.[11,27] STRIIVING was a Phase 3b, randomized, open-label study in 551 HIV-1-infected virologically suppressed participants on CAR consisting of (and no history of resistance to) an NNRTI, PI, or INSTI with 2NRTIs.[12,72] The primary endpoint for ARIA and STRIIVING was the percentage of participants with HIV-1 RNA <50 copies/mL using an Intent-to-Treat exposed (ITT-E), missing, switch or discontinuation equals failure (MSDF, or FDA "snapshot") analysis at 48 weeks and 24 weeks, respectively.[71,72] ADRs related to weight gains or weight loss from ARIA and STRIIVING through 48 weeks are provided below in Table 8.

Table 8. Weight-Related ADRs from ARIA and STRIIVING Trials[20,21]

	ARIA (48 Weeks)		STRIVING (48 Weeks)	
	ABC/DTG/3TC (N = 248); n (%)	ATV/r + TDF/FTC (N = 247); n (%)	ABC/DTG/3TC (N = 248); n (%)	ATV/r + TDF/FTC (N = 247); n (%)
Weight increase				
Grade 1 to 2	0	1 (< 1)	0	0
Grade 3 to 4	0	0	0	0
Weight decrease				
Grade 1 to 2	0	2 (< 1)	0	0

Grade 3 to 4	0	0	0	0

ABC = abacavir; ATV/r = ritonavir-boosted atazanavir; CAR = current antiretroviral regimen; DTG = dolutegravir; FTC = emtricitabine; TDF = tenofovir disoproxil fumarate; 3TC = lamivudine.

POST-HOC ANALYSIS FROM THE NEAT-022 STUDY

NEAT 022 was a randomized, open-label non-inferiority study in participants with cardiovascular risk (Framingham risk score >10% at 10 years and/or >50 years) and HIV-1 RNA <50 copies/mL ≥6 months.[23] Participants switched to DTG-based regimens (n=205) at baseline or continued regimens containing a boosted protease inhibitor (n = 210) through 48 weeks; thereafter, all participants received DTG-based regimens through Week 96. For the co-primary endpoints at Week 48, DTG-containing regimens had noninferior virologic response for the proportion of participants with HIV-1 RNA < 50 copies/mL, and a statistically significant improvement in the mean percentage change from baseline in total cholesterol.

A post-hoc analysis assessed changes in weight and body mass index (BMI) at Week 48 and Week 96 as shown in Table 9.[23] In a multivariate analysis after adjusting for baseline BMI, the only independent baseline factor associated with an increase in BMI was switching to DTG-containing regimens from regimens containing darunavir (P = 0.018).

Table 9. NEAT 022: Median Change From Baseline in Participant Weight and BMI[23]

	Median Change in Weight, kg	*P* value for difference between groups	Median Change in BMI, kg/m^2	*P* value for difference between groups
Early Switch Phase, Week 0 to Week 48				
DTG-containing regimens	0.82	*P* = 0.008	0.272	*P* = 0.008
PI-containing regimens	0.25		0.064	
Late Switch Phase, Week 48 to Week 96				
Continuing DTG-containing regimens	0.03	*P* = 0.002	-0.002	*P* = 0.002
Switch to DTG-containing regimens at Week 48	0.98		0.332	

BMI = Body mass index; DTG = dolutegravir; PI = protease inhibitor.

OBSERVATIONAL DATA

In the absence of clinical trial data specifically addressing changes in weight as a pre-specified endpoint, it is difficult to determine whether such changes in weight are appropriate (representing a return to health), detrimental, or clinically significant in another way. ViiV Healthcare acknowledges that lower levels of evidence (ie retrospective cohort studies and case reports) have reported data on the use of DTG-based regimens and changes in weight (weight increases or weight decreases) in patients with a range of treatment experience.[24-56] Because these studies are less robust in design than evidence from large randomized, controlled trials, the data are not summarized herein; however, the corresponding reference citations are listed at the end of this document.

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In order for ViiV Healthcare to monitor the safety of our products, we encourage healthcare professionals to report adverse events or suspected overdoses to the company at 877–844–8872. Please consult the attached Prescribing Information.

This response was developed according to the principles of evidence-based medicine and, therefore, references may not be all-inclusive.

REFERENCES

1. ClinicalTrials.gov identifier NCT00951015. Available at: https://ClinicalTrials.gov/show/NCT00951015.
2. Wohl DA, Yazdanpanah Y, Baumgarten A, et al. Bictegravir combined with emtricitabine and tenofovir alafenamide versus dolutegravir, abacavir, and lamivudine for initial treatment of HIV-1 infection: week 96 results from a randomised, double-blind, multicentre, phase 3, non-inferiority trial. *The Lancet HIV*. 2019;6:e355-363. doi:http://dx.doi.org/10.1016/S2352-3018(19)30077-3.
3. Stellbrink H-J, Arribas JR, Stephens JL, et al. Co-formulated bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir with emtricitabine and tenofovir alafenamide for initial treatment of HIV-1 infection: week 96 results from a randomised, double-blind, multicentre, phase 3, non-inferiority trial. *The Lancet HIV*. 2019;6:e364-372. doi:http://dx.doi.org/10.1016/S2352-3018(19)30080-3.
4. ClinicalTrials.gov identifier NCT02831673. Available at: https://clinicaltrials.gov/show/NCT02831673.
5. ClinicalTrials.gov identifier NCT02831764. Available at: https://clinicaltrials.gov/show/NCT02831764.
6. Hill A, Venter WF, Delaporte E, et al. Progressive rises in weight and clinical obesity for TAF/FTC/DTG and TDF/FTC/DTG versus TDF/FTC/EFV: ADVANCE and NAMSAL trials. Presented at the 10th International AIDS Society Conference on HIV Science, July 21-24, 2019, Mexico City, Mexico. Presentation MOAX0102LB.
7. Walmsley S, et al. Weight change among treatment naive women initiating dolutegravir in the ARIA study. Presented at the 23rd International AIDS Conference, July 6-10, 2020, San Francisco, California. Poster PEB0238.
8. Kouanfack C, et al. Dolutegravir- versus low-dose Efavirenz-based regimen for the initial treatment of HIV-1 infection in Cameroon: Week 96 results of the ANRS 12313 – NAMSAL trial. Presented at the 23rd International AIDS Conference, July 6-10, 2020, San Francisco, California. Oral OAB04.
9. Orkin C, DeJesus E, Sax PE, et al. Fixed-dose combination bictegravir, emtricitabine, and tenofovir alafenamide versus 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(6):e389-e400. doi:http://dx.doi.org/10.1016/S2352-3018(20)30099-0.
10. Hagins D, et al. Week 48 metabolic health after switch to DTG/3TC vs CAR by baseline regimen (SALSA). Presented at the 29th Conference on Retroviruses and Opportunistic Infections (CROI), February 12-16, 2022, Virtual Event. Poster.
11. van Wyk J, et al. Metabolic health outcomes at week 144 in the TANGO Study, comparing a switch to DTG/3TC versus maintenance of TAF-based regimens. Presented at the 11th IAS Conference on HIV Science, July 18-21, 2021, Virtual Event. E-Poster.
12. van Wyk J, Ajana F, Bisshop F, et al. Efficacy and Safety of Switching to Dolutegravir/Lamivudine Fixed-Dose 2-Drug Regimen vs Continuing a Tenofovir Alafenamide-Based 3- or 4-Drug Regimen for Maintenance of Virologic Suppression in Adults Living With Human Immunodeficiency Virus Type 1: Phase 3, Randomized, Noninferiority TANGO Study. *Clin Infect Dis*. 2020;71(8):1920-1929. doi:http://dx.doi.org/10.1093/cid/ciz1243.
13. ClinicalTrials.gov identifier NCT02422797. Available at: https://ClinicalTrials.gov/show/NCT02422797.
14. ClinicalTrials.gov identifier NCT01227824. Available at: https://ClinicalTrials.gov/show/NCT01227824.
15. ClinicalTrials.gov identifier NCT01449929. Available at: https://ClinicalTrials.gov/show/NCT01449929.
16. ClinicalTrials.gov identifier NCT01263015. Available at: https://ClinicalTrials.gov/show/NCT01263015.
17. ClinicalTrials.gov identifier NCT01231516. Available at: https://ClinicalTrials.gov/show/NCT01231516.
18. ClinicalTrials.gov identifier NCT02429791. Available at: https://ClinicalTrials.gov/show/NCT02429791.
19. ClinicalTrials.gov identifier NCT01328041. Available at: https://ClinicalTrials.gov/show/NCT01328041.
20. ClinicalTrials.gov identifier NCT01910402. Available at: https://ClinicalTrials.gov/show/NCT01910402.
21. ClinicalTrials.gov identifier NCT02105987. Available at: https://ClinicalTrials.gov/show/NCT02105987.
22. ClinicalTrials.gov identifier NCT03446573. Available at: https://ClinicalTrials.gov/show/NCT03446573.
23. Waters L, Assoumou L, Rusconi S, et al. Switch to dolutegravir (DTG) from a boosted protease inhibitor (PI/r) associated with significant weight gain over 48 weeks in NEAT-022, a randomised 96-week trial. Presented at HIV Glasgow; 10/28/2018; Glasgow; UK. Poster 102.
24. Menard A, Meddeb L, Tissot-Dupont H, et al. Dolutegravir and weight gain: An unexpected bothering side effect? *AIDS (London, England)*. 2017;31(10):1499-1500. doi:http://dx.doi.org/10.1097/QAD.0000000000001495.
25. Bhaduri S, Roberts M. Weight gain in patients using integrase inhibitors: An emerging class side effect. Conference presented at 23rd Annual Conference of the British HIV Association (BHIVA); 04/04/2017; Liverpool; UK.
26. Norwood J, Turner M, Bofill C, et al. Weight gain in persons with HIV switched from efavirenz-based to integrase strand transfer inhibitor-based regimens. *Journal of Acquired Immune Deficiency Syndromes*. 2017;76(5):527-531. doi:http://dx.doi.org/10.1097/QAI.0000000000001525.

27. Bakal D, Coelho L, Luz P, et al. Obesity following antiretroviral therapy (ART) initiation is common and influenced by both traditional and HIV-1/ART-specific risk factors. Presented at the 2017 IDWeek Meeting of the Infectious Diseases Society of America (IDSA); 10/04/2017; San Diego, CA; USA.
28. Gibson A, Spivak A, Presson A, Jamjian C. Weight and BMI changes in HIV-infected virologically suppressed adults after switching to an elvitegravir- or dolutegravir-containing regimen. Presented at the 2018 ID Week Meeting of the Infectious Diseases Society of America (IDSA); 10/3/2018; San Francisco, CA; USA. Poster 549.
29. Lake JE, Wu K, Erlandson KM, et al. Risk factors for excess weight gain following switch to integrase inhibitor–based art. Presented at CROI 2019; March 4-7, 2019; Seattle, WA. Poster 669.
30. Bourgi K, Jenkins C, Rebeiro P, et al. Greater weight gain among treatment-naive persons starting integrase inhibitors. Presented at CROI 2019; March 4-7, 2019; Seattle, WA. Poster 670.
31. McComsey G, Eron J, Santiago S, et al. Weight gain during treatment among 3,468 treatment-experienced adults with hiv. Presented at CROI 2019; March 4-7, 2019; Seattle, WA. Poster 671.
32. Kerchberger AM, Sheth AN, Angert CD, et al. Integrase strand transfer inhibitors are associated with weight gain in women. Presented at CROI 2019; March 4-7, 2019; Seattle, WA. Poster 672.
33. Leonard M, Bourgi K, Koethe JR, et al. Pharmacogenetics of weight gain after switch from efavirenz to integrase inhibitors. Presented at CROI 2019; March 4-7, 2019; Seattle, WA. Poster 472.
34. Palella FJ, Rayeed N, Li J, et al. Weight gain among virally suppressed persons who switch to insti-based art. Presented at CROI 2019; March 4-7, 2019; Seattle, WA. Poster 674.
35. Bedimo R, Li X, Adams-Huet B, et al. Differential bmi changes following pi- and insti-based art initiation by sex and race. Presented at CROI 2019; March 4-7, 2019; Seattle, WA. Poster 675.
36. Taramasso L, et al. Predictors of weight gain in patients treated with dolutegravir. Presented at the 17th European AIDS Conference (EACS), November 6-9, 2019, Basel, Switzerland. PE32/3.
37. Lee Y, et al. Good efficacy but side effects including hypercholesterolemia and body weight gain after switching to dolutegravir plus booster protease inhibitor regimen among treatment experienced HIV-positive patients. Presented at the 17th European AIDS Conference (EACS), November 6-9, 2019, Basel, Switzerland. PE2/20.
38. Vizcarra P, et al. Weight gain in people living with HIV switched to dual therapy with dolutegravir plus rilpivirine: changes in body fat mass. Presented at the 17th European AIDS Conference (EACS), November 6-9, 2019, Basel, Switzerland. PE32/6.
39. Hsu R, et al. Characterizations of weight gain following antiretroviral regimen initiation in treatment-naïve individuals living with HIV. Presented at the 17th European AIDS Conference (EACS), November 6-9, 2019, Basel, Switzerland. PE2/32.
40. Ruderman SA, et al. Dolutegravir-based regimens are associated with weight gain over two years following ART-initiation in ART-naïve people living with HIV (PLWH). Presented at the 17th European AIDS Conference (EACS), November 6-9, 2019, Basel, Switzerland. PE2/55.
41. Belkhir L, et al. Weight gain among HIV-positive persons treated with Dolutegravir or Elvitegravir. Presented at the 17th European AIDS Conference (EACS), November 6-9, 2019, Basel, Switzerland. PE32/8.
42. Sekiya, et al. Examination of HIV-infected patients regarding weight gain while using integrase inhibitors in Japan. Presented at the 17th European AIDS Conference (EACS), November 6-9, 2019, Basel, Switzerland. PE9/63.
43. Mugglin C, et al. Changes in weight after switching to dolutegravir containing antiretroviral therapy in the Swiss HIV cohort study Presented at the 17th European AIDS Conference (EACS), November 6-9, 2019, Basel, Switzerland.
44. Vizcarra P, Vivancos MJ, Pérez-Elías MJ, Moreno A, Casado JL. Weight gain in people living with HIV switched to dual therapy: changes in body fat mass. *AIDS (London, England)*. 2020;34(1):155-157. doi:http://dx.doi.org/10.1097/QAD.0000000000002421.
45. Calza L, Colangeli V, Borderi M, et al. Weight gain in antiretroviral therapy-naive HIV-1-infected patients starting a regimen including an integrase strand transfer inhibitor or darunavir/ritonavir. *Infection*. 2019:1-9. doi:http://dx.doi.org/10.1007/s15010-019-01376-5.
46. Rizzardo S, Lanzafame M, Lattuada E, et al. Dolutegravir monotherapy and body weight gain in antiretroviral naïve patients. *AIDS (London, England)*. 2019;33(10):1673-1674. doi:http://dx.doi.org/10.1097/QAD.0000000000002245.
47. Burns JE, Stirrup OT, Dunn D, et al. No overall change in the rate of weight gain after switching to an integrase-inhibitor in virologically suppressed adults with HIV. *AIDS (London, England)*. 2020;34(1):109-114. doi:http://dx.doi.org/10.1097/QAD.0000000000002379.
48. Ruderman SA, Nance, RM, Whitney BM, et al. Race impact on dolutegravir-associated weight gain among previously art-naive PLWH. Presented at the Conference on Retroviruses and Opportunistic Infections, March 8-11, 2020, Boston, MA, USA. Poster 678.
49. Burdet C, Peytavin G, Le M, et al. Drug concentrations and body weight gain in PLWH switched to 3TC & dolutegravir (DTG). Presented at the Conference on Retroviruses and Opportunistic Infections, March 8-11, 2020, Boston, MA, USA. Presentation 677.
50. Koethe J, Bian A, Rebeiro PF, et al. Greater weight gain after switch to InSTI-based regimen from NNRTI vs PI regimens. Presented at the Conference on Retroviruses and Opportunistic Infections, March 8-11, 2020, Boston, MA, USA. Presentation 668.
51. McComsey GA, Althoff KN, Brown TT, et al. Understanding who does and does not gain weight with integrase inhibitors (InSTI). Presented at the Conference on Retroviruses and Opportunistic Infections, March 8-11, 2020, Boston, MA, USA. Presentation 676.
52. Guaraldi G, Calza S, Calcagno A, et al. DTG prescribing patterns in PLWH ≥65 years: the impact of 2DR and weight gain. Presented at the Conference on Retroviruses and Opportunistic Infections, March 8-11, 2020, Boston, MA, USA. Presentation 679.

53. Campbell J, Abudiore O, Amamilo I, et al. Weight gain at 18 months for ART-experienced patients who switched to DTG in Nigeria. Presented at the Conference on Retroviruses and Opportunistic Infections, March 8-11, 2020, Boston, MA, USA. Presentation 681.
54. Ake J, et al. Weight gain and hyperglycemia during the dolutegravir transition in Africa. Presented at the 23rd International AIDS Conference, July 6-10, 2020, San Francisco, California. Oral OAB0602.
55. Mallon P eaWgbaasfTtTPatrIAC, July 6-10, 2020, San Francisco, California. Oral OAB0604. Mallon P, et al. Weight gain before and after switch from TDF to TAF. Presented at the 23rd International AIDS Conference, July 6-10, 2020, San Francisco, California. Oral OAB0604.
56. Ruderman S, et al. Early weight changes associated with bictegravir-based regimens compared to other integrase inhibitors following ART-initiation in ART-naïve people living with HIV. Presented at the 23rd International AIDS Conference, July 6-10, 2020, San Francisco, California. Poster PEC0450.
57. ViiV Healthcare. Global Data Sheet for dolutegravir, Version 0021, August 10, 2022.
58. Mpoudi-Etame, M., et al. Long-Term Outcomes of Dolutegravir and Efavirenz-400 as first-line ART in Cameroon. Presented at the 29th Conference on Retroviruses and Opportunistic Infections (CROI), February 12-16, 2022, Virtual Event. Poster-H04.
59. Venter F, Sokhela S, Fairlie L, et al. The ADVANCE trial: Phase 3, randomised comparison of TAF/FTC+DTG, TDF/FTC+DTG or TDF/FTC/EFV for first-line treatment of HIV-1 infection. Presented at the 23rd International AIDS Conference (Virtual), July 6-10, 2020. Presentation OAXLB0104.
60. Sax PE, Erlandson KM, Lake JE, et al. Weight Gain Following Initiation of Antiretroviral Therapy: Risk Factors in Randomized Comparative Clinical Trials. *Clinical Infectious Diseases*. 2019. doi:http://dx.doi.org/10.1093/cid/ciz999.
61. Erlandson KM, Carter CC, Melbourne K, et al. Weight Change Following Antiretroviral Therapy Switch in People With Viral Suppression: Pooled Data from Randomized Clinical Trials. *Clin Infect Dis*. 2021;73(8):1440-1451. doi:http://dx.doi.org/10.1093/cid/ciab444.
62. ViiV Healthcare. Global Data Sheet for dolutegravir, Version 0020, October 15, 2021.
63. Duwal S, Dickinson L, Khoo S, von Kleist M. Hybrid stochastic framework predicts efficacy of prophylaxis against HIV: An example with different dolutegravir prophylaxis schemes. *PLoS Computational Biology*. 2018;14(6). doi:http://dx.doi.org/10.1371/journal.pcbi.1006155.
64. Raffi F, Jaeger H, Quiros-Roldan E, et al. Once-daily dolutegravir versus twice-daily raltegravir in antiretroviral-naive adults with HIV-1 infection (SPRING-2 study): 96 week results from a randomised, double-blind, non-inferiority trial. *The Lancet Infectious Diseases*. 2013;13(11):927-935. doi:http://dx.doi.org/10.1016/S1473-3099(13)70257-3.
65. Molina JM, Clotet B, van Lunzen J, et al. Once-daily dolutegravir is superior to once-daily darunavir/ritonavir in treatment-naive HIV-1-positive individuals: 96 week results from FLAMINGO. *Journal of the International AIDS Society*. 2014;17(4 Suppl 3):19490. doi:http://dx.doi.org/10.7448/IAS.17.4.19490.
66. Walmsley S, Baumgarten A, Berenguer J, et al. Dolutegravir plus abacavir/lamivudine for the treatment of HIV-1 infection in antiretroviral therapy-naive patients: Week 96 and week 144 results from the SINGLE randomized clinical trial. *Journal of Acquired Immune Deficiency Syndromes*. 2015;70(5):515-519. doi:http://dx.doi.org/10.1097/QAI.0000000000000790.
67. Cahn P, Madero S, Arribas J, et al. Non-inferior efficacy of dolutegravir (DTG) plus lamivudine (3TC) versus DTG plus tenofovir/emtricitabine (TDF/FTC) fixed dose combination in antiretroviral treatment-naive adults with HIV-1 infection - 48-week results from the GEMINI studies. Presented at the 22nd International AIDS Conference (IAS); July 23-27, 2018; Amsterdam, the Netherlands. Abstract B33.
68. Cahn P, Pozniak AL, Mingrone H, et al. Dolutegravir versus raltegravir in antiretroviral-experienced, integrase-inhibitor-naive adults with HIV: Week 48 results from the randomised, double-blind, non-inferiority SAILING study. *The Lancet*. 2013;382(9893):700-708. doi:http://dx.doi.org/10.1016/S0140-6736(13)61221-0.
69. Castagna A, Maggiolo F, Penco G, et al. Dolutegravir in antiretroviral-experienced patients with raltegravir-and/or elvitegravir-resistant HIV-1: 24-week results of the phase III VIKING-3 study. *Journal of Infectious Diseases*. 2014;210(3):354-362. doi:http://dx.doi.org/10.1093/infdis/jiu051.
70. ClinicalTrials.gov identifier NCT04021290. Available at: https://clinicaltrials.gov/ct2/show/NCT04021290.
71. Orrell C, Hagins DP, Belonosova E, et al. Fixed-dose combination dolutegravir, abacavir, and lamivudine versus ritonavir-boosted atazanavir plus tenofovir disoproxil fumarate and emtricitabine in previously untreated women with HIV-1 infection (ARIA): week 48 results from a randomised, open-label, non-inferiority, phase 3b study. *The Lancet HIV*. 2017;4(12):e536-e546. doi:http://dx.doi.org/10.1016/S2352-3018(17)30095-4.
72. Trottier B, Lake JE, Logue K, et al. Dolutegravir/abacavir/lamivudine versus current ART in virally suppressed patients (STRIIVING): a 48-week, randomized, non-inferiority, open-label, Phase IIIb study. *Antiviral Therapy*. 2017;22(4):295-305. doi:http://dx.doi.org/10.3851/IMP3166.