

Supplementary material

Table 1. RCT in Experienced PLWH

Year of publication and duration of study	Study Name and authors	Duration	Study design and Primary end point	Baseline characteristics	Results
Switch to INSTI					
2018 May 2014-November 2015	NEAT 022 substudy [14]	96W	Multicenter (Europe), n = 415 (1) immediate switch to DTG = DTG-I (n=205) VS (2) Remain on PI/r 48W → DTG at 48W= DTG-D (n = 210)	Male: 89%; White: 85%; Median BMI: 25,9kg/m²; Suppressed patients: 100%; Backbone: TDF/FTC: n (%) (1) n = 135 (65,4) (2) n = 135 (64,3) ABC/3TC (1) n = 63 (30,7) (2) n = 67 (31,9) Other (1) n = 8 (3,0) (2) n = 8 (3,8)	<u>Median weight change (kg)</u> W0 to W48: (1) + 0,82 (2) + 0,25 <i>p</i> = 0,008 W48 to W96: (1) + 0,003 (2) + 0,98 <i>P</i> = 0,002 <u>Mean BMI change (kg/m²)</u> W0 to W48: (1) + 0,272 (<i>p</i> = 0,003) (2) + 0,064 (<i>p</i> = 0,471) (1) vs (2) <i>p</i> = 0,008 W48 to W96: (1) - 0,002 (<i>p</i> = 0,984) (2) + 0,332 (<i>p</i> = 0,004) (1) vs (2) <i>p</i> = 0,002
2020 August 2018-March 2019	BRAAVE [15]	48W	Phase 3b; multicenter (US); n = 495 (1) BIC 50mg/FTC 200mg/TAF25mg (n = 330) VS (2) Baseline regimen (2NRTI + third agent) (n = 165) → delayed BIC/FTC/TAF at W24	Women: 32%; Black or African American: 100%; Suppressed patients: 100% -Median weight (kg): (1) 88; (2) 89 -Median BMI (kg/m²): (1) 29,2; (2) 29,3 <u>Baseline regimen</u> - <i>baseline NRTI backbone: n (%)</i> FTC/TAF: (1) 224 (68) (2) 107 (65) FTC/TDF: (1) 56 (17) (2) 34 (21) ABC/3TC: (1) 44 (13) (2) 24 (15) Other: (1) 4 (1) (2) 0 (0) - <i>baseline 3rd agents: n (%)</i> INSTIs: (1) 202 (61) (2) 99 (60) NNRTI: (1) 100 (30) (2) 51 (31) PIs: (1) 30 (9) (2) 14 (9)	W24 <u>Median weight change (kg)</u> (1) + 0,9, (2) + 0,2, <i>p</i> = 0,09 <u>Subgroup analysis:</u> *By sex: -male: no difference between (1) and (2) -women: +1,0 (1) vs -0,4 (2) <i>p</i> = 0,03 *By NRTI: - TDF → TAF: + 1,8 - TAF → TAF: + 0,8 - ABC → TAF: + 0,7 <i>p</i> = 0,0235 for TDF vs TAF <i>p</i> = 0,89 for ABC vs TAF W48 <u>Median weight change (kg)</u> (1) + 0,9kg
2020 and 2022 January 2018-April 2019	TANGO [16, 17]	To 200W	Phase 3; multicenter (international); n= 741 (1) Switch DTG/3TC (n=369) VS (2) Remain on a TAF-based regimen (n = 372)	Women: (1) n = 25 (6,8%), (2) n = 33 (8,9%) Blacks: (1) n = 50 (13,6%), (2) n = 58 (15,6%) Suppressed patients: 100% <u>Baseline regimen</u> - baseline TAF backbone: 100% (switch TDF → TAF ≥ 3 months before screening) - baseline 3 rd agent INSTI: (1) n = 289 (78,3%) (2) n = 296 (79,6%) EVG/c: (1) n = 243 (65,9%) (2) n = 249 (66,9%) NNRTI: (1) n = 51 (14%) (2) n = 48 (13%) PI: (1) n = 29 (8%) (2) n = 28 (8%)	W96 <u>Mean weight gain (kg)</u> (1) +0,81 (n = 343) (2) +0,76 (n = 343) <i>Prior TAF duration < 1y:</i> (1) + 1,45 (2) + 1,35 <i>Priori TAF duration ≥ 1y:</i> (1) +0,60 (2) +0,60 <i>Boosted baseline regimen:</i> (1) +0,81 (2) +0,88 <i>Unboosted baseline regimen:</i> (1) +0,81 (2) +0,40 <u>Weight change ≥ 10%</u> (1) 3% (n = 11) (2) 4% (n = 13) Missing data with COVID-19 W144 <u>Median weight gain (kg)</u> (1) +2,2 (2) +1,7 <i>P</i> = 0,31 <u>Weight change ≥ 10% (% of participants)</u> (1) 13 (42/316) (2) 12 (37/303)
2021 November 2019-April 2021	SALSA [18]	48W	Phase 3; multicenter (international); n = 493 (1) switch DTG/3TC (n = 246) VS (2) current ART (n = 247)	Women: (1) 44%, (2) 34%; White: (1) 61%, (2) 58%; African/American heritage: (1) 18%, (2) 19% Median weight (kg): (1) 73 (2) 75 Median BMI (kg/m²): (1) 25 (2) 26 Suppressed patients: 100% <u>Baseline regimen</u> - <i>baseline 3rd agent: n (%)</i> NNRTI Overall: 247 (50) (1) 123 (50) (2) 124 (50) INSTI Overall: 196 (40) (1) 98 (40) (2) 98 (40) PI Overall: 50 (10%) (1) 25 (10) (2) 25 (10) - <i>NNRTI at screening in ≥ 30% of participants: n (%)</i> EFV Overall: 152 (31) (1) 79 (32) (2) 73 (30) - <i>INSTIs at screening in ≥ 30% of participants: n (%)</i> DTG: Overall: 86 (17) (1) 45 (18) (2) 41 (17) EVGc: Overall: 51 (10) (1) 24 (10) (2) 27 (11) BIC Overall: 50 (10) (1) 24 (10) (2) 26 (11) RAL Overall: 10 (2) (1) 6 (2) (2) 4 (2) - <i>NRTI at screening in ≥ 30% of participants: n (%)</i> FTC Overall: 305 (62) (1) 149 (61) (2) 156 (63) TDF Overall: 218 (44) (1) 109 (44) (2) 109 (44) 3TC Overall: 185 (38) (1) 96 (39) (2) 89 (36) TAF Overall: 174 (35) (1) 83 (34) (2) 91 (37)	W48 <u>Mean weight change (kg)</u> (1) +2,1 (2) +0,6 <i>P</i> < 0,001 By baseline TAF use: (1) n = 83: +1,6kg (2) n = 91: +1,4kg By baseline TDF use: (1) n = 108: +2,4kg (2) n = 106: +0,1kg <u>Mean BMI change (kg/m²)</u> (1) 0,7 (2) 0,2 <i>p</i> < 0,001 <u>Weight gain ≥ 10% (% of patients)</u> (1) 12 (27/230) (2) 4 (9/224) By baseline TAF use: (1) 8 (2) 7 By baseline TDF use: (1) 14 (2) 3

2020 October 2016-May 2018	ATLAS [19]	48W	Phase 3; multicenter (international); n = 618 (1) current therapy (n = 308) VS (2) shift to LA CAB/1 month + LA RPV (n = 308)	Women: n (%) (1) 104 (34), (2) 99 (32) Black (1) 77 (25), (2) 62 (20) Median BMI (kg/m²) (1) 26, (2) 26 Suppressed patients: 100% <u>Baseline regimen</u> - <i>baseline 3rd agent: n (%)</i> INSTI: (1) 99 (32) (2) 102 (33) NNRTI: (1) 155 (50) (2) 155 (50) PI: (1) 54 (18) (2) 51 (17) - <i>PI+NRTIs: n (%)</i> *ATV/r: (1) 16 (5) (2) 18 (6) + 3TC/ABC: (1) 5 (2%) (2) 10 (3%) + 3TC/ABC/AZT: (1) 1 (< 1) (2) 0 + 3TC/AZT: (1) 3 (1) (2) 2 (1) + 3TC/TDF: (1) 1 (< 1) (2) 1 (< 1) +ABC/TDF: (1) 1 (< 1) (2) 0 +FTC/TDF: (1) 4 (1) (2) 5 (2) +FTC/TAF: (1) 1 (< 1) (2) 0 *DRV/r or c (1) 12 (4) (2) 14 (5) + FTC/TAF: (1) 0 (2) 1 (< 1) +FTC/TDF: (1) 9 (3) (2) 7 (2) +3TC/ABC: (1) 2 (1) (2) 2 (1) +3TC/AZT: (1) 1 (< 1) (2) 2 (1) + 3TC/TDF: (1) 0 (2) 2 (1) * LPV/r (1) 26 (8) (2) 19 (6) + 3TC/ABC: (1) 7 (2) (2) 3 (1) +3TC/AZT: (1) 14 (5) (2) 9 (3) +3TC/PSZ: (1) 0 (2) 2 (1) +3TC/TDF: (1) 2 (1) (2) 2 (1) +FTC/TDF (1) 2 (1) (2) 3 (1) +TDF: (1) 1 (< 1) (2) 0 - NNRTI + NRTI: n (%) (1) 155 (50) (2) 155 (50) *EFV (1) 105 (34) (2) 100 (32) + FTC/TDF: (1) 75 (24) (2) 74 (24) +3TC/ABC: (1) 13 (4) (2) 15 (5) +3TC/AZT: (1) 13 (4) (2) 5 (2) +3TC/TDF: (1) 3 (1) (2) 5 (2) +3TC/ddI: (1) 1 (< 1) (2) 1 (< 1) * NVP (1) 15 (5) (2) 15 (5) + 3TC/ABC: (1) 7 (2) (2) 6 (2) +3TC/AZT: (1) 0 (2) 1 (< 1) +3TC/TDF: (1) 1 (< 1) (2) 0 +FTC/TAF: (1) 1 (< 1) (2) 1 (< 1) +FTC/TDF: (1) 6 (2) (2) 7 (2) *RPV (1) 35 (11) (2) 40 (13) + FTC/TAF: (1) 1 (< 1) (2) 2 (< 1) +FTC/TDF: (1) 32 (10) (2) 37 (12) + 3TC/ABC: (1) 2 (1) (2) 1 (< 1) - INSTI+NRTIs: n (%) (1) 18 (6) (2) 24 (8) *RAL: (1) 18 (6) (2) 24 (8) +3TC/ABC: (1) 4 (1) (2) 4 (1) +3TC/AZT: (1) 1 (< 1) (2) 0 +FTC/TAF: (1) 1 (< 1) (2) 2 (1) +FTC/TDF: (1) 12 (4) (2) 18 (6) * DTG (1) 6 (2) (2) 8 (3) +FTC/TAF: (1) 0 (2) 3 (1) +FTC/TDF: (1) 6 (2) (2) 5 (2) *EVG/c (1) 75 (24) (2) 70 (23) + FTC/TAF: (1) 49 (16) (2) 40 (13) +FTC/TDF: (1) 26 (8) (2) 30 (10)	W48 <u>Median weight gain (kg)</u> (1) 0,3 (2) 1,8
2020 June 2017-November 2017	WISEND [20]	144W	Phase 3; Zambia; n = 1201 Switch NNRTI based regimen (3TC/TDF/NVP or EFV) to: Arm A (VL < 1000 copies/mL): (1) DTG + TAF/FTC (TAFED) (n = 209) VS (2) DTG + TDF/3TC (TLD) (n = 209). Arm B (VL > 1000 copies/mL): (3) DTG + TAF/FTC (TAFED) (n = 211) (4) DTG + TDF/3TC (TLD) (n = 208) (5) LPV/r + AZT/3TC (n = 167) (6) ATV/r + AZT/3TC (n = 197)	Women: (1) 58%, (2) 67%, (3) 61%, (4) 59%; Zambian population; Median BMI (kg/m²): (1) 22, (2) 23, (3) 21, (4) 21, (5) 21, (6) 22 - <i>baseline VL (copies/mL):</i> *VL < 50: n (%) (1) 162 (78) (2) 169 (81) *VL ≥ 50: n (%) (1) 47 (22) (2) 40 (19) *VL ≥ 1000 < 100000: n (%) (3) 169 (80) (4) 149 (72) (5) 116 (69) (6) 114 (73) * VL ≥ 100000: n (%) (3) 42 (20) (4) 59 (28) (5) 51 (31) (6) 53 (27)	W48 <u>Mean weight change (kg)</u> <u>Arm A:</u> (1) Overall: + 1,1 (VL < 50 copies/mL: 76%) (2) Overall + 2,8 (VL < 50 copies/mL: 81%) <u>Arm B:</u> (3) *Overall: + 5,4 (VL < 50 copies/mL: 82%) *Women: + 5,7 *Men: +3,4 (4) *Overall: + 5,0 (VL < 50 copies/mL: 72 %) * Women: + 3,1 * Men: +4,6 (5) *Overall: + 2,0 (VL < 50 copies/mL: 56%) * Women: + 2,8 * Men: +2,1 (6) *Overall: + 2,8 (VL < 50 copies/mL: 71%) * Women: + 2,6 * Men: +3,2
2020 June 2017-November 2017	GS-US-380-4030 [21]	48W	Phase 3 - multicenter (international) - n = 565	Women: (1) 14%, (2) 15%; Black: (1) 24%, (2) 22%; White: (1) 71%, (2) 72%; Median weight: (1) 81kg, (2) 82kg; Median BMI: (1) 26kg/m², (2) 27kg/m²; Suppressed patients: 100%	W48 <u>Median weight gain (kg)</u> (1) +1,3

			Switch DTG/FTC/TAF or TDF to (1) BIC/FTC/TAF (n = 284) VS (2) DTG/FTC/TAF (n = 281)	<u>Baseline regimen</u> -TAF/FTC backbone (1) 68% (2) 69%	(2) +1,1 <i>p</i> = 0,46 <u>By baseline NRTI:</u> -TDF/FTC: +2,2 -TAF/FTC: +0,6 <i>p</i> < 0,001
Switch to NNRTI					
2021 June 2015-February 2017	DRIVE-SHIFT [22]	144W	Phase 3; Multicenter (international); n = 670 2NRTIs + PI/b or + EVG/c or + NNRTI Switch to: (1 = ISG) DOR 100mg/3TC 300mg/TDF 300mg (n = 447) VS (2 = DSG) Continue baseline regimen (n = 223) W24 (1 = ISG) Immediate switch group (ISG) W0 to W144 VS (2 = DSG) Delayed Switch Group (DSG) W24 to W144	Men: 84,5%; White: 76,4% - At the time of switch: *BMI < 18,5: 2,2% *BMI ≥ 18,5 to < 25: 48,1% *BMI ≥ 25 to < 30: 33,0% *BMI ≥ 30: 16,7% <u>Baseline regimen</u> - Baseline 3 rd agent - bPI: n (%) (1) 316 (70,7) (2) 156 (70) DRV: (1) 166 (37,1) (2) 82 (36,8) ATV: (1) 96 (21,5) (2) 43 (19,3) LPV: (1) 54 (12,1) (2) 31 (13,9) - NNRTI: (1) 106 (23,7) (2) 55 (24,7) EFV: (1) 78 (17,4) (2) 36 (16,1) NVP: (1) 17 (3,8) (2) 12 (5,4) RPV: (1) 11 (2,5) (2) 7 (3,1) - INSTI (= EVG/c): (1) 25 (5,6) At 144w: 20 (+ TAF: 17) (2) 12 (5,4) At 144w: 9 (+TAF: 7) <u>Backbone NRTI: n (%)</u> TDF/FTC: (1) 330 (73,8) (2) 154 (69,1) TAF/FTC: (1) 22 (4,9%) (2) 11 (4,9%) TDF/3TC: (1) 10 (2,2) (2) 10 (4,5) ABC/3TC: (1) 61 (13,6) (2) 28 (12,6) AZT/3TC: (1) 23 (5,1) (2) 19 (8,5)	W144 <u>Mean weight gain (kg)</u> (1) *Overall: +1,4 *Men: +1,4 *Women: +1,2 *Black: +1,4 *Non-black: 1,4 *Hispanic/Latino: +1,6 *Other ethnicity: +1,3 *bPI: +1,4 *NNRTI: +1,5 *INSTI (=EVG/c) + TAF (n = 17/20): +0,8 (2) *Overall: +1,2 *Men: +1,2 *Women: +1,0 *Black: +1,3 *Non-black: 1,2 *Hispanic/Latino: +1,5 *Other ethnicity: +1,2 *bPI: + 1,3 *NNRTI: +1,3 *INSTI (= EVG/c) + TAF (n = 7/9): +0,6 <u>Weight change category: % of participants</u> ≤ -10%: (1) 3,9 (2) 5,6 > -10% to ≤ -5%: (1) 10,6 (2) 4,0 > -5% to ≤ 0%: (1) 29,3 (2) 28,8 > 0% to < 5%: (1) 29,9 (2) 33,3 ≥ 5% to < 10%: (1) 17,9 (2) 20,3 ≥ 10%: (1) 8,4 (2) 7,9 <u>Change in BMI category: % of participants</u> Overall - no change: 82,6 - non-obese at switch (n = 445) → obese: 4 - obese at switch (n = 89) → non-obese: 9
Pooled RCT					
2021	Erlandson [23]	96W in 7 studies 48W in 5 studies	Pooled analysis of 12 RCT; n = 7306 (1) switch ART (n = 4166) - switch NRTIs + 3 rd agent (n = 1949) - switch NRTI only (n = 1326) - switch 3 rd agent only (n = 891) VS (2) remaining on ART (n = 3150)	10/12 RCT: - Men: majority (women ≤ 10-20%) - White: majority (Black ≤ 10-30%) - Obesity ≥ 15-30% 2 RCT/12: - GS-US- 380-1961: only women and majority of Black participants - GS-US- 292-1826: older participants; < 3% of Black participants	W48 <u>Median weight gain (kg)</u> Overall (1) +1,6 VS (2) + 0,4 <i>p</i> < 0,0001 <u>Weight gain (kg) by ART switch</u> NNRTI switch - switch EFV→ RPV: +1,5 vs stay on EFV (<i>p</i> < 0,001) - switch EFV→ EVG/c: + 0,9 vs stay on EFV (<i>p</i> < 0,001) - switch RPV → EVG/c: - 1,7 vs stay on RPV (<i>p</i> = 0,01) - switch NVP → EVG/c: similar weight vs stay on NVP PI switch - switch bPI → EVG/c or BIC vs stay on bPI: no significantly change INSTI switch - switch DTG → BIC vs stay on DTG: no significantly change - switch EVG/c → BIC vs stay on EVG/c: + 0,7 (<i>p</i> = 0,034) NRTI switch - switch TDF → TAF: + 1,6 (<i>p</i> < 0,001) - switch ABC → TAF: precise data on weight gain not available (<i>p</i> < 0,001) <u>Weight gain (kg) by maintain ART</u> Maintain NNRTI - similar weight gain for all NNRTI SBR; - stay on RPV vs stay on EVG/c: greater weight gain (precise data on weight gain not available) (<i>p</i> = 0.046). Maintain INSTI - stay on DTG VS stay on EVG/c: +0,6 (<i>p</i> = 0.02) Maintain NRTI - stay on TDF or ABC vs stay on TAF: no weight change <u>Weight gain by sex</u> - Women: +0,3kg vs men (<i>p</i> = 0,0046) - Black vs non-Black: no difference - Black males: +0,3kg vs non-Black males (<i>p</i> = 0,041) - Non-Black women: +0,5kg vs non-black males (<i>p</i> = 0,013) <u>Weight gain ≥ 10% (% of patients)</u> Overall: 4,6% (1) 6,4% (2) 2,2% <u>Risk factors:</u> - age ≤ 35y - lower baseline weight and BMI - switch EFV → RPV or EVG/c - switch TDF →TAF W96 <u>Median weight gain (kg)</u> (1) + 2,0 VS (2) + 0,5 <i>p</i> < 0,0001 <u>Change in BMI (% of patient)</u> Obesity (BMI: ≥ 30) (1) 21% → 25% (2) 21% → 21% Overweight (BMI: ≥ 25 - < 30) (1) 37% → 40% (2) 38% → 42%

W: Week; ART: AntiRetroviralTherapy; VL: Viral Load; y: years; BMI: Body Mass Index; US : United States; SBR: Stable Baseline Regimen; (b)PI: (boosted) Protease Inhibitor; r: ritonavir; LPV: Lopinavir; ATV: Atazanavir; c: Cobicistat; NRTI: Nucleoside (tide) Reverse Transcriptase Inhibitor; FTC: Emtricitabine; ABC: Abacavir ; TAF: Tenofovir Alafenamide Fumarate; TDF: Tenofovir Disoproxil Fumarate; AZT: Zidovudine; 3TC: Lamivudine; PSZ: Phosphazide; ddl: Didanosine; NNRTI: Non-Nucleoside Reverse Transcriptase Inhibitor; EFV: Efavirenz; RPV: Rilpivirine; DOR: Doravirine; NVP: Nevirapine; INSTI: Integrase Strand Transfer Inhibitor; DTG: Dolutegravir; BIC: Bictegravir; EVG/c: Elvitegravir/cobicistat; RAL: Raltegravir; LA: Long Acting; CAB: Cabotegravir.

Table 2. Cohorts studies in Experienced PLWH

Year of publication (and duration of study)	Study Name and authors	Duration	Study design and primary endpoint	Baseline characteristics	Results
Switch TDF to TAF					
2021 (2015-2019)	OPERA [24]	48 months prior to switching up to 36 months after switch	- Multicentric (US) - n = 6919 Switch TDF to TAF (1) + maintained NNRTI (n = 1452) (2) + maintained bPI (n = 746) (3) + maintained INSTI (n = 3281) (4) + switch to INSTI (n = 1429)	Men: 80%; Women: (1) 19%, (2) 21%, (3) 15%, (4) 18%; Black: (1) 41%, (2) 39%, (3) 37%, (4) 38% -median BMI (kg/m²): 27 -mean weight gain before switch (kg/y): 0,42 - suppressed patients: 100% <u>Baseline regimen before switch:</u> (1) maintained NNRTI: RPV: 85% (2) maintained bPI: DRV/r: 68% (3) maintained INSTI: EVG/c: 73% (4) + switch to INSTI: - bPI: DRV/r: 42%; ATV/r: 44% - NNRTI: EFV: 84%	<u>Weight change before and after switch from TDF to TAF (kg/y)</u> <u>Maintained agent:</u> Global average: -60 to 0 months: 0,48 0 to 9 months: 2,43 > 9 months: 0,24 INSTI (n = 3281): -60 to 0 months: 0,42 0 to 9 months: 2,64 > 9 months: 0,29 NNRTI (n = 1452) -60 to 0 months: 0,66 0 to 9 months: 2,25 > 9 months: 0,20 bPI (n = 746): -60 to 0 months: 0,31 0 to 9 months: 1,98 > 9 months: -0,11 <u>Maintained INSTI:</u> EVG/c (n = 2389): -60 to 0 months: 0,71 0 to 9 months: 2,51 > 9 months: 0,36 DTG (n = 643): -60 to 0 months: 0,73 0 to 9 months: 2,38 > 9 months: - 0,18 RAL (n = 249): -60 to 0 months: -0,44 0 to 9 months: 1,80 > 9 months: 0,63 <u>+ switch to INSTI (n = 1429):</u> EVG/c (n = 1120): -60 to 0 months: 0,24 0 to 9 months: 2,55 > 9 months: 0,26 DTG (n = 174): -60 to 0 months: 0,22 0 to 9 months: 3,09 > 9 months: - 0,23 BIC (n = 129): -60 to 0 months: 0,01 0 to 9 months: 4,47 > 9 months: -9,97 <u>Average adjusted weight gain (kg)</u> <u>Maintained all other ARVs</u> +12 months *INSTI: +1,6 *bPI: + 1,1 *NNRTI: +1,5 +24 months: *INSTI: +2,1 *bPI: +1,3 *NNRTI: +1,5 <u>Switch core agent</u> +12 months *EVG/c: +1,6 *DTG: +1,5 +24 months: *EVG/c: +2,0 *DTG: +1,6
2020	Mc Comsey [25]	12 months post-switch	- Multicentric (10 US HIV treatment centers) - n = 970 (1) switch ABC → TAF (n = 142) VS (2) switch TDF → TAF (n = 828)	Women: (1) 13%, (2) 16% White: (1) 60%, (2) 55% - BMI (kg/m²) * < 18,5: (1) 4% (2) 5% * 18,5-24,9: (1) 32% (2) 32% * 25-29,9: (1) 38% (2) 33% * ≥ 30: (1) 26% (2) 31% - suppressed patients: 100% - + switch to INSTI: (1) 84% (DTG: 96%; RAL: 4%) (2) 14% (DTG: 11%; RAL: 10%; EVG: 79%)	<u>Mean weight gain (kg) at 1y</u> (1) +0,2 (2) +1,4 <i>p</i> = 0,039 <u>Weight gain > 10% (% of patients)</u> (1) 6% (2) 10% Not statistically significant <u>Weight gain > 3% (% of patients)</u> (1) 27% (2) 40% <i>p</i> = 0,003
Switch INSTI +/- TAF					
2020 (1997 to 2017)	Lake et al. [26]	2y before and after switch INSTI	- Observational study among AIDS Clinical Trials Group (ACTG) participants in ACTG protocols A5001 and A5322 - n = 691	Men: 81%; non-white: 50%; median BMI: 26,4kg/m²; suppressed patients: 100% <u>Baseline regimen before switch:</u> *PI: 68% *NNRTI: 31% *other non-INSTI: 2% <u>NRTI backbone before switch, maintained after switch:</u> *ABC: 62% *TDF: 61% *TAF: 57% <u>Switch regimen:</u> *RAL: n = 539 *EVG: n = 222 *DTG: n = 211	<u>Annualized weight gain (kg/y)</u> <u>Overall</u> Prior INSTI switch: + 0,4 After INSTI switch: + 0,6 Women. After INSTI switch: + 1,3 Black race. After INSTI switch: + 0,9 Age ≥ 60y. After INSTI switch: + 1,2 <u>Pre-post switch to INSTI difference</u> DTG (n = 198): +1,0 (<i>p</i> < 0,001) EVG (n = 204): + 0,5 (<i>p</i> = 0,1) RAL (n = 289): -0,2 (<i>p</i> = 0,4) <u>By regimen at switch:</u> <i>NNRTI: switch to</i> DTG: + 1,2 (<i>p</i> = 0,01) EVG: + 1,3 (<i>p</i> = 0,01) RAL: -0,2 (<i>p</i> = 0,6) <i>PI: switch to</i> DTG: +0,9 (<i>p</i> = 0,04) EVG: +0,1 (<i>p</i> = 0,8) RAL: -0,2 (<i>p</i> = 0,3) <i>NRTI backbone at switch to any INSTI:</i> ABC: +0,9 (<i>p</i> = 0,004) TAF: +0,8 (<i>p</i> = 0,1) TDF: -0,2 (<i>p</i> = 0,3) <u>Weight absolute slope (kg/y)</u> PI (n = 527): BEFORE switch: Overall: +0,80 (<i>p</i><0,001) Women: + 0,94 Non-Whites: +1,04 Age ≥ 50y: +0,70 AFTER switch: Overall: +0.34 (<i>p</i> < 0,001) Women: +0,49 Non-Whites: +0,44 Age ≥ 50y: +0,04 *Switch PI to DTG: -0,04 (<i>p</i> < 0,001) *Switch PI to RAL: + 0,17 (<i>p</i> < 0,001) *Switch PI to EVG: + 0,89 (<i>p</i> = 0,11) NNRTI (n = 343): BEFORE switch: Overall: +0,63 (<i>p</i> < 0,001) Women: +0,14 Non-Whites: +0,76 Age ≥ 50y: +0,21 AFTER switch: Overall: +1,13 <i>p</i> < 0,001 Women: + 1,58 (<i>p</i> < 0,001) Non-Whites: +2,03 (<i>p</i> < 0,001) Age ≥ 50y: + 1,38 (<i>p</i> < 0,001)
2020 (January 1 st , 2007 and December 31 st , 2014.)	NA-ACCORD [27]	2y before and after switch INSTI	- North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). - n = 870 Switch from an NNRTI or PI to INSTI-based ART	Men: 83%; White: 59%; Median BMI: 26kg/m² <u>Regimen switch:</u> *NNRTI → INSTI (n = 343) RAL: n = 146 DTG: n = 81 EVG: n = 117 *PI → INSTI (n = 527) RAL: n = 285 DTG: n = 95 EVG: n = 146	PI (n = 527): BEFORE switch: Overall: +0,80 (<i>p</i><0,001) Women: + 0,94 Non-Whites: +1,04 Age ≥ 50y: +0,70 AFTER switch: Overall: +0.34 (<i>p</i> < 0,001) Women: +0,49 Non-Whites: +0,44 Age ≥ 50y: +0,04 *Switch PI to DTG: -0,04 (<i>p</i> < 0,001) *Switch PI to RAL: + 0,17 (<i>p</i> < 0,001) *Switch PI to EVG: + 0,89 (<i>p</i> = 0,11) NNRTI (n = 343): BEFORE switch: Overall: +0,63 (<i>p</i> < 0,001) Women: +0,14 Non-Whites: +0,76 Age ≥ 50y: +0,21 AFTER switch: Overall: +1,13 <i>p</i> < 0,001 Women: + 1,58 (<i>p</i> < 0,001) Non-Whites: +2,03 (<i>p</i> < 0,001) Age ≥ 50y: + 1,38 (<i>p</i> < 0,001)

					*Switch NNRTI to DTG (n = 176): +1,73 ($p < 0,001$) *Switch to EVG (n = 263): +1 ($p = 0,07$) *Switch to RAL (n = 431): +0,97 ($p = 0,21$)
2020 (2006 to 2015)	Kerchberger [28]	Mean of 2y of follow-up	- Multicentric (US) - Data already collected from WLHIV in the previously described Women's Interagency HIV Study (WIHS) - n = 1118 (1) switch or add an INSTI to ART (SWAD group) n = 234 VS (2) remained on non-INSTI ART (STAY group) n = 884	Women: 100% African American: (1) 59,8% (n = 140), (2) 61,1% (n = 540) White: (1) 19,7% (n = 46), (2) 14,3% (n = 126); Suppressed patients: (1) 93,2%, (2) 96,2% <u>Baseline ART regimen</u> *NNRTI: (1) 35,5% vs (2) 53,4% $p < 0,0001$ *PI (1) 68,8% vs (2) 46,6% $p < 0,0001$ *ABC (1) 27,4% vs (2) 17,1% $p = 0,0004$ *TDF (1) 65% vs (2) 80,5% $p < 0,0001$ STAY group, - 97% (n = 857) had no change to their anchor drug class during follow-up - 3% (n = 22) switched to/added either an NNRTI or a PI. - 1.1% (n = 10): + ABC - 1.7% (n = 15): +TDF - 8.7% (n = 77): + TAF SWAD group: - 42% (n = 97) switched to/added DTG - 23% (n = 52) switched to/added EVG - 36% (n = 85) switched to/added RAL - 15% (n = 36): + ABC - 8% (n = 18): + TDF - 12% (n = 29): + TAF	<u>Mean increase in weight (kg)</u> (1) + 2,4 (2) + 0,2 $p < 0,0001$ <u>Weight increase $\geq$ 7% (% of patients)</u> (1) 22% (n = 52) (2) 14% (n = 124) $p < 0.0001$ <u>Changes in weight (kg) stratified by clinical characteristics</u> By age $\geq$ 50y: (1) +2,3 (2) -0,3 $p < 0,001$ By race: *white/other/non-Hispanics (n = 172): (1) +1,8 (2) +0,2 *Black non-Hispanic (n = 680) (1) +3 (2) +0,6 $p < 0,001$ *Hispanic (n = 266) (1) +1,8 (2) -0,6 $p < 0,01$ By baseline BMI (kg/m²) *BMI< 30 (n = 584): (1) +2,7 (2) +0,4 $p < 0,0001$ *BMI $\geq$ 30 (n = 507) (1) +2,1 (2) +0,4 $p < 0,05$ Baseline VL (copies/mL): *Detectable (n = 208): (1) +1 (2) +0,3 *Undetectable (n = 910) (1) +2,7 (2) +0,1 $p < 0,0001$ By baseline CD4 (cells/mm³): * < 350 (n = 153): (1) +1,6 (2) -0,1 * $\geq$ 350 (n = 957) (1) +2,4 (2) +0,3 $p < 0,0001$ By baseline ART regimen: *NNRTI (n = 526): (1) +3,1kg (2) +0,5kg $p < 0,01$ *PI (n = 543) (1) +2,1kg (2) +0 ,04kg $p < 0,001$ INSTI type (SWAD group only) DTG (n = 97): +1,7 RAL (n = 85): +1,3 EVG (n = 52): +2,7 <u>Mean change in BMI (kg/m²)</u> (1) 0,9 (2) 0,1 $p < 0,001$ <u>Mean change in PBF (%)</u> (1) +1,7 (2) + 0,3 $p < 0,01$ <u>Change in body circumference mesures (cm): (1) vs (2)</u> - Waist circumference: +2 ($p < 0,0001$) - Hip circumference: +1,9 ($p < 0,0001$) - Arm circumference: +0,6 ($p < 0,001$) - Tight circumference: +1 ($p < 0,01$) - Waist to hip ratio: 0,002
2019 (March to July 2018)	Kuo et al. [29]	48W	-Taiwan -n = 693 Switch to EVG/c/TAF/FTC	Women: 34% Mean BMI at switch (kg/m²): 23,8 TDF before switch: 96%	<u>Mean change in weight (kg) before (-48W) vs after switch (+48W)</u> - all: +0,54 vs +1,75 ($p < 0,0001$) - priori NNRTI (n = 337): +0,54 vs +2,07 ($p < 0,01$) - priori PI (n = 219): +0,38 vs +1,5 ($p < 0,01$) - priori INSTI (n = 137): +0,76 vs +1,37 ($p = 0,31$)
2021 (January 2015 – January 2019)	TRIO [30]	12 months	- Multicenter (US) - n = 2272 <u>Switch to:</u> - EVG: 39% (n = 887) - BIC: 31% (n = 713) - DTG: 28% (n = 631) - RAL: 2% (n = 41) <u>Switch TDF to TAF at the same time:</u> - overall: 47% - + switch to *EVG: 87% (n = 768)-*BIC: 18% (n = 129) *DTG: 23% (n = 142) *RAL: 56% (n = 23)	Women: EVG: 12% BIC: 11% DTG: 18% RAL: 27% White: EVG: 55% BIC: 60% DTG: 48% RAL: 66% Mean weight (kg): 84 Suppressed patients: 100% <u>Baseline regimen:</u> -INSTI: 64% (n = 1447) -TDF: 57% - prior switch TDF to TAF: 47% (more common in patients on EVG) <u>Significantly differences in Baseline characteristics, % of patients ($p < 0,05$)</u> -< 50y: EVG: 56% vs DTG :46% -white: BIC: 60% vs DTG: 48% -black: DTG: 40% vs EVG: 30% vs BIC: 24% -female: EVG: 12% vs BIC: 11% vs DTG: 18% - CD4 < 200 cells/μL: EVG: 1% vs BIC: 2% vs DTG: 6% vs RAL: 4%	12 months <u>Mean weight gain (kg)</u> Overall: + 1,3 EVG: +1,5 BIC: +0,9 DTG: +1,2 RAL: 1,9 <u>Weight gain $\geq$ 3% (% of patients)</u> EVG: 41% BIC: 35% EVG vs BIC: $p = 0,015$ EVG: 41% DTG: 37% RAL: 37% <u>Variables associated with risk of weight gain $\geq$ 3%: aRR:</u> - switch from TDF to TAF: 1,22 (1.06, 1.41) $p = 0,006$ - priori INSTI: 0,77 (0.61, 0.97) $p = 0,029$ - baseline BMI underweight or normal vs overweight or obese: 1,17 (1.04, 1.31) $p = 0,009$ - baseline CD4 < 200 cells/μL: 1,33 (1.02, 1.73) $p = 0,036$ - age < 50y: 1,16 (1.03, 1.3) $p = 0,012$ - Black vs white: 1,13 (1, 1.28) $p = 0,043$ <u>Weight gain $\geq$ 5% (% of patients)</u> EVG: 24% BIC: 22% DTG: 27% RAL: 24% <u>Variables associated with risk of weight gain $\geq$ 5% (aRR):</u> Women: 1,3 Black: 1,2 Baseline BMI underweight/normal: 1,4 Switch from TDF to TAF: 1,3 <u>Weight gain $\geq$ 10% (% of patients)</u> EVG: 8% BIC: 6% DTG: 10% DTG vs BIC: $p = 0,046$ RAL: 7%

					Variables associated with risk of weight gain ≥ 10% (aRR): Women: 2,2 Baseline BMI underweight/normal: 2,3 Prior non-INSTI regimen: 2,2 Switch from TDF to TAF: 1,6
2021 (June 2015 – May 2016)	GEPO cohort [31]	Average follow-up of 2,6y	- Multicenter (Italian) - n = 568 INSTI-naïve (INSTI-n) → (1) INSTI-n (n = 427) VS (2) DTG-switchers (DTG-s) (n = 141)	Mean age (y): (1) 73,3 (2) 73,5 Men: n (%): (1) 360 (84,3) (2) 112 (79,4) Mean weight (kg) (1) 74,5 (2) 71,8 BMI (kg/m²) (1) n (%) * < 18,5: 7 (2,8) * 18,5 – 30: 206 (82,4) * > 30: 37 (14,8) (2) n (%) * < 18,5: 2 (1,9) * 18,5 – 30: 89 (85,6) * > 30: 13 (12,5) Suppressed patients at baseline (%): (1) 95 (2) 92,9 Suppressed patients at last visit (%) (1) 96,3 (2) 96,2 - current CD4 cells count/μL (1) 650,7 (2) 652,9 - nadir CD4 cells count/μL (1) 246,94 (2) 204,17 <u>ART regimen at baseline:</u> n (%) PI: (1) 191 (44,7) (2) 77 (54,6) NNRTI: (1) 215 (50,4) (2) 49 (34,8) TDF: (1) 148 (34,7) (2) 44 (31,2) ABC: (1) 129 (30,2) (2) 53 (37,6) - <u>ART regimen at last visit:</u> n (%) PI: (1) 133 (31,1) (2) 8 (5,7) NNRTI: (1) 216 (50,6) (2) 13 (9,2) TAF: (1) 141 (33) (2) 36 (25,5) TDF: (1) 38 (8,9) (2) 0 ABC: (1) 103 (24,1) (2) 43 (30,5)	<u>Delta weight between weight at last follow-up and baseline weight (kg)</u> (1) 0,02 (<i>p</i> = 0,633) (2) -0,04 (<i>p</i> = 0,755) <u>Weight gain ≥ 5% (%)</u> (1) 9,3 vs (2) 15,1 <i>p</i> = 0,175 <u>Time to achieve weight gain ≥ 5%</u> (1) vs (2): no significant differences (<i>p</i> = 0,93) 2DR vs 3DR: no significant differences (<i>p</i> = 0,56) TAF vs TDF: no significant differences (<i>p</i> = 0,56) <u>Prevalence of BMI > 30kg/m² at last visit: n (%)</u> (1) 33 (13,1) (2) 13 (12,5) <i>p</i> = 0,997
2019 (2007 - 2017)	HOPS [32]	Mean duration: - INSTI use after switch: 2.4y - non-INSTI use after switch: 2.6y	- Multicenter (US) - n = 653 <u>INSTI naïve patients switched to</u> (1) INSTI-based regimen (n = 368) VS (2) non-INSTI-based regimen (n = 285)	Women (1) 17,7% (2) 20,4% Non-Hispanic Black (1) 22,8% (2) 27,4% BMI (kg/m²) * < 25: (1) 40,2% (2) 37,2% * 25-29,9: (1) 38,3% (2) 40% * ≥ 30: (1) 21,5% (2) 22,8% Suppressed patients: 100% <u>Baseline regimen</u> * NNRTI: 50,2% (n = 143) * PI: 48,1% (n = 137) + ≥ 1 NRTI: 95,8% (n = 273) <u>INSTI regimen after switch</u> *RAL: 48,6% (n = 179) *EVG: 21,7% (n = 80) *DTG: 29,6% (n = 109)	<u>Mean weight change (kg)</u> (1) + 1,2 vs (2) + 0,3 <i>P</i> = 0,05 <u>BMI slope per month</u> RAL Pre-RAL: 0,005 (<i>p</i> < 0,001) Post switch RAL: 0,009 (<i>p</i> < 0,001) EVG Pre-EVG: 0,002 (<i>p</i> = 0,05) Post switch EVG: -0,002 (<i>p</i> = 0,67) DTG Pre-DTG: 0,003 (<i>p</i> < 0,001) Post switch DTG: 0,020 (<i>p</i> < 0,001); DTG vs RAL (<i>p</i> = 0,03); DTG vs EVG/c (<i>p</i> =0,003) Non-INSTI Pre-non-INSTI: 0,009 (<i>p</i> < 0,001) Non-INSTI: 0,005 (<i>p</i> < 0,001)
2021 (2007-2018)	HOPS [33]		- Multicenter (US) - n = 736 non-INSTI baseline regimen (1) switch to INSTI (n = 441) * RAL: 40,4% * EVG: 25,4% * DTG: 32,4% * INSTI + TAF: n = 188 vs (2) remain on non-INSTI baseline regimen (n = 295) * post-switch non-INSTI+TAF: n = 128	Women: n (%) (1) 82 (18,6) (2) 59 (20) Non-Hispanic Black: (1) 110 (24,9) (2) 80 (27,1) Suppressed patients: 100% INSTI naïve: 100% BMI (kg/m²): n (%) * < 25: (1) 175 (39,7) (2) 113 (38,3) * 25-29,9: (1) 165 (37,4) (2) 112 (38) > 30: (1) 101 (22,9) (2) 70 (23,7) <u>Baseline ART regimen</u> Mean duration (y): (1) 5,4 (2) 5,8 *PIs: n (%) (1) 189 (42,9) (2) 139 (47,1) *NNRTIs: n (%) (1) 238 (54) (2) 154 (52,2) * NRTIs: n (%) (1) 429 (97,3) (2) 283 (95,9) *TAF: n (%) (1) 188 (42,6) (2) 128 (43,4) <u>Post-switch ART regimen</u> Mean duration (y): (1) 2,5 (2) 2,6 *PIs: n (%) (1) 48 (10,9) (2) 108 (36,6) *NNRTIs: n (%) (1) 43 (9,8) (2) 173 (58,6) * NRTIs: n (%) (1) 420 (95,2) (2) 274 (92,9)	Pre-switch <u>Change in weight pre-switch (kg)</u> (1) 2,0 (2) 2,2 <u>BMI slope per month</u> (1) 0,0005 (<i>p</i> = 0,36) (2) 0,0073 (<i>p</i> < 0,001) Post-switch <u>BMI slope per month</u> INSTI vs non-INSTI: 0,00712 (<i>p</i> < 0,001) (1) +/- TAF: < 8 months after switch * INSTI + TAF: 0,0620 (<i>p</i> < 0,001) * INSTI: 0,0541 (<i>p</i> < 0,001) ≥ 8 months after switch * INSTI + TAF: 0,0108 (<i>p</i> = 0,02) * INSTI: 0,0029 (<i>p</i> = 0,05) By INSTI vs pre-switch * RAL: 0,00989 (<i>p</i> < 0,001) vs 0,00746 (<i>p</i> < 0,001) * DTG: 0,01045 (<i>p</i> < 0,001) vs 0,00022 (<i>p</i> = 0,77) * EVG: 0,00694 (<i>p</i> = 0,09) vs 0,00243 (<i>p</i> = 0,02) By INSTI post-switch * RAL vs DTG: -0,00056 (<i>p</i> = 0,86) * RAL vs EVG: 0,00295 (<i>p</i> = 0,49) * DTG vs EVG: 0,00351 (<i>p</i> = 0,49) (2) * non-INSTI+TAF: 0,0096 (<i>p</i> = 0,03) * non-INSTI: 0,0019 (<i>p</i> = 0,12)
INSTI use					
2019	Swiss cohort [34]	18 months pre and post-switch	- Observational cohort - Multicenter (Switzerland) - n = 2186 Weight change (1) pre-switch VS (2) post-switch to DTG-regimen	Men: 75%; White: 81%; Median weight (kg): 73; Median BMI (kg/m²): 24; Suppressed patients: 100% <u>Baseline regimen:</u> no data available	<u>Median weight gain (kg/y)</u> Overall (1) 0,47 (2) 0,72 <i>p</i> = 0,029 Women (1) 0,44 (2) 0,41 <i>p</i> = 0,923 Men (1) 0,49 (2) 0,81 <i>p</i> = 0,009 Black (1) 1,06 (2) 0,85 <i>p</i> = 0,545 Non-Black (1) 0,40 (2) 0,70 <i>p</i> = 0,011 - switch to DTG + TAF (n = 72) (1) 0,33 (2) 1,43 <i>p</i> = 0,117 - switch to DTG without TAF (1) 0,48 (2) 0,70 <i>p</i> = 0,046 <u>Weight gain > 5%</u> N = 477 Risk factors: women, black, smokers

2021 (2015-2019)	REPRIEVE [35]		- Cross-sectional analysis - Multicenter (international) - n = 4498 (1) INSTI use > 6 months (n = 1848) VS (2) Non-INSTI use (n = 2652)	Women: (1) 20% (2) 25% Black/African American: 40% Mean BMI (kg/m²) (1) 28,2 (2) 26,9 Mean WC (cm): (1) 97,7 (2) 94 Suppressed patients: VL < 400 copies/mL: 87% <u>Baseline regimen</u> *NNRTI: 62% *PI: 36%	<u>Mean BMI (kg/m²)</u> (1) vs (2): +1,6 <u>Mean WC (cm)</u> (1) vs (2): +3,6 (1) + women: +5,0 <u>Difference (1) VS (2) for BMI (kg/m²) at quantile 0,9</u> - all: 3,1 - female: 3,9 - male: 2,0 <u>for WC (cm) at quantile 0,9</u> - all: 7,2 - female: 9,8 - male: 5,6
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W: Week; M: Months; VL: Viral Load; ART: AntiRetroviralTherapy; cm: centimeter; BMI: Body Mass Index; y: year(s); PBF: Percentage Body Fat; WC: Waist Circumference; aRR: adjusted Rate Ratio; 2DR: two-drug regimens; 3DR: three-drug regimens; WLHIV: Women Living With HIV. NRTI: Nucleoside (tide) Reverse Transcriptase; TDF: Tenofovir Disoproxil fumarate; TAF: Tenofovir Alafenamide Fumarate; 3TC: lamivudine; ABC: Abacavir; NNRTI: Non-Nucleoside Reverse Transcriptase; EFV: Efavirenz; RPV: Rilpivirine; (b)PIs: (boosted) Protease inhibitors; ATV: Atazanavir; DRV: Darunavir; r: ritonavir; INSTI: Integrase Strand Transfer Inhibitor; DTG: Dolutegravir; RAL: Raltegravir; EVG: Elvitegravir; c: cobicistat; BIC: Bictegravir.