Evolution of weight under Dual Therapy without Tenofovir Compared to Triple Therapy: Week 96 Results from the MODERATO Trial (ANRS -MIE 12372)

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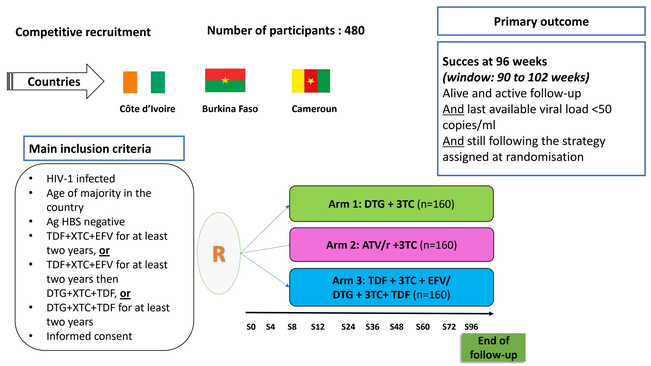
BACKGROUND

Moderato trial proves the non-inferiority of dual Therapy DTG+3TC or ATV/r + 3TC comparing to 3-drug current antiretroviral regimens at week 96, (IAS2025: 5282). Dual therapies, particularly the DTG/3TC combination, are now recommended by the WHO as an alternative to TDF-based triple ART for virologically controlled patients and without active hepatitis B. We have worked on the issue of weight gain under dual therapy in sub-Saharan Africa countries.

METHODS

We conducted a study in three sub-Saharan Africa countries, randomizing HIV-1 adults on TDF/3TC/EFV for ≥2 years, without prior virological failure, antigen HBS negative and with BMI data at all visits. We compared changes in weight between those switching to dual therapy (DTG/3TC) or (ATV/r/3TC) and those continuing triple ART, using mixed-model repeated measures, and we assessed the prognostic factors associated with weight gain of more than 10% between baseline and W96 using the binary logistic regression.

STUDY DESIGN



RESULTS

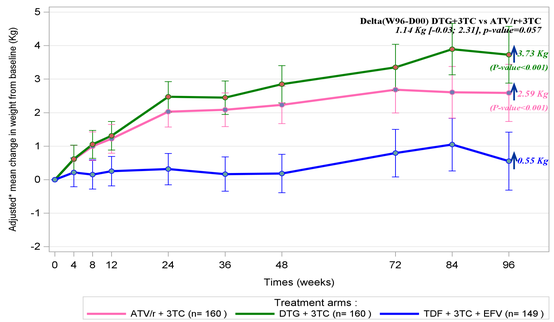
Baseline Characteristics 1/2

	DTG+3TC (N=160)	ATV/r + 3TC (N=160)	TDF + 3TC + EFV (N = 149)	TOTAL (N=469)
Gender, n (%)				
Female	121 (76%)	123 (77%)	124 (83%)	368 (79%)
Age (years)				
Median [IQR]	50 [44 – 55]	50 [46 – 57]	49 [42 – 54]	50 [44 – 56]
Min – Max	28 - 75	23 – 76	21 – 70	21 –76
CD4 at inclusion (cells count)				
Median [IQR]	709 [526 – 914]	721 [532 – 924]	762 [627 – 970]	736 [558 – 943]
Min – Max	203 – 2107	205 – 1933	260 – 1732	203 – 2107
HIV-1 RNA (copies/ml) at inclusion				
Median [IQR]	20 [20 – 20]	20 [20 – 20]	20 [20 – 20]	20 [20 – 20]
Min – Max	0 – 45	0 – 50	0 – 49	0 – 50
Duration on ARV treatment (years)				
Median [IQR]	8.6 [5.0 – 12.8]	8.6 [5.2 – 12.3]	8.8 [4.9 – 13.2]	8.7 [5.0 – 12.8]
Min – Max	2.8 – 20.5	2.2 – 20.3	2.2 – 18.4	2.2 – 20.5

Baseline Characteristics 2/2

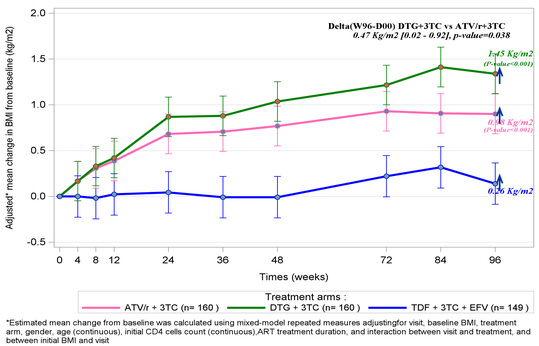
	DTG + 3TC (N = 160)	ATV/r + 3TC (N = 160)	TDF + 3TC + EFV (N = 149)	TOTAL (N=469)
Weight (Kg)				
Median [IQR]	68 [57 – 78]	70 [60 – 79]	69 [59 – 80]	69 [58 – 79]
Min - Max	37 – 111	39 – 138	41 – 130	37 – 138
BMI (Kg/m2)				
Median [IQR]	25 [21 – 28]	26 [22 – 29]	26 [22 – 30]	25 [22 – 29]
Min - Max	16 – 40	16 – 49	17 – 46	16 –49
BMI in class				
Underweight (<18.5 kg/m2)	17 (11%)	8 (5%)	9 (6%)	34 (7%)
Normal (18.5 – 25 kg/m2)	67 (42%)	65 (41%)	58 (39%)	190 (41%)
Overweight (25 – 30 kg/m2)	46 (29%)	58 (37%)	41 (27%)	145 (31%)
Obese (>30 kg/m2)	30 (19%)	29 (18%)	41 (27%)	100 (21%)
Waist circumference (cm)				
Median [IQR]	88 [79 - 95]	89 [81 - 96]	89 [81 - 98]	88 [80 - 97]
Min - Max	60 - 134	66 - 126	66 - 123	60 – 134
Hip circumference (cm)				
Median [IQR]	100 [92 – 108]	103 [94 – 108]	102 [94 – 110]	101 [94 – 109]
Min - Max	76 - 123	61 - 139	74 - 135	61 - 139

Evolution of mean weight changes (Kg) by treatment arm



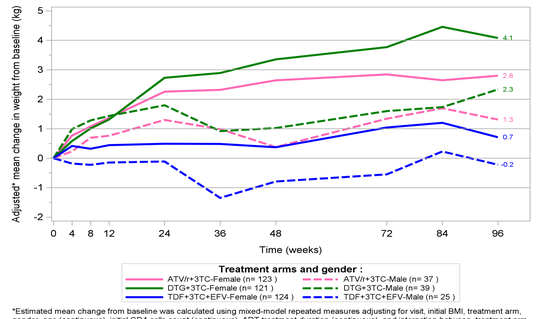
*Estimated mean change from baseline was calculated using mixed-model repeated measures adjusting for visit, baseline weight (continuous), initial BMI, treatment arm, gender, age (continuous), initial CD4 cells count (continuous), ART treatment duration, and interaction between treatment arm and visit , and between baseline weight (continuous) and visit

Evolution of BMI (Kg/m²) by treatment arm



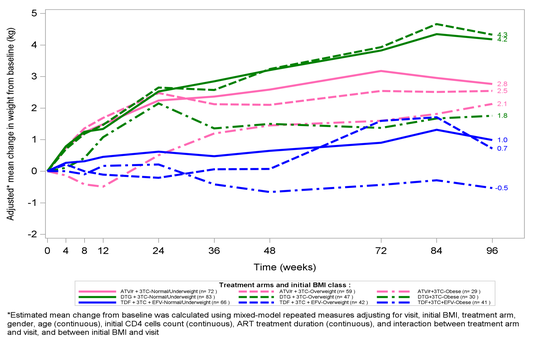
*Estimated mean change from baseline was calculated using mixed-model repeated measures adjustingfor visit, baseline BMI, treatment arm, gender, age (continuous), initial CD4 cells count (continuous),ART treatment duration, and interaction between visit and treatment, and between initial BMI and visit

Evolution of average weight changes by gender and treatment arm



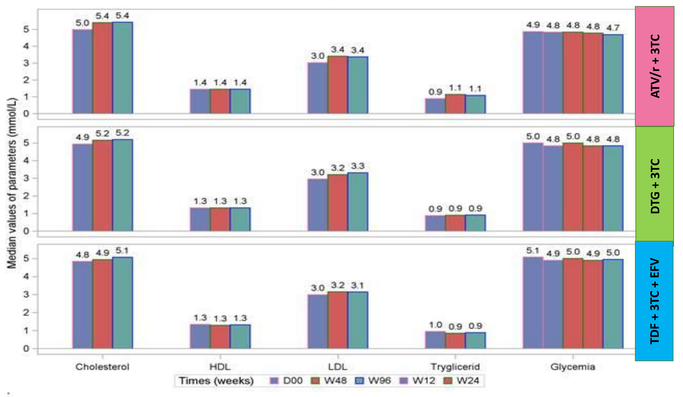
*Estimated mean change from baseline was calculated using mixed-model repeated measures adjusting for visit, initial BMI, treatment arm, gender, age (continuous), initial CD4 cells count (continuous), ART treatment duration (continuous), and interaction between treatment arm and visit, and between initial BMI and visit

Evolution of average weight changes by initial BMI and treatment arm



*Estimated mean change from baseline was calculated using mixed-model repeated measures adjusting for visit, initial BMI, treatment arm, gender, age (continuous), initial CD4 cells count (continuous), ART treatment duration (continuous), and interaction between treatment arm and visit, and between initial BMI and visit

Evolution of glycemia and lipids parameters by treatment arm



BMI classes evolution from baseline to week 96

	DTG + 3TC	ATV/r + 3TC	TDF + 3TC + EFV	Total
Underweight/Normal -> Underweight/Normal	64 (40,8)	56 (35,9)	59 (39,6)	179 (38,7)
Underweight/Normal -> Overweight	16 (10,2)	15 (9,6)	6 (4,0)	37 (8,0)
Overweight -> Overweight	29 (18,5)	43 (27,6)	33 (22,2)	105 (22,7)
Overweight -> Obese	17 (10,8)	9 (5,8)	5 (3,4)	31 (6,7)
Obese -> Obese	27 (17,2)	24 (15,4)	33 (22,2)	84 (18,2)
Reduction in BMI grade	4 (2,6)	9 (5,8)	13 (8,7)	26 (5,6)
Total	**157 (100,0)**	**156 (100,0)**	**149 (100,0)**	**462 (100,0)**

Prognostic factors associated with weight gain of more than 10% between baseline and W96: binary logistic regression

	aOR [95%CI]	P-value
Treatment arm		**0.0001**
TDF + 3TC + EFV	1.00	
ATV/r + 3TC	3.78 [1.75 - 8.19]	0.0007
DTG + 3TC	5.12 [2.4 - 10.92]	<.0001
BMI class		**0.0009**
Obese	1.00	
Underweight/Normal	5.17 [2.08 - 12.86]	0.0004
Overweight	2.84 [1.09 - 7.41]	0.0328
Gender		**0.0055**
Male	1.00	
Female	2.75 [1.35 - 5.63]	
Duration on ARV regimen		**0.0244**
>= 10years	1.00	
]5-10 years[	0.73 [0.39 - 1.38]	0.3353
<= 5years	1.83 [1.00 - 3.33]	0.0499

CONCLUSIONS

Dual therapies, particularly the DTG/3TC combination, are now recommended by the WHO in 2025 and can be used for treatment simplification in persons stables on TLD. MODERATO trial shows that switching to dual maintenance therapy without Tenofovir is non inferior to 3RDs at W96. However, we have observed that with the following prognostic factors, such as female gender, having a underweight/normal or overweight BMI, or being on ART for less than 5 years, there is a greater risk of weight gain with the switch to dual therapy. The possibility of maintaining access to 3DRs with NNRTIs in virologically controlled patients at risk of weight gain should be discussed.

ACKNOWLEDGEMENTS

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