D²EFT Body Composition Sub-study week 96 results

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Background

INSTIs have been associated with greater weight increases than other antiretrovirals. D²EFT is a multi-national trial in which HIV-infected adults with first-line NNRTI failure were randomized to an open-label second-line regimen of dolutegravir (DTG) with fixed tenofovir (TDF) plus lamivudine or emtricitabine (TDF/XTC) versus DTG + darunavir/ritonavir (DRV/r) versus standard of care DRV/r+2NRTIs. The study provided an ideal opportunity to investigate weight increases in a prospective, randomized fashion. At 96 weeks rates of viral suppression in both DTG-containing regimens of D²EFT were superior to DRV/r+2NRTIs[1].

Aims

To investigate the role of contemporary ART on body composition (total & regional [arm, leg & truncal] fat & lean tissue mass) assessed by whole-body dual-energy X-ray absorptiometry (DXA) by comparing over 96 weeks the effects of DTG+DRV/r versus DRV/r+2NRTIs versus DTG+2NRTIs on measured parameters.

Research Hypothesis

Participants randomized to either of the DTG-containing regimens will demonstrate greater changes in body composition parameters than those randomized to DRV/r+2NRTIs.

Methods

Sites with access to DXA whole-body composition analysis could participate. The study was offered to consecutive clinic patients.

Inclusion criteria

- Fulfil criteria for D²EFT randomization
- Able to undergo DXA screening

Exclusion criteria

- Unwilling to comply with study requirements

Patients consent before randomization into D²EFT & attended visits at weeks 0, 48 & 96. Body habitus & body composition measures were assessed over 96 weeks. Changes from baseline were summarized by treatment arm & compared using linear regression. Models were adjusted for age, sex, baseline CD4 cell count & baseline outcome value.

Results

Between November 2020 & December 2021, 149 participants from 6 sites in Africa & Asia were recruited. Mean baseline & body composition variables are shown in Table 1.

Table 1. Baseline characteristics of 149 participants

Characteristic	DRV/r+2NRTI (n42) (SOC)	DTG+TDF/XTC (n=61)	DTG+DRV/r (n=46)	Total (N=149)
Male‡	23 (54.8)	27 (44.3)	24 (52.2)	74 (49.7)
Age (years)	38.3 (10.4)	38.7 (8.7)	38.5 (11.8)	38.8 (9.7)
Race/ethnicity‡ Asian Black	 7 (16.7) 35 (83.3)	 9 (14.8) 51 (83.6)	 11 (23.9) 35 (76.1)	 27 (118.1) 121 (81.2)
Weight (kg)	62.3 (9.9)	62.0 (13.4)	61.5 (16.5)	61.9 (13.5)
Waist measure (cm)	82.2 (10.7)	80.4 (11.4)	80.9 (13.4)	81.0 (11.8)
Hip measure (cm)	92.0 (9.6)	93.5 (11.1)	92.0 (11.9)	92.6 (10.9)
Waist-to-hip ratio	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)
BMI (kg/m²)	23.1 (3.6)	23.3 (4.8)	22.8 (5.9)	23.1 (4.9)
ART duration (years)	7.1 (3.8)	6.9 (4.2)	6.4 (4.6)	6.8 (4.2)
Thymidine use‡ Past Current	 9 (21.4) 2 (4.8)	 13 (21.4) 1 (1.6)	 3 (6.5) (0.0)	 25 (16.8) 4 (6.5)
HIV RNA (copies/mL)	148,134 (646,941)	50,890 (109,710)	228,150 (953,707)	133,026 (635,417)
CD4 cell count (mm³)	266 (248)	289 (201)	312 (237)	290 (225)
Limb fat (kg)	23 (54.8)	27 (44.3)	24 (52.2)	74 (49.7)
Trunk fat (kg)	38.3 (10.4)	38.7 (8.7)	38.5 (11.8)	38.8 (9.7)
Total body fat (kg)	19.1 (7.7)	19.8 (9.5)	20.8 (17.2)	19.9 (11.9)
Total lean mass (kg)	40.8 (6.6)	39.5 (6.6)	39.4 (10.4)	39.8 (7.9)
Total BMD g/cm ²	2.3 (0.4)	2.2 (0.4)	2.2 (0.5)	2.2 (0.4)

Values are mean (standard deviation); ‡ are n(%)

At week 96, mean(SD) weight had increased 3.8kg (5.4) for SOC, 5.4kg (6.8) for DTG+TDF/XTC & 7.1kg (5.4) for DTG+DRV/r/; mean(SD) BMI had increased 1.4kg/m² (2.0), 2.1kg/m² (2.6) & 2.7kg/m² (2.1), respectively (Table 2).

Table 2. Change from baseline to week 96 in body habitus parameters

Parameter	DRV/r+2NRTIs	DTG+TDF/XTC	DTG+DRV/r	Overall
Weight (kg)	3.8 (5.4)	5.4 (6.8)	7.1 (5.4)	5.5 (6.1)
BMI (kg/m²)	1.4 (2.0)	2.1 (2.6)	2.7 (2.1)	2.1 (2.3)
Waist measure (cm)	4.1 (6.4)	6.3 (7.4)	6.4 (5.5)	5.7 (6.7)
Hip measure (cm)	3.3 (5.9)	4.8 (5.7)	4.6 (9.3)	4.3 (7.0)
Waist-to-hip ratio	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)

Values are mean (standard deviation)

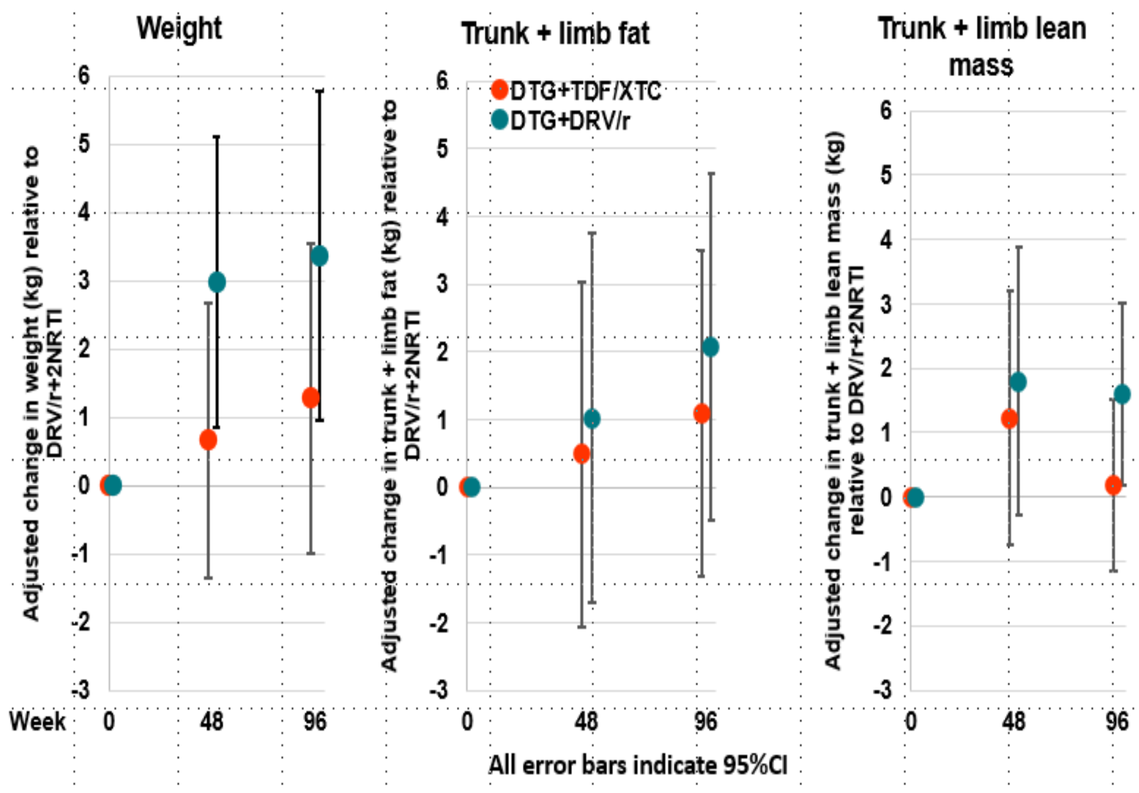
Adjusted changes in body habitus & body composition parameters at 96 weeks are shown in Table 3 & Figure 1. Compared to DRV/r+2NRTIs, mean changes in weight & BMI were greater with DTG+DRV/r (3.4kg [95%CI 1.0, 5.8]; p=0.006) & (1.3kg/m² [95%CI 0.4, 2.2]; p=0.004), respectively but did not differ significantly with DTG+TDF/XTC.

Table 3. Adjusted changes in body habitus & body composition parameters at week 96

Parameter	DTG+TDF/XTC	DTG+DRV/r
Weight (kg)	1.28 (-0.99, 3.54), 0.27	3.37 (0.96, 5.77), 0.006
BMI (kg/m²)	0.58 (-0.26, 1.42), 0.17	1.33 (0.43, 2.22), 0.004
Waist measure (cm)	1.54 (-0.86, 3.95), 0.21	2.3 (-0.25, 4.85), 0.077
Hip measure (cm)	1.42 (-1.36, 4.20), 0.31	1.27 (-0.69, 4.22) 0.40
Limb fat (kg)	1.08 (-0.19, 2.36), 0.10	1.09 (-0.27, 2.46), 0.12
Trunk fat (kg)	0.09 (-1.34, 1.51), 0.90	1.02 (-0.05, 2.54), 0.19
Total body fat (kg)	1.16 (-1.28, 3.59), 0.35	0.42 (-2.18, 3.02),0.75
Total lean mass (kg)	0.40 (-1.12, 1.91), 0.61	1.99 (0.38, 3.60), 0.16
Total limb + trunk fat (kg)	1.09 (-1.32, 3.49), 0.37	2.07 (-0.49, 4.63) 0.112
Total limb + trunk lean (kg)	0.18 (-1.16, 1.51), 0.79	1.59 (0.17, 3.00), 0.03

All values are presented as co-efficient (95% CI), p value & are adjusted for age, sex, baseline CD4 & baseline outcome value. Reference group is DRV/r+2NRTIs.

Figure 1. Adjusted changes from baseline in weight & body composition measures



Conclusions

The greater increases in weight in the DTG-containing arms relative to the DRV/r+2NRTIs arm are consistent with previous clinical data. However, there is really no clear pattern that this is limb mass versus trunk mass or limb fat versus limb lean mass. New strategies to counter the tendency to weight gain with these highly effective & robust DTG-containing regimens are required.

References

1. D²EFT: Dolutegravir & darunavir in adults failing therapy 96-week results. AS-AIDS-2024 -05785.