

Switching from Combivir [CBV] (AZT/3TC) to Truvada [TVD] (TDF/FTC) Preserves Limb Fat: Results of a DEXA Sub-Study of a 48 Week Randomised Study

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Background

- Dual nucleosides/tides remain the backbone of HAART regimens
- Thymidine analogues (both d4T and AZT) have been associated with lipoatrophy and are not recommended as initial therapy^{1,2}
- Switching from a thymidine analogue to tenofovir in individuals with lipoatrophy is associated with an improvement in limb fat³ and maintenance of virological control^{3,4}
- The management of patients currently suppressed on AZT without lipoatrophy is not established

Figure 1. Results from Studies of Limb Fat Change with Tenofovir-Based Regimens

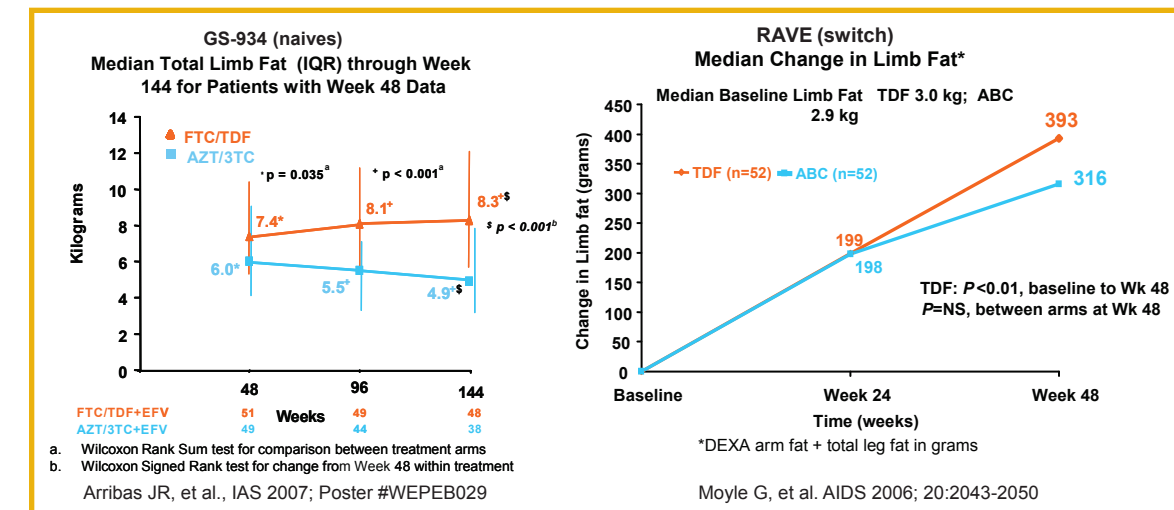
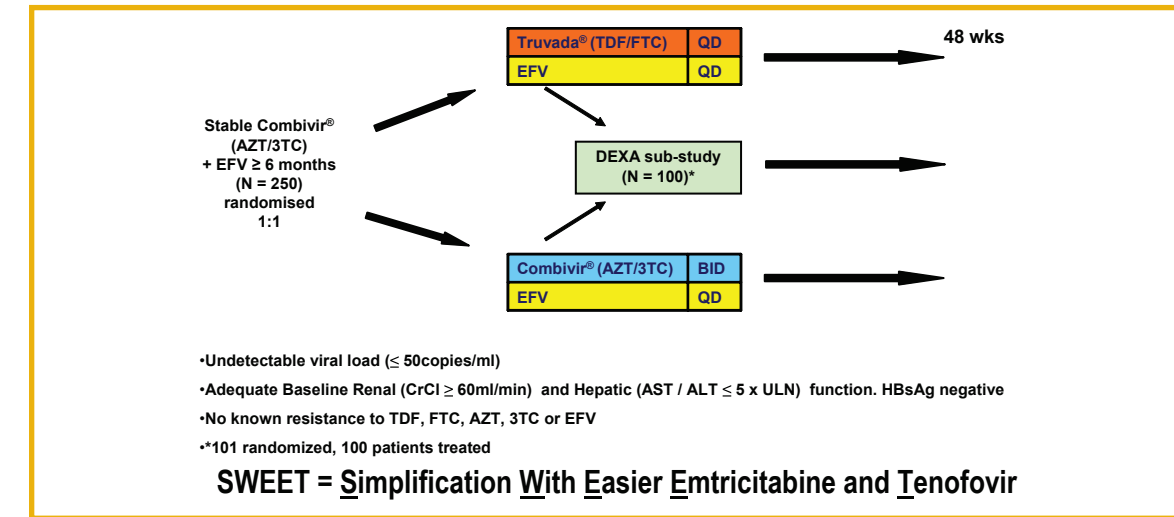


Figure 2. SWEET Study Design



Objectives

- DEXA Sub-study:**
- To assess whether therapy simplification with Truvada[®] leads to improved fat recovery and fat sparing relative to AZT-based therapy
 - To assess whether there is a change in bone mineral density (BMD) in the lumbar spine and pelvic parameters with Truvada compared to AZT-based therapy
- Total Study Group:**
- To assess the renal safety of Truvada compared to AZT-based therapy
 - To compare the immunological and virological outcomes for patients in the total study group

Methods

- 48 week multicentre, prospective, open label, randomised (1:1) study
- 24 sites in UK and Ireland
- 234 subjects enrolled and received at least one dose of study drug
- All subjects in specific centres were given the option to participate in the DEXA sub-study at screening
- Subjects in this analysis had paired Baseline and Week 48 assessments
- No requirement for clinical signs of lipoatrophy

Results

Table 1. Baseline Characteristics^a

	All Subjects		DEXA Sub-Study	
	Truvada [®]	Combivir [®]	Truvada [®]	Combivir [®]
Number of subjects	117	117	46	54
Median age in yrs (IQR)	41 (36,48)	42 (36,49)	43 (37,47)	42 (36,50)
Race				
Black	36 (31%)	44 (38%)	9 (20%)	13 (24%)
White	77 (66%)	68 (58%)	36 (78%)	39 (72%)
Other	4 (3%)	5 (4%)	1 (2%)	2 (4%)
Gender				
Male	101 (86%)	96 (82%)	41 (89%)	47 (87%)
HIV RNA				
< 50 copies/ml	112 (96%)	109 (93%)	43 (93%)	51 (94%)
< 400 copies/ml	115 (98%)	111 (95%)	44 (96%)	52 (96%)
Median CD4 count (c/mm ³) (IQR)	413 (313, 534)	393 (300, 539)	439 (320, 534)	413 (322, 618)
Median BMI (kg/m ²) (IQR)	23.8 (21.7, 25.6)	24.5 (22.3, 27.2)	24.1 (21.8, 25.2)	24.7 (22.4, 27.2)
Median Limb Fat (kg) (IQR)			4.90 (3.41, 7.23)	4.82 (3.95, 6.85)
Median years prior AZT (IQR)	2.9 (2.2, 4.5)	3.4 (1.9, 4.5)	2.9 (2.2, 4.3)	2.9 (1.8, 4.5)
Prior D4T use	18 (15%)	8 (7%)	11 (24%)	2 (4%)

a. Treated (TRT) analysis set

Figure 3. Subject Disposition at Week 48

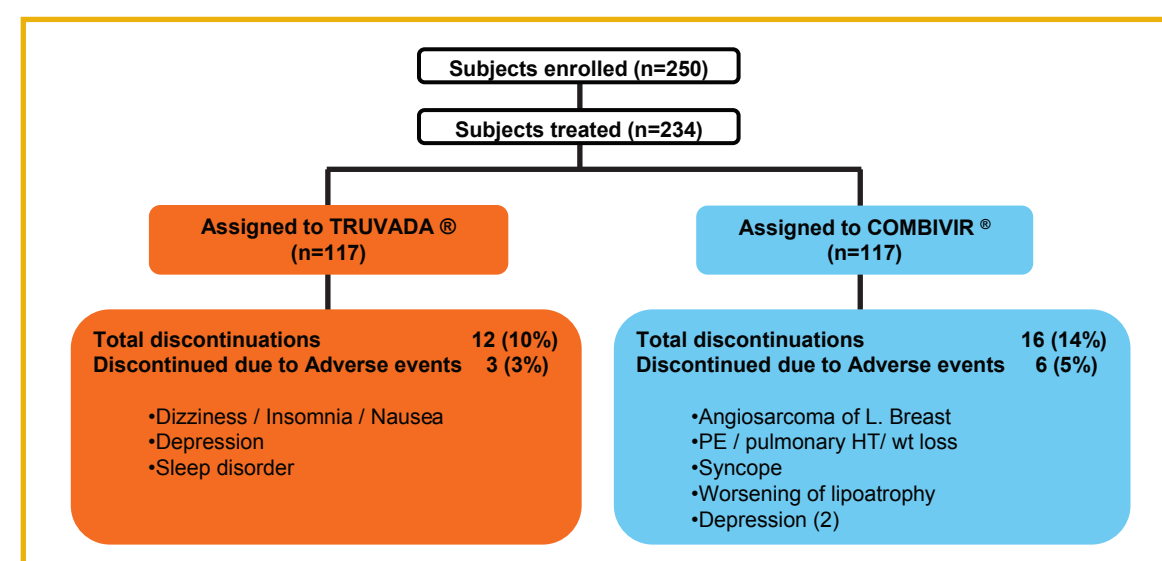
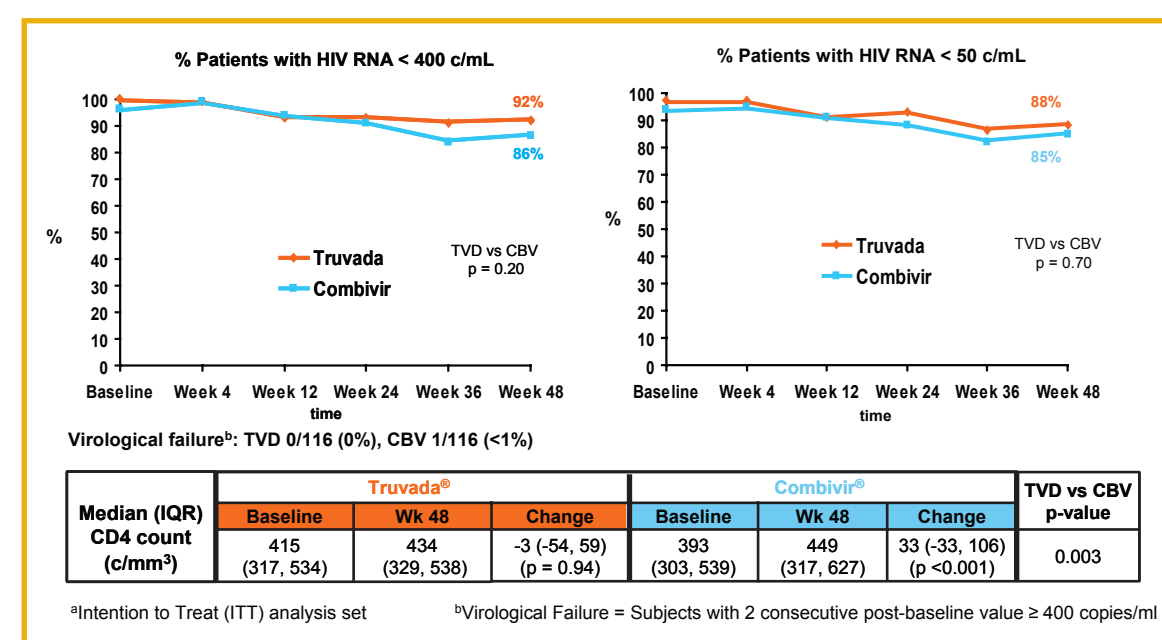


Figure 4. Viral Suppression^a and CD4 Change at Week 48



^aIntention to Treat (ITT) analysis set

^bVirological Failure = Subjects with 2 consecutive post-baseline value ≥ 400 copies/ml

Figure 5. Median Total Limb Fat (kg) and Median Whole Body Fat (kg): Week 48 Change from Baseline

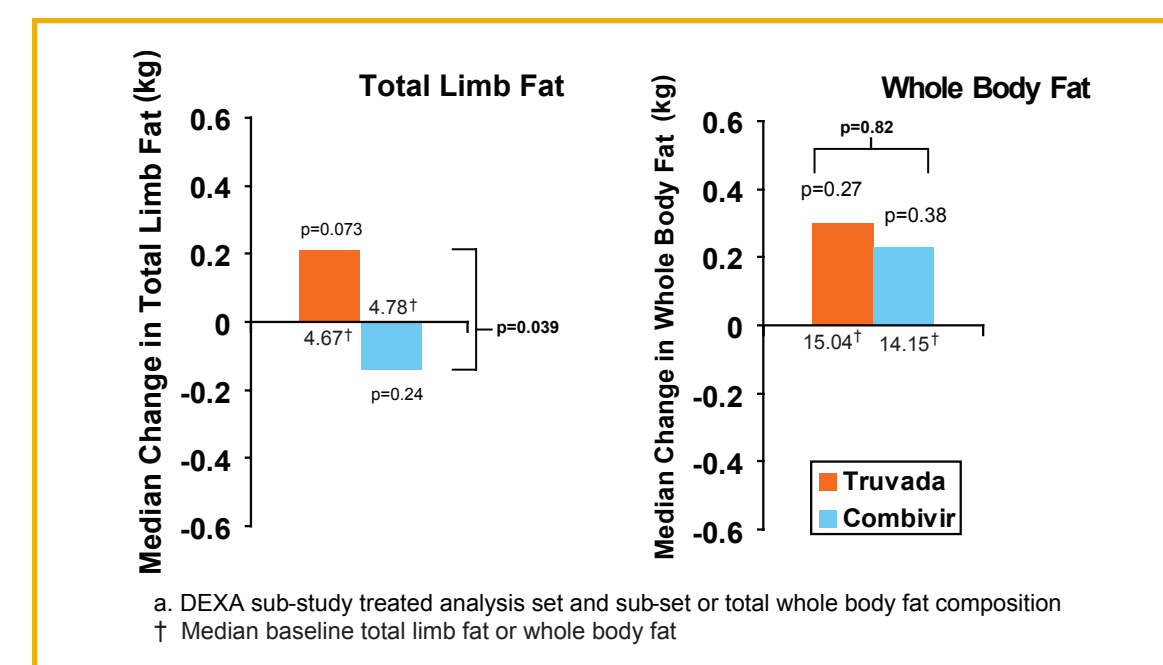


Figure 6. Effect of Previous AZT Exposure on Total Limb Fat^a

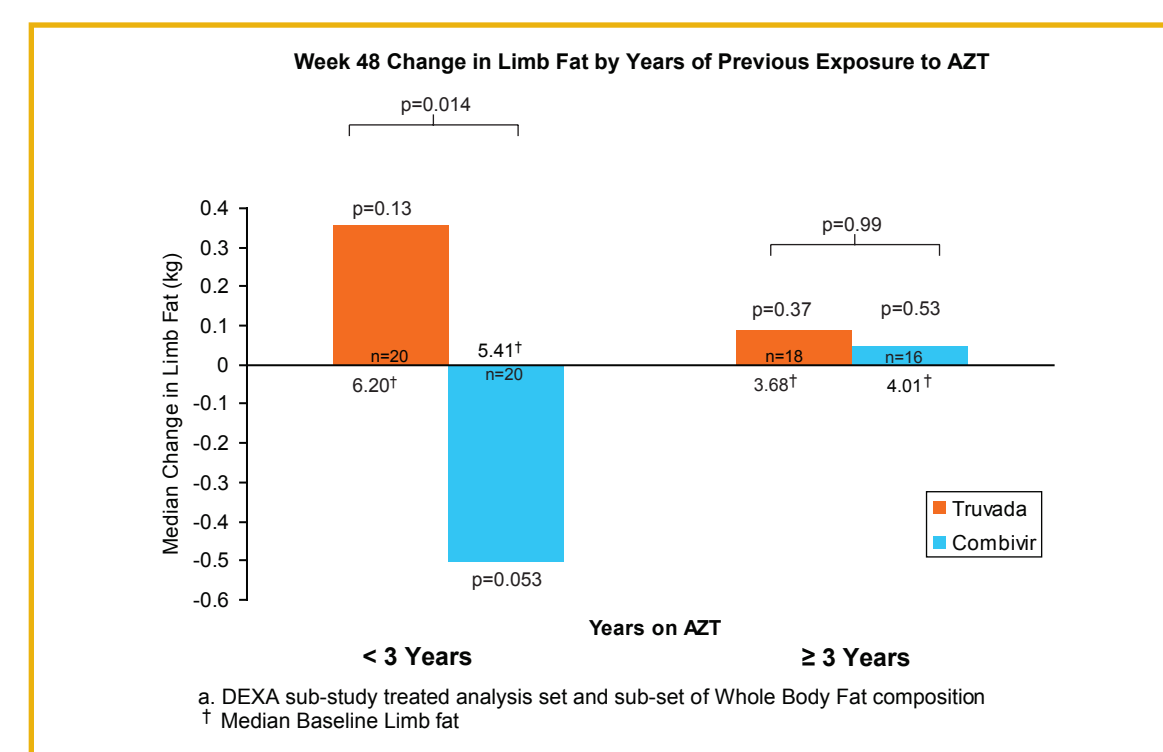
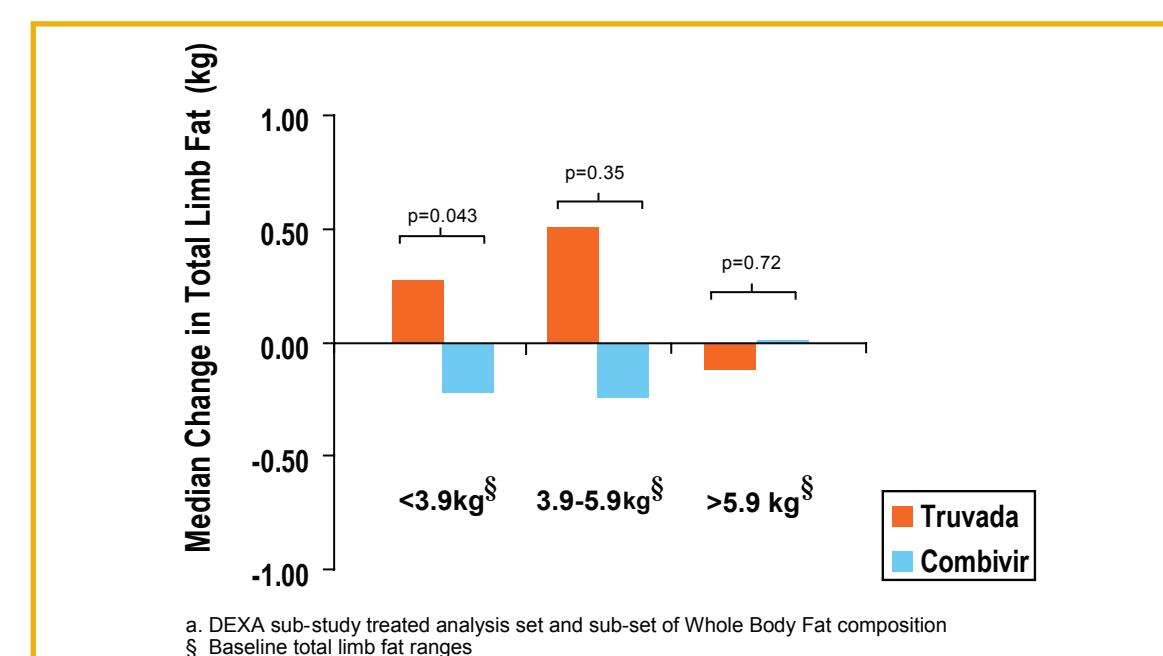


Figure 7. Effect of Baseline Total Limb Fat on Change in Total Limb Fat at Week 48^a



a. DEXA sub-study treated analysis set and sub-set of Whole Body Fat composition

§ Baseline total limb fat ranges

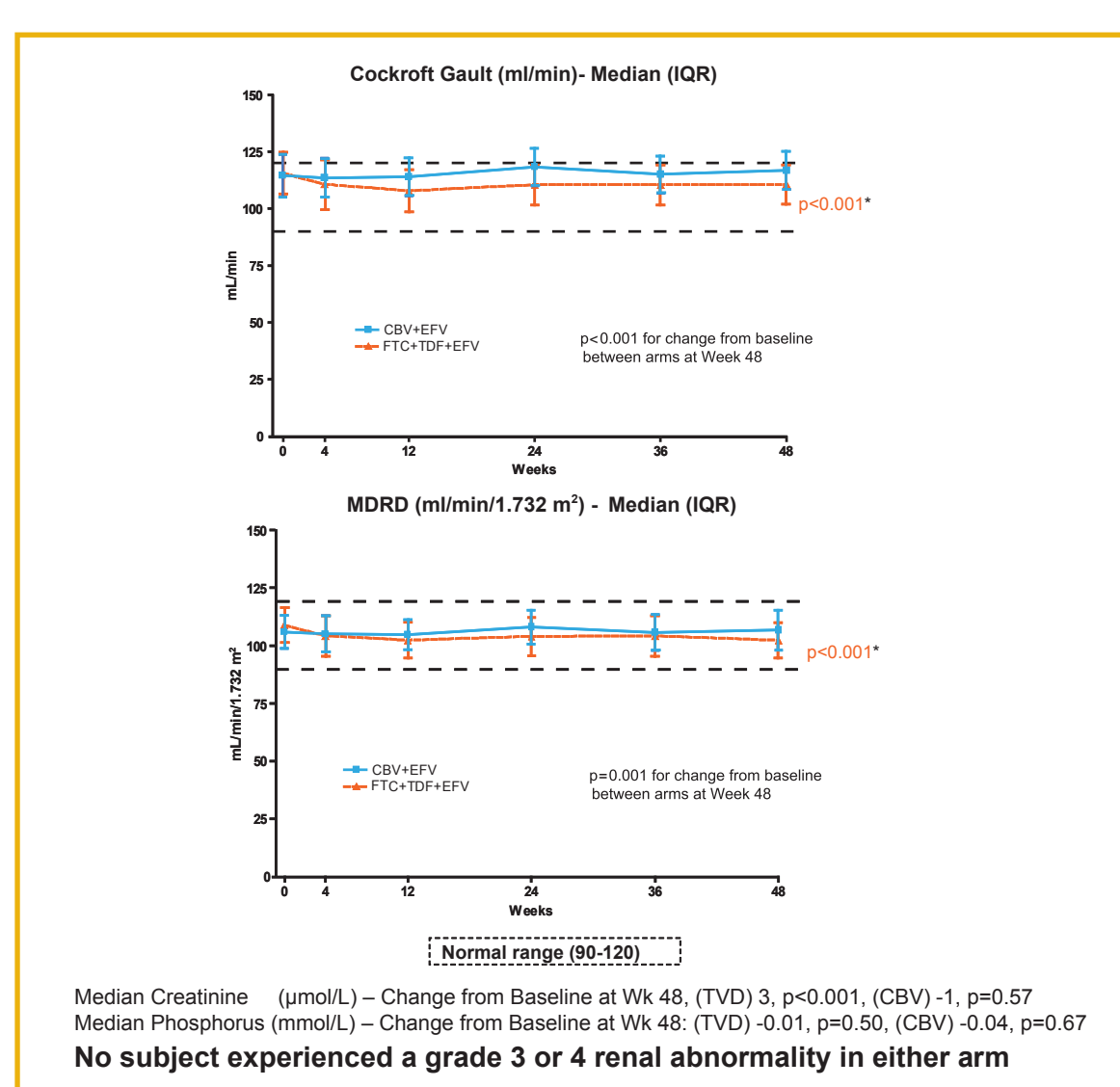
Table 2. Median (IQR) BMD (g/cm²)^a

	Baseline		Wk 48		Change		% Change	
	Truvada [®]	Combivir [®]	Truvada [®]	Combivir [®]	Truvada [®]	Combivir [®]	Truvada [®]	Combivir [®]
Pelvic								
Truvada [®] n=38	1.141 (1.079, 1.258)	1.159 (1.111, 1.258)	1.142 (1.067, 1.267)	1.187 (1.098, 1.296)	-0.008 (-0.039, 0.015) (p = 0.14)	-0.032 (-0.027, 0.034) (p = 0.63)	-0.617 (-3.650, 1.447) (p=0.16)	-0.232 (-2.252, 3.023) (p=0.51)
Combivir [®] n=36								
P-values TVD vs CBV At 48 Wks					0.19	0.16		
Lumbar								
Truvada [®] n=38	1.024 (0.956, 1.161)	1.085 (1.028, 1.191)	1.064 (0.940, 1.156)	1.096 (1.005, 1.246)	-0.024 (-0.052, 0.067) (p = 0.96)	-0.001 (-0.029, 0.081) (p = 0.45)	-2.172 (-4.402, 6.923) (p=0.83)	-0.073 (-2.343, 7.922) (p=0.37)
Combivir [®] n=36								
P-values TVD vs CBV At 48 Wks					0.36	0.32		

a. DEXA sub-study treated analysis set

- Over the study period there were no significant change in lumbar spine or pelvic BMD
- Lumbar Spine BMD correlates with Hip BMD⁵
- The lack of significant lumbar spine BMD changes from baseline in the DEXA sub-study group suggests that patients did not have an increased relative risk of fracture due to study drugs at 48 weeks

Figure 8. Renal Function - Median eGFR by Cockcroft Gault & MDRD



Median Creatinine (µmol/L) – Change from Baseline at Wk 48, (TVD) 3, p<0.001, (CBV) -1, p=0.57

Median Phosphorus (mmol/L) – Change from Baseline at Wk 48: (TVD) -0.01, p=0.50, (CBV) -0.04, p=0.78

No subject experienced a grade 3 or 4 renal abnormality in either arm

^aWeek 48 change from baseline in FTC+TDF+EFV arm

Conclusions

Switching from Combivir[®] to Truvada[®] in persons receiving EFV:

- Maintains virological control
- Preserves limb fat and leads to limb fat recovery – Earlier switch results in greater limb fat increase
- Preserves bone mineral density
- Preserves renal function

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Acknowledgements

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