

# Lipid Changes in a Randomised, 48-week, Open Label Comparative Study of Tenofovir DF vs. Abacavir as Substitutes for a Thymidine Analog in Persons with Lipoatrophy: The RAVE Study

G Moyle<sup>1</sup>, C Sabin<sup>2</sup>, J Cartledge<sup>3</sup>, M Johnson<sup>2</sup>, E Wilkins<sup>4</sup>, D Churchill<sup>5</sup>, P Hay<sup>6</sup>, A Fakoya<sup>7</sup>, M Murphy<sup>8</sup>, G Scullard<sup>9</sup>, C Leen<sup>10</sup>, and G Reilly<sup>11</sup> for the RAVE study

<sup>1</sup>Chelsea and Westminster Hosp, London; <sup>2</sup>Royal Free & UC Medical School, London; <sup>3</sup>Camden PCT, London; <sup>4</sup>North Manchester Hosp; <sup>5</sup>Lawson Unit Royal Sussex County Hosp; <sup>6</sup>St Georges Hosp, London; <sup>7</sup>Newham General, London; <sup>8</sup>St Barts & The London; <sup>9</sup>St Mary's Hosp, London; <sup>10</sup>Western General Hosp, Edinburgh; <sup>11</sup>Gilead Sciences, UK

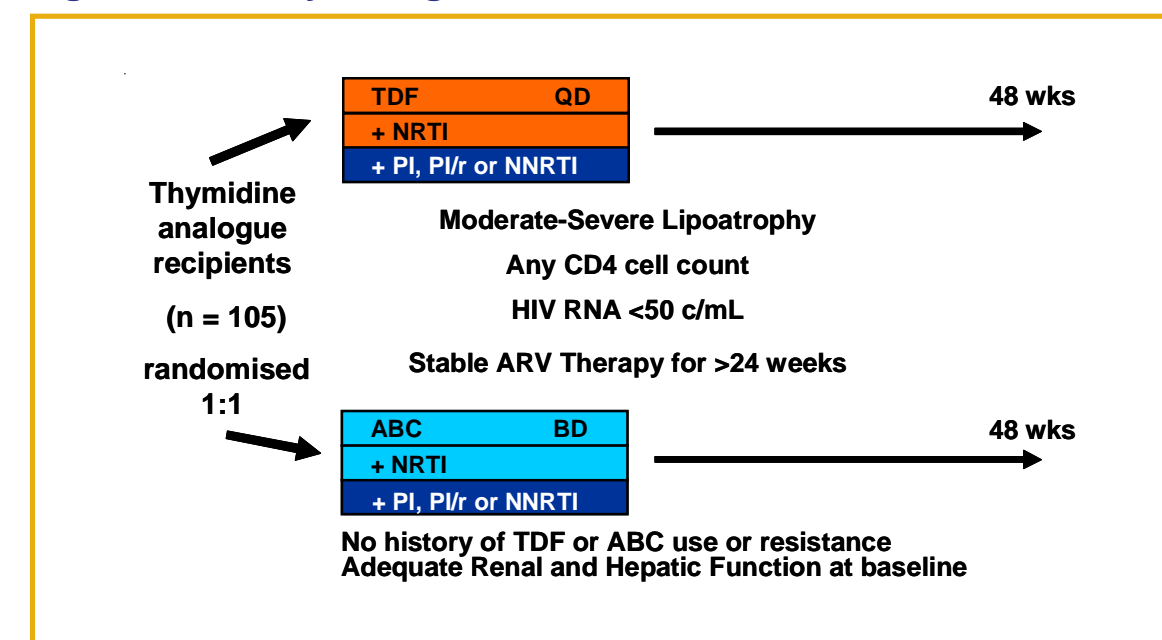


Gilead Sciences, Inc.  
333 Lakeside Drive  
Foster City, CA 94404  
Tel: (650)574-3000  
Fax: (650)578-9264

## Background

- Thymidine analog therapy is associated with peripheral fat loss and dyslipidemia
- Duration of exposure to HAART has been associated with increased risk of CV disease. This may, in part, be mediated through ART-associated dyslipidemia
- In initial treatment regimens tenofovir DF (TDF) is associated with smaller changes in total cholesterol and triglycerides than either d4T or AZT
- The lipid profile of abacavir (ABC) relative to thymidine analogs has not been well characterised

Figure 1. Study Design



## Methods

- Trial endpoints: change in total limb fat mass (by DEXA) and lipids from baseline to 48 weeks
- Changes in lipids were approximately normally distributed
- Changes in values over 48 weeks were tested for significance using paired t-tests; the changes in the two treatment groups were compared using unpaired t-tests
- Analyses of changes in lipids were based on all values as measured, disregarding any information on the use of lipid-lowering therapy
- All analyses were performed on an intention-to-treat basis. Missing values were imputed using a last-observation-carried-forward approach

Table 1. Baseline Characteristics

	TDF (n = 52)	ABC (n = 53)
Male sex	94%	87%
White race	85%	83%
Median age (years)	42	43
Nadir CD4 (median, IQR)	114 (0, 818)	154 (2, 783)
Current CD4 (median, IQR)	522 (314, 724)	478 (340, 653)
Years on ART (median, IQR)	5.7 (0.8, 11.5)	4.9 (0.8, 8.1)
Current PI-sparing regimen	63%	74%
Current thymidine analog		
d4T	77%	59%
AZT	23%	41%

Table 2. Baseline Metabolics (Median)

	TDF (n = 52)	ABC (n = 53)
Total Cholesterol [mg/dL](mmol/L)	216.2 (5.6)	204.6 (5.3)
HDL-C [mg/dL](mmol/L)	50.2 (1.3)	50.2 (1.3)
LDL-C [mg/dL](mmol/L)	127.4 (3.3)	115.8 (3.0)
Triglycerides [mg/dL](mmol/L)	177.0 (2.0)	150.5 (1.7)
Insulin (IU/l)	8.8	7.2
Fasting Glucose [mg/dL](mmol/L)	91.9 (5.1)	93.7 (5.2)
Lactate [mg/dL](mmol/L)	13.5 (1.5)	11.7 (1.3)

Table 3. Patient Disposition through Week 48

	TDF (n = 52)	ABC (n = 53)
<b>N (%) discontinued study</b>	3 (6%)	8 (15%)
Lost to follow-up	-	1 (2%)
Patient withdrew consent	1 (2%)	2 (4%)
Protocol violation	-	2 (4%)
Adverse event	1 (2%)	3 (6%) <sup>a</sup>
Other	1 (2%)	-
<b>Median time to discontinuation (weeks, range)</b>	36 (4, 39)	19 (1.6, 40)

a. All discontinuations due to adverse events in ABC group were due to hypersensitivity reaction, TDF related discontinuation was secondary to diarrhoea

## Results

Figure 2. Median Change in Limb Fat DEXA arm fat + total leg fat in grams (ITT M = F analysis)

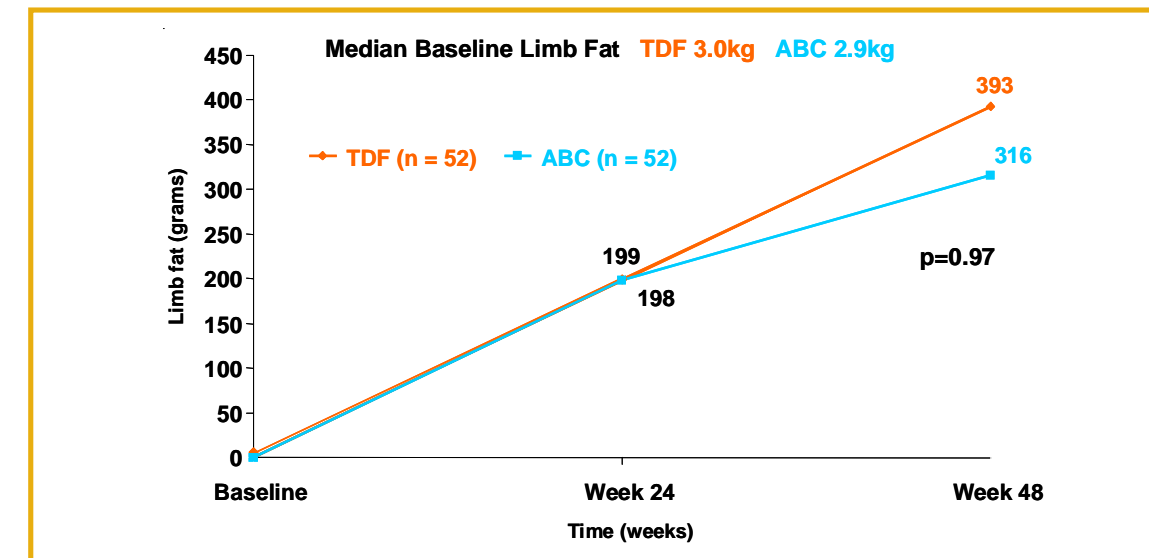


Figure 3. Median Changes at Week 48 in Limb Fat by Baseline Characteristics

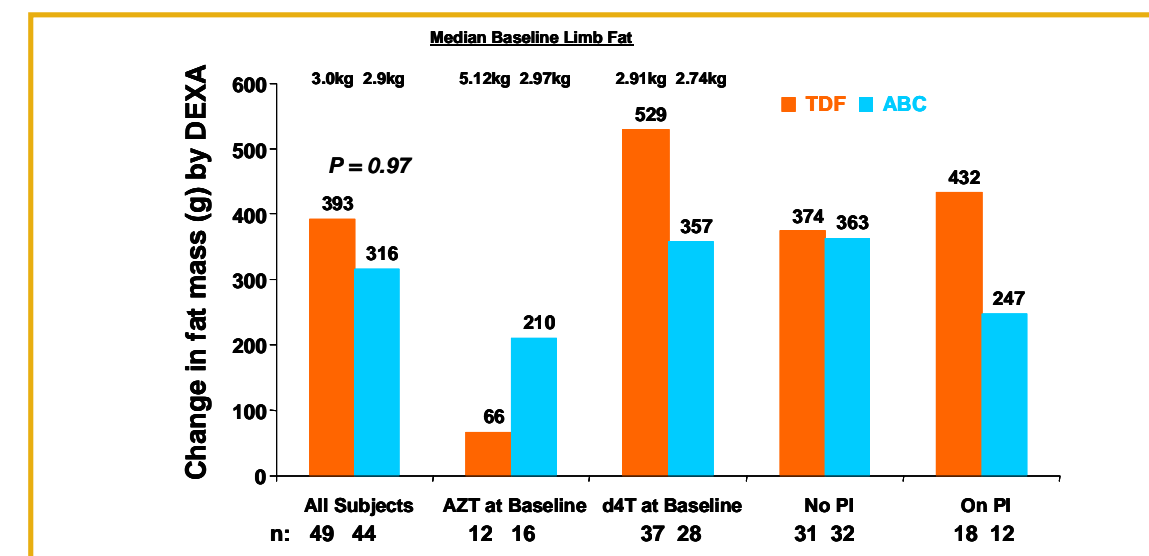
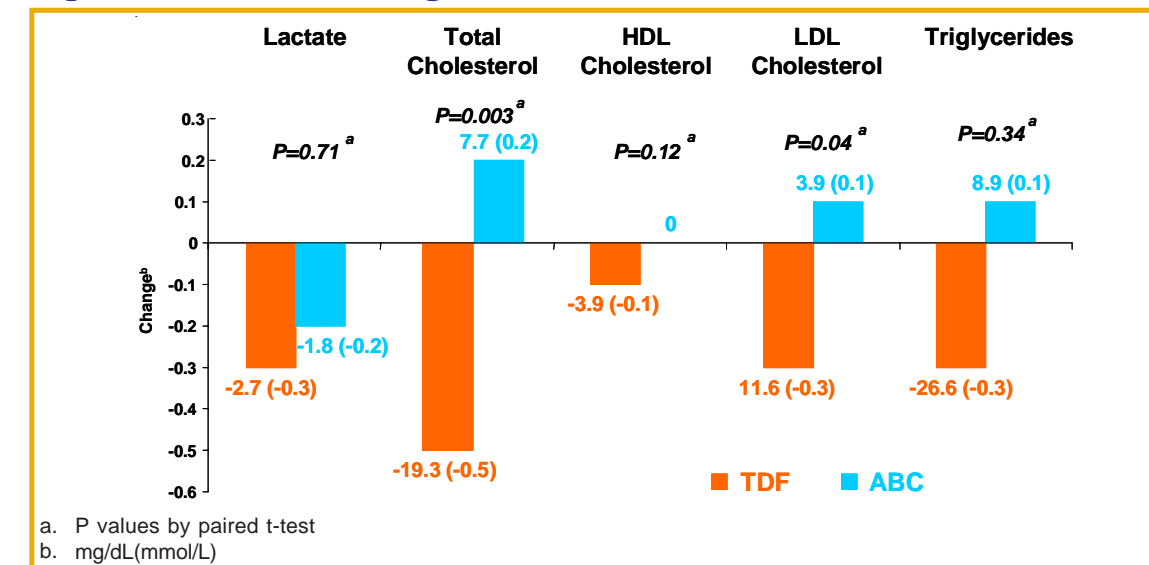


Figure 4. Mean Change in Metabolic Outcomes to Week 48



- All individuals included. Lipid lowering therapy commenced during study for TDF n=1, at 273 days, ABC n=8, at median 91.5 days
- Includes fasting and non-fasting samples. Observations are similar when only fasting samples are included

Figure 5. Mean Fasting Cholesterol (mmol/L) by Baseline Thymidine Analog

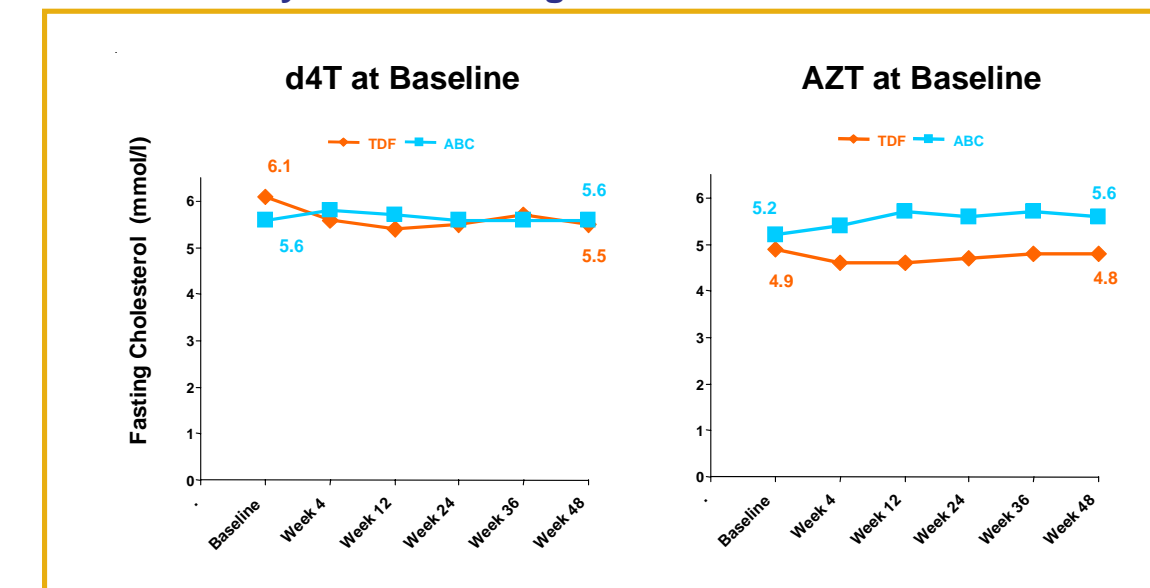


Figure 6. Mean Fasting LDL-c (mmol/L) by Baseline Thymidine Analog

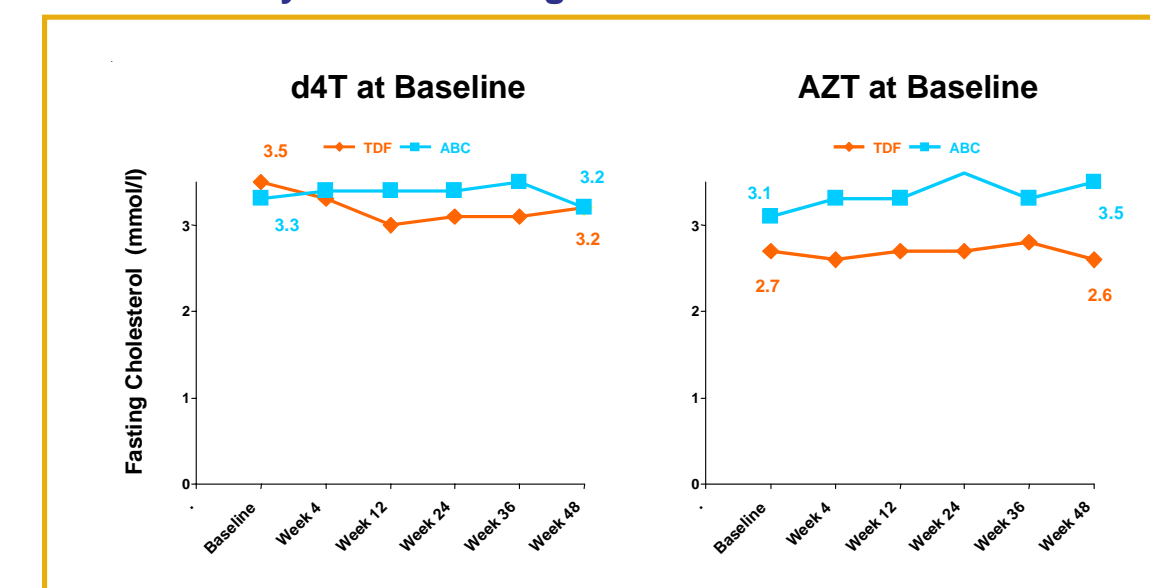


Figure 7. Mean Fasting HDL-c (mmol/L) by Baseline Thymidine Analog

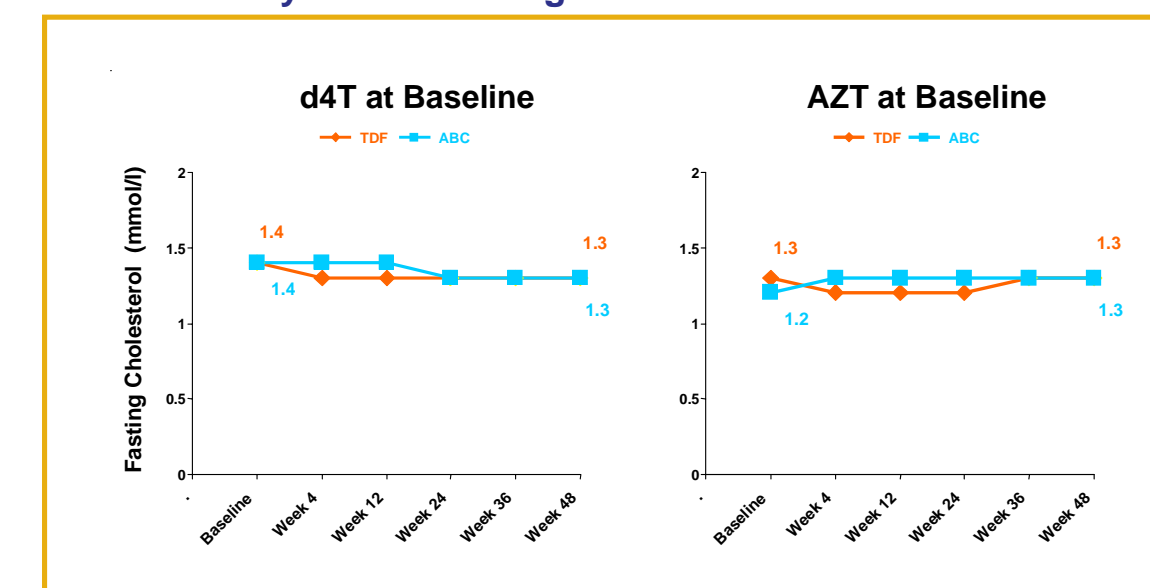
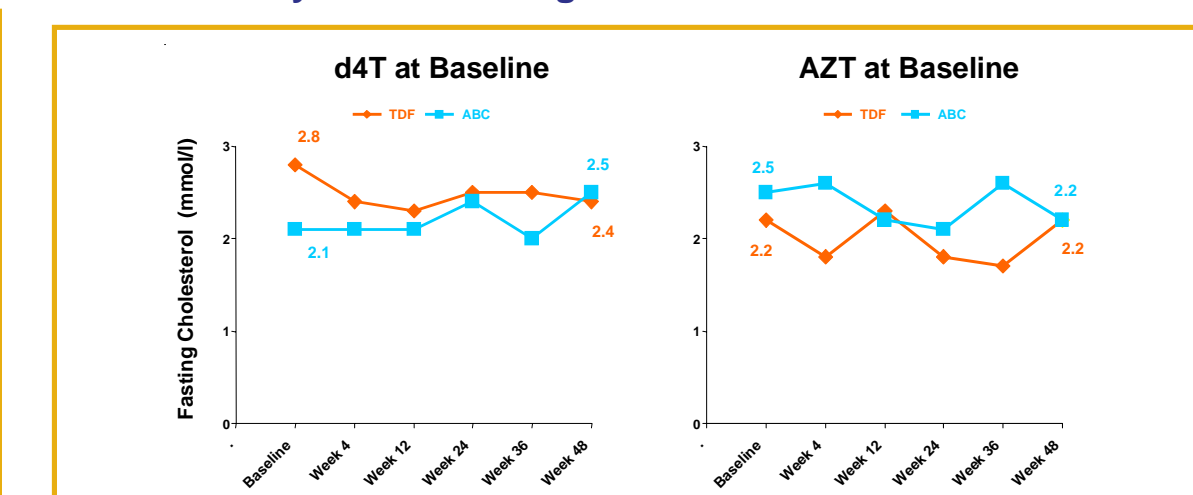
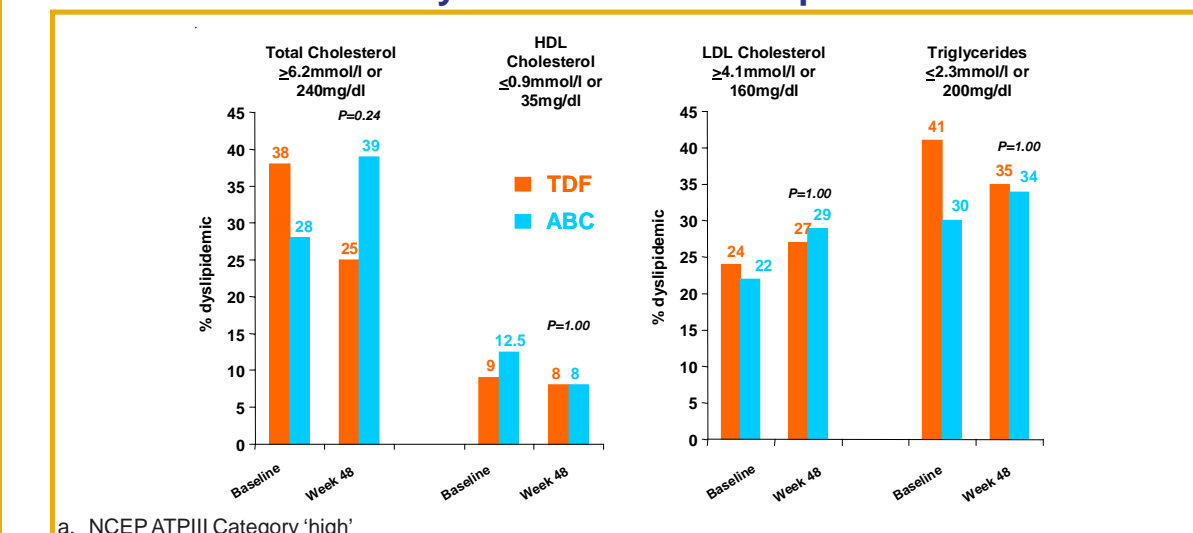


Figure 8. Mean Fasting Triglycerides (mmol/L) by Baseline Thymidine Analog



- All data LOCF. All individuals included. Lipid lowering therapy commenced during study for TDF n=1, at 273 days, ABC n=8, at median 91.5 days
- Includes fasting and non-fasting samples. Observations are similar when only fasting samples are included

Figure 9. RAVE: % Patients with Dyslipidemia<sup>a</sup> at Baseline and Week 48 by Randomized Group



## Conclusions

- TDF and ABC similarly allow restoration of limb fat over 48 weeks when switching from thymidine analogs in persons with lipoatrophy
- Lipid changes favored the TDF arm. Fewer TDF patients initiated lipid lowering therapy
- Baseline lipids were generally higher in the d4T arm
- Falls in total cholesterol and TGs were predominately seen in individuals on d4T at baseline