A Randomized Comparison of Continued Zidovudine Plus Lamivudine BID (AZT/3TC) versus Switching to Tenofovir DF Plus Emtricitabine (FTC/TDF) each plus Efavirenz (EFV) in Stable HIV Infected Persons: 48 Week Study - Results of a Planned 24 Week Analysis

Poster Number
WEPEB028
4th International AIDS Society Conference on HIV Pathogenesis, Treatment, and Prevention
July 22-25, 2007
Sydney, Australia

G Moyle,[1] M Fisher,[2] and the SWEET Study Group[3]

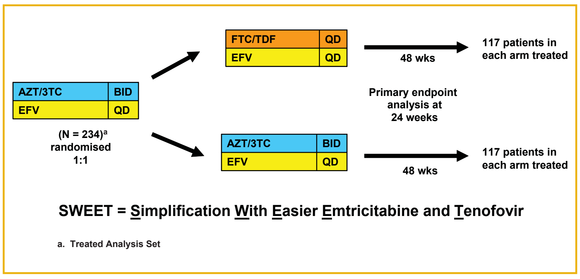
[1]Chelsea and Westminster Hospital, London, UK; [2]Brighton and Sussex University Hospitals, UK

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

Background

- Long-term success with antiretroviral therapy requires maintenance of adherence and avoidance of long term toxicities
- Comparative data suggests FTC/TDF provides at least similar virological control to AZT/3TC but with lower observed rates of haematological and metabolic adverse events[1]
- We sought to investigate if these benefits were observed when FTC/TDF was used to replace AZT/3TC

Figure 1. SWEET Study Design



Objectives

- Primary Objective:
  - To determine if switching from AZT/3TC to FTC/TDF leads to changes in absolute haemoglobin at 24 weeks
- Secondary Objectives:
  - To determine if switching from AZT/3TC to FTC/TDF leads to:
    - An improvement in lipid profile or a delay in the time to lipid elevation
    - Delays the time to treatment failure by improving virological efficacy, durability and safety
  - To compare the immunological and virological outcomes for patients

Methods

- Key inclusion criteria:
  - HIV+ subjects with viral loads < 50 c/mL on last 2 consecutive testings and < 400 copies/ml for ≥ 3 months
  - Subjects maintained on stable antiretroviral therapy consisting of EFV given with AZT/3TC for at least 6 months
  - Concomitant lipid lowering therapy permitted if stable for ≥ 12 weeks prior to Baseline and remain stable throughout study
- Analysis Methods:
  - Analysis of Hb at Wk 24 utilises last observation carried forward (LOCF)
  - Hb and all other tests are summarized for Treated Analysis Set (Subjects who took at least one dose of study drug)
  - Viral load (M=F) and CD4 are summarized for ITT analysis set (excluding any subjects in All Treated set who had BL viral load > 1,000 c/mL)
  - LDL-c calculated Friedewald's Formula:
    LDL-c (when TG < 400 mg/dL) = Total Cholesterol – HDL-c – TG/5

Results

Table 1. Baseline Characteristics[a]

	FTC/TDF	AZT/3TC
Number of subjects	117	117
Age (yrs) - Mean (Range)	42 (20,69)	42 (24,72)
Race		
Asian	3 (3%)	4 (3%)
Black	36 (31%)	44 (38%)
White	77 (66%)	68 (58%)
Other	1 (< 1%)	1 (< 1%)
Sex		
Male	101 (86%)	96 (82%)
Female	16 (14%)	21 (18%)
HIV RNA		
< 50 copies/ml	112 (96%)	109 (93%)
< 400 copies/ml	115 (98%)	111 (95%)
Mean Body Mass Index (kg/m²)	24	25
Years on AZT – Median (q1, q3)	2.9 (2.2, 4.5)	3.4 (1.9, 4.5)

a. Treated Analysis Set

Table 2. Selected Haematological Parameters: Week 24 - Change from Baseline[a]

	Baseline		Wk 24 – Change from Baseline[a]		FTC/TDF vs AZT/3TC p-value
	FTC/TDF	AZT/3TC	FTC/TDF	AZT/3TC	
Hb (g/dL) - Mean LOCF[a,b]	14.4	14.0	0.46 (p < 0.001)	0.10 (p = 0.19)	< 0.001
MCV (fL) - Median[b]	112	110	-19 (p < 0.001)	0 (p = 0.49)	< 0.001
WBC (x10⁹/L) - Median[b]	4.66	4.43	0.24 (p < 0.001)	0.16 (p = 0.13)	0.17
Platelet Count (x10⁹/L) - Median[b]	260	250	-13 (p < 0.001)	0 (p = 0.95)	0.012
CD4 (cells/µL) - Median[c]	415	393	-8 (0.51)	21 (0.28)	0.20

a. LOCF: Last Observation Carried Forward; paired t-test for within group and two sample t-test for between group comparison are used. Only one subject had a history of Erythropoietin (for anemia due to chronic illness) more than 10 month prior to screening for the study.
b. Treated Analysis Set
c. ITT Analysis Set
Note: P-values are from Wilcoxon signed rank test for within group (change from baseline) and Wilcoxon Rank Sum test for between groups

Results (cont'd)

Figure 2. Haemoglobin: Week 24 - Change from Baseline[a]

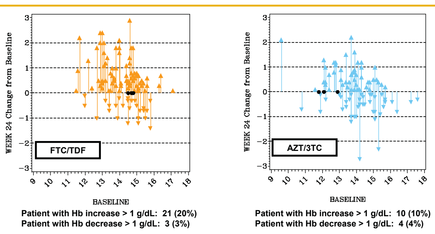


Table 3. Metabolic Parameters: Median (IQR) Baseline & Week 24[a,b]

		FTC/TDF			AZT/3TC		
		N	(mmol/L)	(mg/dL)	N	(mmol/L)	(mg/dL)
Total Cholesterol	BL	108	5.47 (4.72, 6.18)	212 (183, 239)	105	5.08 (4.53, 6.03)	196 (175, 233)
	Wk 24	106	5.13 (4.29, 5.83)	198 (166, 225)	100	5.04 (4.46, 5.81)	195 (172, 225)
Calculated LDL-c	BL	101	3.25 (2.53, 3.79)	126 (98, 147)	101	2.99 (2.59, 3.62)	116 (100, 140)
	Wk 24	100	2.88 (2.35, 3.80)	111 (91, 147)	98	2.94 (2.44, 3.60)	114 (94, 139)
HDL-c	BL	108	1.31 (1.08, 1.61)	51 (42, 62)	105	1.30 (1.13, 1.56)	50 (44, 60)
	Wk 24	104	1.29 (1.07, 1.53)	50 (41, 59)	100	1.28 (1.07, 1.55)	49 (4, 60)
Triglycerides	BL	108	1.60 (1.05, 2.56)	142 (93, 227)	105	1.32 (1.01, 2.26)	117 (89, 200)
	Wk 24	106	1.36 (0.84, 2.16)	120 (74, 191)	100	1.58 (1.04, 2.20)	140 (92, 195)

a. Treated Analysis Set, Fasted
b. Metabolic Parameters: Median (IQR) Baseline & Week 24

Figure 3. Metabolic Parameters: Week 24 - Median Change from Baseline[a]

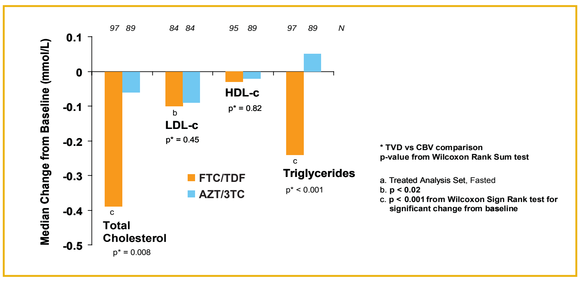


Figure 4. Total Cholesterol: Week 24 - Change from Baseline[a]

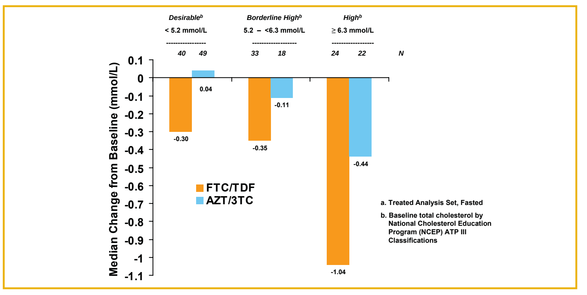


Table 4. Viral Suppression[a]

HIV-1 RNA at Week 24	FTC/TDF N=116	AZT/3TC N=116	FTC/TDF vs AZT/3TC p-value[b]
< 50 copies/mL	108 (93%)	102 (88%)	0.26
≥ 50 copies/mL	0 (0%)	3 (3%)	
Early discontinuation	6 (5%)	10 (9%)	
Missing	2 (2%)	1 (<1%)	
By Week 24			
Treatment Failure[c]	7/116 (6%)	16/116 (14%)	0.077
Virologic Failure[d]	0/115 (0%)	4/112 (4%)	0.058

a. ITT Analysis Set
b. Fisher's Exact test
c. Treatment Failure: 2 consecutive values ≥ 50 copies/ml OR an early discontinuation within 24 weeks OR last observed post-baseline value ≥ 50 copies/ml followed by lost to follow-up
d. Virologic Failure: 2 consecutive values ≥ 50 copies/ml

Conclusions

- **Switching from AZT/3TC to FTC/TDF in persons receiving EFV:**
  - **Improves haemoglobin levels**
  - **Improves key lipid parameters**
  - **Maintains virological control**

References

1. Gallant JE, DeJesus E, Arribas JR, Pozniak AL, Gazzard B, Campo RE, et al. Tenofovir DF, emtricitabine, and efavirenz vs. zidovudine, lamivudine, and efavirenz for HIV. N Engl J Med 2006;354 (3):251-60.

ACKNOWLEDGEMENTS:

[3]The SWEET Study Group:

J Ainsworth (North Middlesex, London), J Anderson (Homerton University, London), G Brook (Central Middlesex, London), A de Burgh Thomas (Gloucester Royal), S Das (Coventry & Warwickshire), J Dhar (Leicester Royal Infirmary), M Fisher (Brighton & Sussex University), R Fox (Gartnavel General), V Harindra (St. Mary's, Portsmouth), P Hay (St. Georges, London), M Johnson (Royal Free, London), M Kapembwa (Northwick Park, London), M Kingston (Manchester Royal Infirmary), N Larbalestier (St. Thomas's, London), C Leen (Western General, Edinburgh), R Maw (Royal Victoria, Belfast), G Moyle (Chelsea & Westminster, London), F Mulcahy (St. James's, Dublin), E Ong (Newcastle General), C Orkin (Barts & Royal London), M Shahmanesh (Selly Oak, Birmingham), D White (Birmingham Heartlands), E Wilkins (North Manchester General), I Williams (University College London), Gilead Sciences Limited, Cambridge.