SWIFT: Switching from Lamivudine/Abacavir to Emtricitabine/Tenofovir Improved Lipids While Maintaining Virologic Suppression in Older HIV Subjects

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Background

- DHHS[1] and IAS-USA[2] guidelines list FTC/TDF as the preferred NRTI backbone and 3TC/ABC as an alternative backbone
- In prior treatment naïve and experienced studies, use of FTC/TDF has been associated with less virologic failure[3,4], a favorable lipid profile[3-6], and no increased MI risk[7] compared to 3TC/ABC
- These guidelines and published studies may prompt clinicians to consider switching virologically stable patients from 3TC/ABC to FTC/TDF
- However, there are limited data on the impact of switching from 3TC/ABC to FTC/TDF, particularly in older HIV+ subjects
- The SWIFT study was designed as a head-to-head switch study to evaluate this approach to treatment

Endpoints

Primary Endpoint

- Proportion of subjects with HIV-1 RNA < 200 c/mL through Week 48 based on TLOVR (virologic failure, premature discontinuation for any reason, ARV modifications = TLOVR failure)

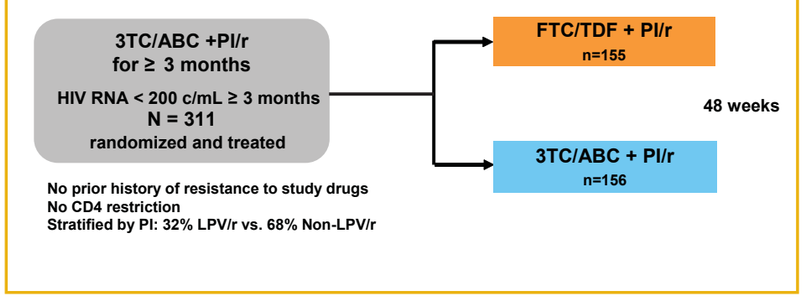
Secondary Endpoints

- Proportion who experienced virologic failure with HIV-1 RNA ≥ 200 c/mL through Week 48 (defined as confirmed HIV-1 RNA ≥ 200 c/mL, or last on-study HIV-1 RNA ≥ 200 c/mL)
- Change from baseline in CD4 cell count at Week 48
- Safety and tolerability through Week 48
- Change from baseline in GFR by Cockcroft Gault and MDRD at Week 48
- Change from baseline in fasting lipid parameters (TC, LDL, HDL, TG, and TC/HDL ratio) at Week 48

Methods

- Prospective, open-label, multicenter, randomized, Phase 4, 48-week study conducted in Canada, Puerto Rico, and the United States
- The FTC/TDF arm would be declared non-inferior to the 3TC/ABC arm if the lower bound of the 95% CI of the difference in TLOVR response rates (FTC/TDF –3TC/ABC) was greater than −12%
- Virologic failure (VF) was estimated by Kaplan Meier product limit method and Log-Rank test was used for detecting treatment differences through Week 48

Figure 1. Study Design



Results

Table 1. Baseline Characteristics

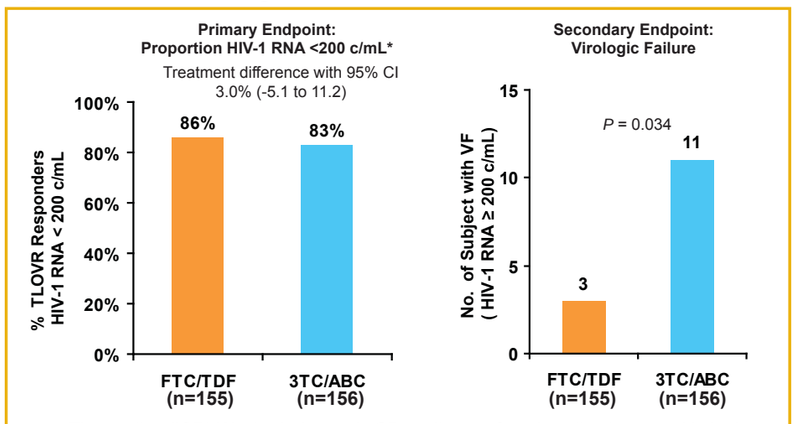
Characteristic	FTC/TDF n=155	3TC/ABC n=156
Age, median (IQR), years	46 (22 - 66)	46 (22 - 75)
Male gender, n (%)	129 (83)	134 (86)
Race, n (%)		
White	96 (62)	106 (68)
African American	43 (28)	44 (28)
HIV RNA c/mL, n (%)		
<50	139 (90)	145 (93)
50 to < 200	13 (8)	10 (6)
200 to < 400	2 (1)	1 (1)
≥ 400	1 (1)	0
Time since first ARV therapy, median (IQR), years	4 (2.5, 6.9)	3.7 (2.5, 6.7)
CD4 cell count, median (IQR), cells/mm³	532 (354, 725)	532 (382, 728)
Lipid modifying agent, n (%)	67 (43)	80 (51)
Comorbidities, n (%)	108 (70)	116 (74)

Table 2. Baseline Characteristics by Age

Characteristics	FTC/TDF		3TC/ABC	
	≥ 50 Years (n = 60)	< 50 Years (n = 95)	≥ 50 Years (n = 53)	< 50 Years (n =103)
Age, mean (range), years	55 (50 – 66)	41 (22 – 49)	57 (50 – 75)	41 (22 – 49)
Male gender, n (%)	51 (85)	78 (82)	44 (83)	90 (87)
Race, n (%)				
White	39 (65)	57 (60)	38 (72)	68 (66)
African American	19 (32)	24 (25)	14 (26)	30 (29)
HIV RNA c/mL, n (%)				
<50	56 (93)	83 (87)	51 (96)	94 (91)
50 to < 200	2 (3)	11 (12)	2 (4)	8 (8)
200 to < 400	1 (2)	1 (1)	0	1 (1)
> 400	1 (2)	0	0	0
CD4 cell count, median (IQR), cells/mm³	492 (294, 669)	538 (376, 769)	567 (421, 757)	523 (357, 712)
Lipid modifying agent, n (%)	32 (53)	35 (37)	34 (64)	46 (45)
Comorbidities, n (%)	51 (85)	57 (60)	47 (89)	69 (67)

Results (cont'd)

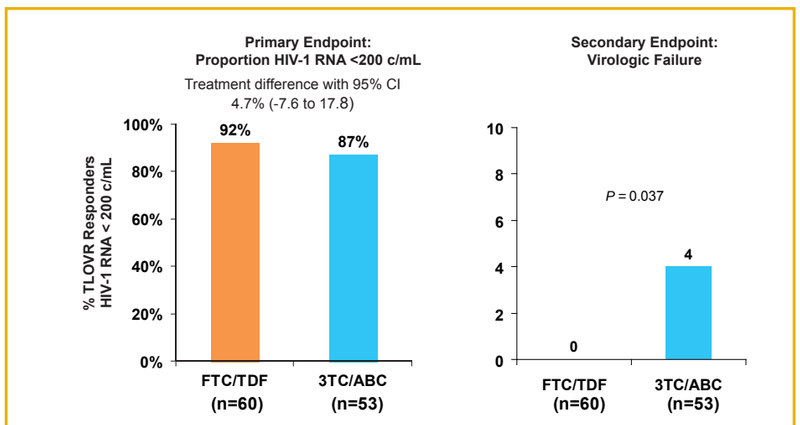
Figure 2. TLOVR, Virologic Failure, and CD4 Count through Week 48



- The median (IQR) Week 48 change in CD4 cell count from baseline increased in both arms, by 8 (-49, 80) cells/mm³ with FTC/TDF and 39 (-41, 125) cells/mm³ with 3TC/ABC (*P* = 0.10 for comparison between treatment groups)

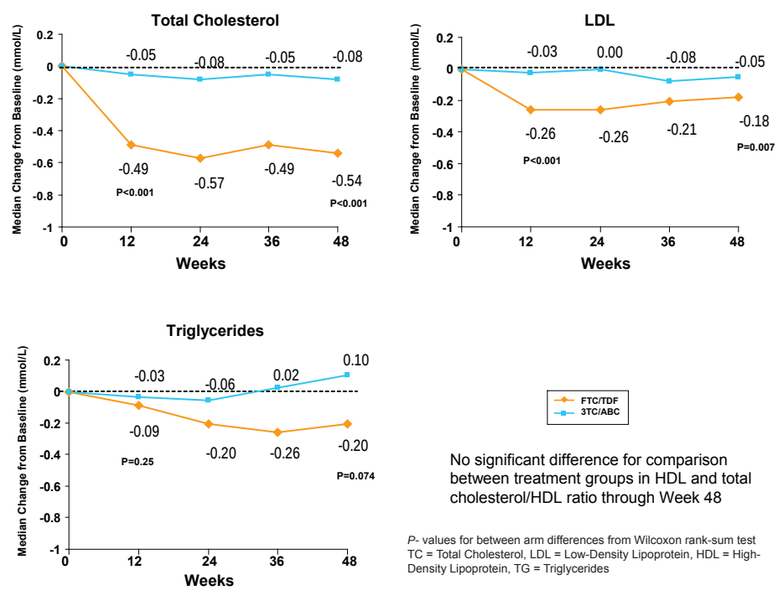
*TLOVR failure includes: virologic failure, premature discontinuation for any reason, ARV modifications

Figure 3. TLOVR, Virologic Failure, and CD4 Count through Week 48 for Subjects ≥ 50 Years



- In subjects ≥ 50, the median (IQR) Week 48 change in CD4 cell count from baseline increased in both arms, by 27 (-31, 77) cells/mm³ with FTC/TDF and 38 (-62, 146) cells/mm³ with 3TC/ABC (*P* = 0.54 for comparison between treatment groups)
- Discontinued study prematurely, n (%): age ≥ 50 years: 10 (8.8); age < 50 years: 24 (12.1)

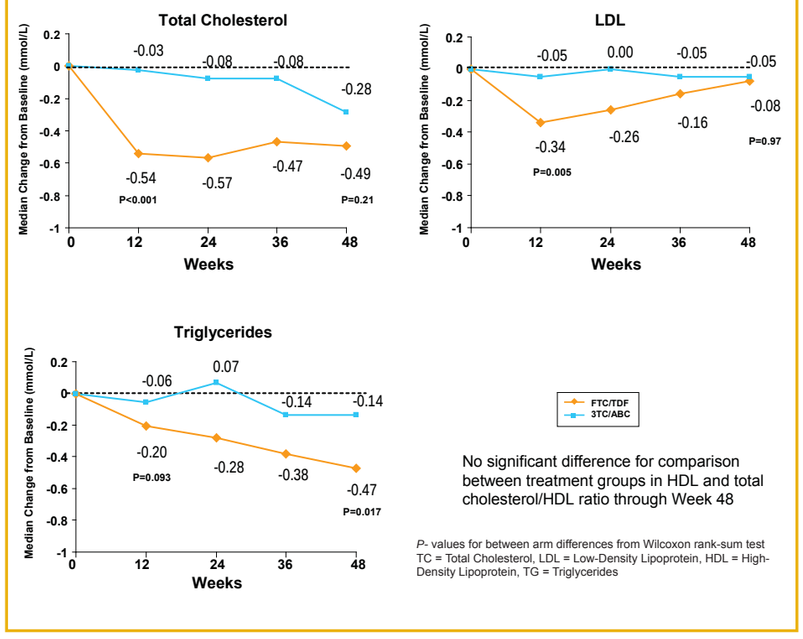
Figure 4. Change from Baseline in Lipids through Week 48 All Subjects



No significant difference for comparison between treatment groups in HDL and total cholesterol/HDL ratio through Week 48

P- values for between arm differences from Wilcoxon rank-sum test
TC = Total Cholesterol, LDL = Low-Density Lipoprotein, HDL = High-Density Lipoprotein, TG = Triglycerides

Figure 5. Change from Baseline in Lipids through Week 48 in Subjects ≥ 50 Years



No significant difference for comparison between treatment groups in HDL and total cholesterol/HDL ratio through Week 48

P- values for between arm differences from Wilcoxon rank-sum test
TC = Total Cholesterol, LDL = Low-Density Lipoprotein, HDL = High-Density Lipoprotein, TG = Triglycerides

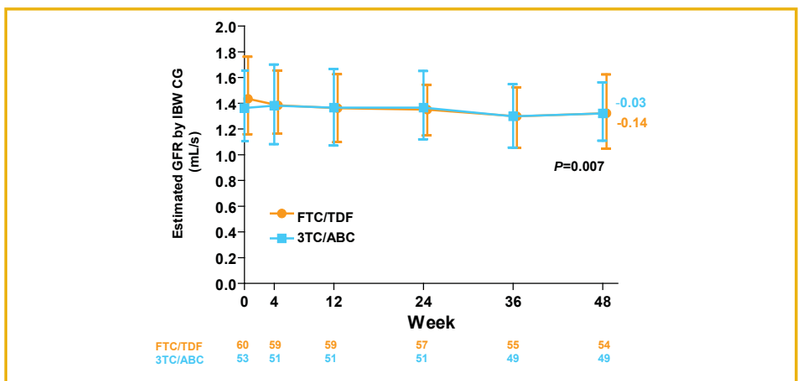
Table 3. Change from Baseline in CHD Risk by Framingham Score at Week 48

CHD Risk by 10-Year Framingham Score	FTC/TDF	3TC/ABC
Overall	n = 138	n = 136
Mean (SD)	-1.2 (4.39)	-0.3 (4.00)
P-value*	0.006	0.40
≥ 50 years	n = 60	n = 53
Mean (SD)	-2.1 (5.46)	-1.1 (5.62)
P-value*	0.008	0.18
< 50 years	n = 95	n = 103
Mean (SD)	-0.5 (3.42)	0.1 (2.74)
P-value*	0.18	0.69

**P* -values for comparison from baseline to Week 48 within treatment arms

- No significant difference for comparison between treatment groups in CHD risk by Framingham score

Figure 7. Renal Function by eGFR through 48 Weeks for Subjects ≥ 50 Years



- < 50 years: eGFR is -0.14 mL/s in FTC/TDF and -0.11 mL/s in 3TC/ABC (*P* = 0.21)
- Overall population: eGFR is -0.14 mL/s in FTC/TDF and -0.08 mL/s in 3TC/ABC (*P* = 0.012)

Plotted median at each visit; *P*-values for comparison between treatment groups on change from baseline to Week 48 are from Wilcoxon Rank-Sum test

Table 4. Adverse Events Summary

	FTC/TDF n=155 n (%)	3TC/ABC n=156 n (%)
Number of subjects with any treatment-emergent AE	112 (72)	120 (77)
≥ 50 years*	46 (77)	43 (81)
< 50 years‡	66 (70)	77 (75)
All Grades of Treatment-emergent AEs Reported for ≥ 5% of Patients		
Upper Respiratory Tract Infection	14 (9)	14 (9)
Diarrhea	13 (8)	11 (7)
Headache	8 (5)	5 (3)
Cough	8 (5)	8 (5)
Grade 3 or 4 AE	13 (8)	16 (10)
≥ 50 years*	5 (8)	9 (17)
< 50 years‡	8 (8)	7 (7)
Grade 3 or 4 AE related to Study Drug	1 (1)	0
Serious AE	12 (8)	11 (7)
AE Leading to Study Drug Discontinuation	7 (5)	3 (2)
Renal events*	1	1
Death†	1	2
Other‡	5	0

*≥ 50 years: n = 113; FTC/TDF (n = 60); 3TC/ABC (n = 53);
‡< 50 years: n = 198; FTC/TDF (n = 95); 3TC/ABC (n = 103);
**Renal events: One 52-year old subject discontinued FTC/TDF due to elevation in Cr from 1.0 to 1.3 mg/dl; One 53-year old subject discontinued 3TC/ABC due to renal failure/dehydration
†Deaths: FTC/TDF arm 1 suicide; 3TC/ABC arm 1 homicide, 1 lymphoma;
ΨOther: Multiple CNS symptoms and rash; malaise and lower baack pain; decreased weight; cellulitis and streptococcal sepsis; and rash

Conclusions

In older HIV+ population ≥ 50 years old, switching to FTC/TDF from 3TC/ABC through Week 48:

- **Maintains virologic suppression and is non-inferior**
- **Results in less virologic failure and similar increases in CD4 count**
- **Results in numerically lower total cholesterol and significantly lower median triglycerides**
  - **With a rapid decline by Week 12 in total cholesterol, LDL, and triglycerides**
- **Improves 10-year Framingham CHD risk category in those who switched to FTC/TDF**
- **Shows lower eGFR in both arms, statistically greater in the FTC/TDF arm, but no difference in discontinuations due to renal adverse events**
- **Is safe and well tolerated with similar adverse events**

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