SWIFT Study: Switching from Lamivudine/Abacavir (3TC/ABC) to Emtricitabine/ Tenofovir DF (FTC/TDF) Based Regimen Improves Lipid Parameters While Maintaining Virologic Suppression

E DeJesus,[1] RE Campo,[2] F Bredeek,[3] H Wang,[4] L Dau, J Flaherty,[4] and TA Fralich[4]

[1]Orlando Immunology Ctr, Orlando, FL, USA; [2]Univ of Miami Sch of Med, Miami, FL, USA;
[3]Metropolis Med, San Francisco, CA, USA; [4]Gilead Sciences, Inc., Foster City, CA, USA

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GILEAD

Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404
Tel: (650) 522-1864
email: lauren.dau@gilead.com

Background

- DHHS[1] and IAS-USA[2] guidelines list FTC/TDF as the preferred NRTI backbone and 3TC/ABC as an alternative backbone; EACS[3] guidelines recommends both agents for antiretroviral-naïve subjects
- ACTG 5202[4] demonstrated shorter time to virologic failure in subjects with high viral load (>100,000 c/mL) and BICOMBO[5] showed more virologic failures while on 3TC/ABC compared to FTC/TDF
- Subjects in treatment-naive and -experienced studies (ACTG 5202, BICOMBO, ROCKET I, and ROCKET II) experienced lipid benefits on FTC/TDF compared to 3TC/ABC[4-7]
- These guidelines and published studies may prompt clinicians to consider switching virologically stable patients from 3TC/ABC to FTC/TDF
- 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)

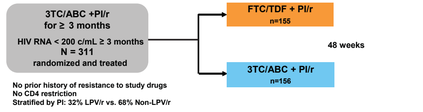
Secondary Endpoints

- 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



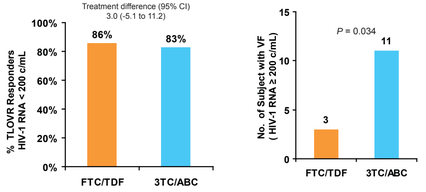
	LPV/r	ATV+RTV	FPV+RTV 100mg	FPV+RTV 200mg	DRV+RTV
FTC/TDF	48/155 (31%)	62/155 (40%)	22/155 (14%)	12/155 (8%)	9/155 (6%)
3TC/ABC	53/156 (34%)	60/156 (38%)	12/156 (8%)	19/156 (12%)	11/156 (7%)

Results

Table 1. Baseline Characteristics

Characteristic	FTC/TDF n=155	3TC/ABC n=156
Age, median (IQR), years	46 (40, 52)	46 (41, 53)
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)

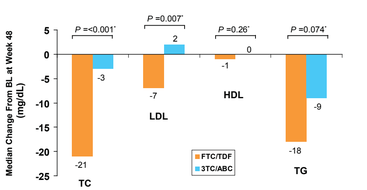
Figure 2. Virologic Response through Week 48



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

- 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/FTC (*P*=0.10 for between group comparison)

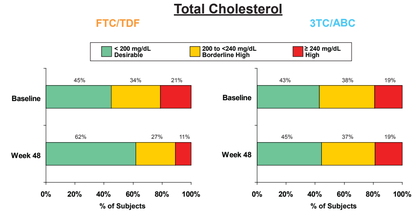
Figure 3. Change from Baseline in Fasting Lipids at Week 48



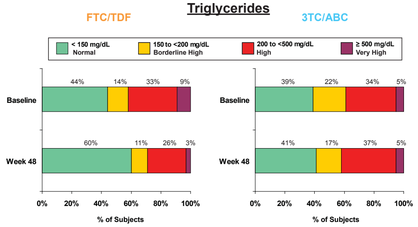
No significant difference between groups in total cholesterol/HDL ratio at Week 48

*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 4. Fasting TC and TG by NCEP Classification[8]



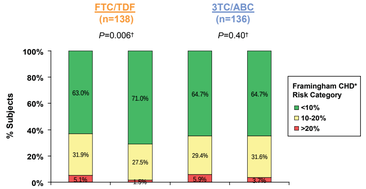
- At baseline, no difference in distribution across Total Cholesterol NCEP categories comparing FTC/TDF and 3TC/ABC (*P* = 0.92)
- At Week 48, statistically significant difference in distribution across Total Cholesterol NCEP categories comparing FTC/TDF and 3TC/ABC (*P* = 0.005)



- At baseline, no difference in distribution across Triglyceride NCEP categories comparing FTC/TDF and 3TC/ABC (*P* = 0.91)
- At Week 48, statistically significant difference in distribution across Triglyceride NCEP categories comparing FTC/TDF and 3TC/ABC (*P* = 0.003)

No difference in LDL, HDL, TC:HDL ratio

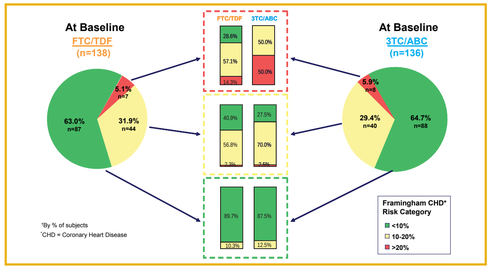
Figure 5. Change in 10-Year CHD* Risk Category by Framingham Score



No difference in median change from baseline between treatment arms (*P*=0.22‡)

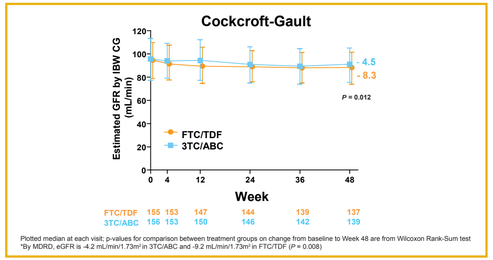
*CHD = Coronary Heart Disease
†P-value from Wilcoxon signed-rank test for within group comparison on Framingham score
‡P-value from Wilcoxon rank-sum test for between group comparison on Framingham score

Figure 6. Categorical Shifts by Framingham Scores from Baseline to Week 48†



†By % of subjects
*CHD = Coronary Heart Disease

Figure 7. Renal Function by eGFR* through 48 Weeks



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
*By MDRD, eGFR is -4.2 mL/min/1.73m² in 3TC/ABC and -9.2 mL/min/1.73m² in FTC/TDF (*P* = 0.008)

Table 3. 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)
All Grades of Treatment-emergent AEs Reported for ≥ 5% of Patients		
Diarrhea	13 (8)	11 (7)
Headache	8 (5)	5 (3)
Cough	8 (5)	8 (5)
Grade 3 or 4 AE	13 (8)	16 (10)
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

*Renal events: One subject discontinued FTC/TDF due to elevation in Cr from 1.0 to 1.3 mg/dl; One subject discontinued 3TC/ABC due to renal failure/dehydration
†Deaths: FTC/TDF arm 1 suicide; 3TC/ABC arm 1 homicide, 1 lymphoma
‡Other: Multiple CNS symptoms and rash; malaise and lower back pain; decreased weight; cellulitis and streptococcal sepsis; and rash

Conclusions

Switching to FTC/TDF from 3TC/ABC through Week 48:

- **Maintains virologic suppression, is non-inferior, and results in less virologic failure**
- **Significantly improves lipids including**
  - **Median fasting TC and LDL**
  - **NCEP classification for TC and TG**
- **Improves 10-year Framingham CHD risk category in those who switched to FTC/TDF**
  - **Improves from baseline in both the >20% risk and 10-20% risk categories**
- **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**

References

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5. Martinez E, et al. BICOMBO, IAS 2007
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