Switching to Atripla® (EFV/FTC/TDF) from ABC/3TC FDC (Kivexa®/Epzicom®) + Efavirenz (EFV) Improves Lipid Levels Towards NCEP Recommendations: Primary Endpoint Results of a 24-week Randomised Study

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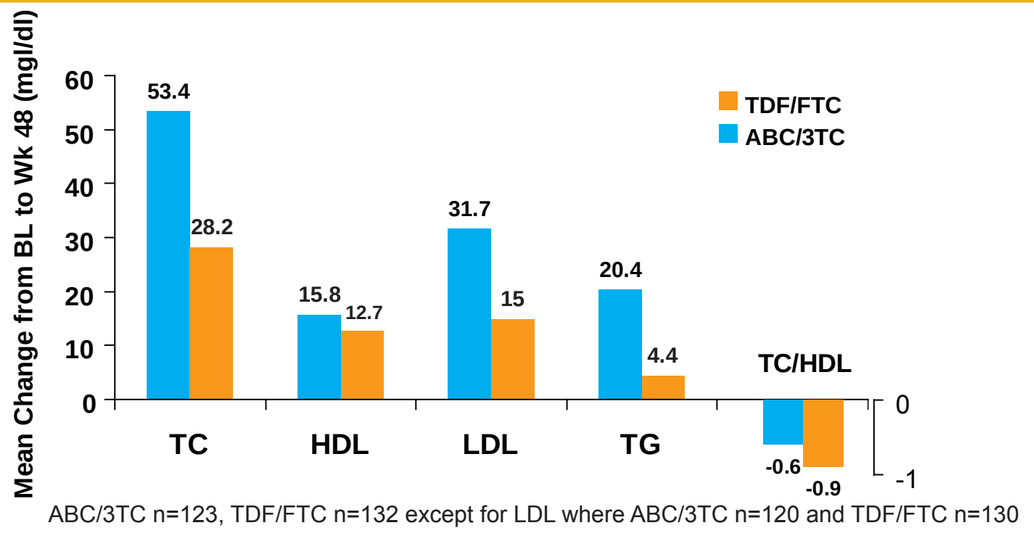
Background

- Dyslipidaemia contributes to CV risk[1] in HIV infection
- Tenofovir DF-based regimens may have a favourable lipid profile relative to abacavir-based regimens[2]
- We investigated changes in fasting total cholesterol (TC) in hypercholesterolaemic participants switching to the single tablet regimen of Atripla [ATR] from Kivexa + efavirenz [KVX+EFV]

ASSERT Study

Lipid Effects of ABC/3TC vs TDF/FTC

- Greater increases from baseline were seen in the ABC/3TC arm compared with the TDF/FTC arm



ABC/3TC n=123, TDF/FTC n=132 except for LDL where ABC/3TC n=120 and TDF/FTC n=130

Stellbrink HJ, et al., EACS 2009; Oral #PS10/1

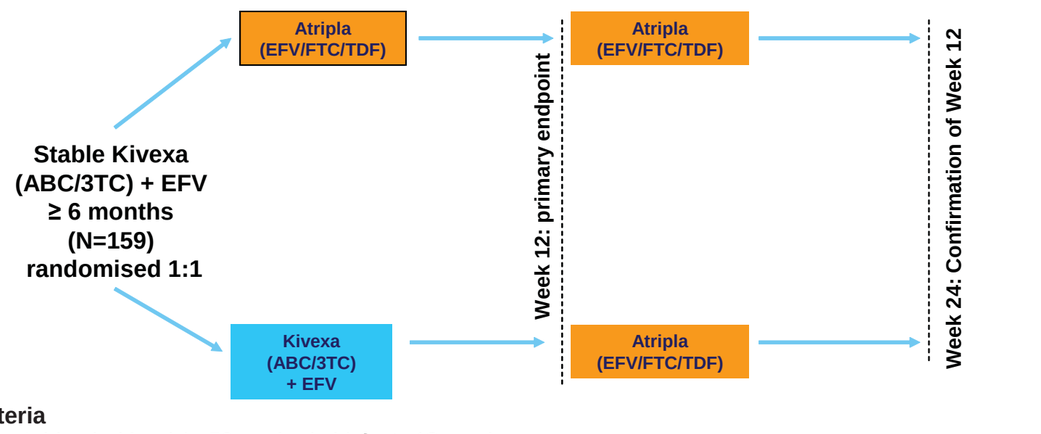
Objectives

- Primary Objective
  - Determine whether switching from Kivexa + Efavirenz to QD Atripla leads to a reduction in fasting total cholesterol at 12 weeks
- Secondary Objectives
  - Evaluation of fasting metabolic parameters (e.g., LDL, HDL, triglycerides, non-HDL cholesterol and cholesterol ratios)
  - Evaluation of efficacy and safety
  - Evaluation of changes in the 10-year risk for coronary heart disease outcomes as measured by Framingham risk score

Methods

- 159 participants stable on KVX+EFV for ≥ 6 months with HIV RNA < 50 copies/mL for ≥ 12 weeks and cholesterol ≥ 5.2 mmol/L randomised to switch to ATR or continue KVX +EFV
- 157 /159 randomised participants were treated (two KVX+EFV participants were not dosed)
- At Week 12, participants randomised to KVX+EFV were switched to ATR and all participants continued through to Week 24
- The primary endpoint was change in fasting TC from baseline to Week 12
- Fasting lipid parameters were assessed using NCEP thresholds

Figure 1. Study Design



Entry criteria
- Undetectable viral load (< 50 copies/mL) for ≥ 12 weeks
- Total cholesterol at Screening ≥ 5.2 mmol/L
- Baseline renal function (CrCl) ≥ 60mL/min and hepatic function (AST / ALT) ≤ 5 x ULN

Results

Table 1. Baseline Participant Characteristics[a]

	ATR	KVX + EFV
Number of Participants	79	78
Median age in yrs (IQR)	42 (36, 48)	44 (40, 50)
Race		
White	45 (57.0%)	48 (61.5%)
Black	29 (36.7%)	27 (34.6%)
Asian	2 (2.5%)	0
Other	3 (3.8%)	3 (3.9%)
Gender		
Male	61 (77.2%)	64 (82.1%)
HIV RNA[b]		
< 50 copies/mL	76/79 (96.2%)	71/77 (92.2%)
< 400 copies/mL	79/79 (100%)	77/77 (100%)
Median BMI (kg/m²) (IQR)	25.7 (23.5, 29.3)	25.8 (23.7, 28.0)
Median Fasting Total Cholesterol (IQR)[c]	6.62 (5.97, 7.26)	6.19 (5.80, 6.78)
Number of Participants on Prior Lipid Modifying Agents	9 (11.4%)	13 (16.7%)

a. Treated Analysis Set
b. One participant in Kivexa arm did not have a baseline viral load sample
c. Three participants in the Kivexa arm did not have fasting cholesterol at baseline, one participant in the Kivexa arm had a baseline TC <4.2mmol/L. These participants were excluded from the Modified ITT Analysis set (MITT)

Table 2. Patient Disposition at Week 12[a]

N (%)	ATR (N=79)	KVX + EFV (N=78)
Participants Completing 12 Weeks of Study	**78 (98.7%)**	**74 (94.9%)**
Treatment Discontinuation (Prior to Week 12)	**1 (1.3 %)**	**4 (5.1%)**
Adverse Events[b]	1 (1.3%)	1 (1.3%)
Pregnancy	0	0
Protocol Violation	0	2 (2.5%)
Withdrew Consent	0	0
Investigator's Decision	0	1 (1.3%)

a. Treated Analysis Set
b. Adverse Events leading to study drug discontinuation:
- ATR arm - anxiety / heartburn / night sweats / general body pain/ palpitations
- KVX arm - depression

Results (cont'd)

Figure 2. Fasting Metabolic Parameters: Week 12 Change from Baseline

(MITT Analysis Set (LOCF) Excluding participants who started/modified lipid lowering medications during the study)

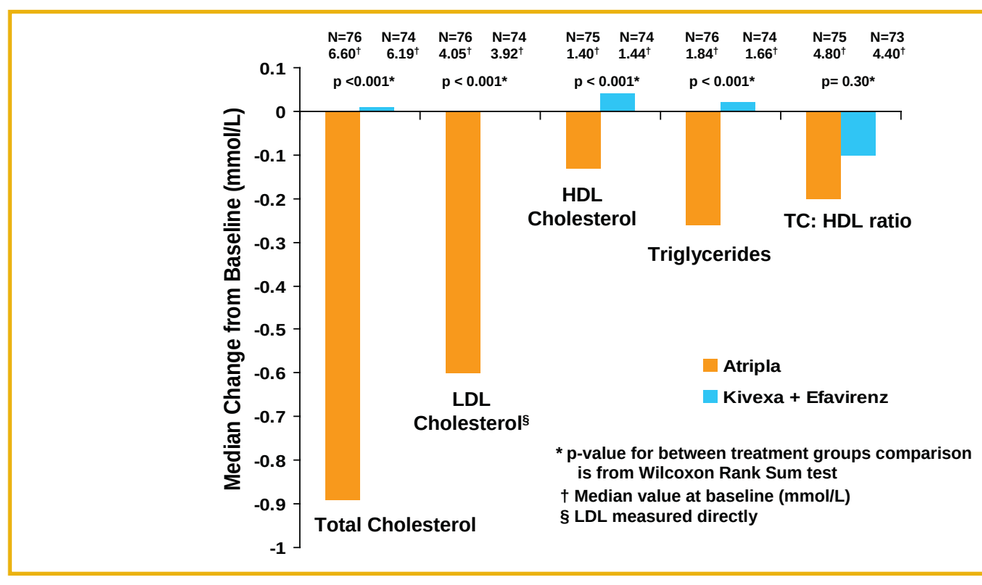


Figure 3. Total Cholesterol by NCEP Thresholds

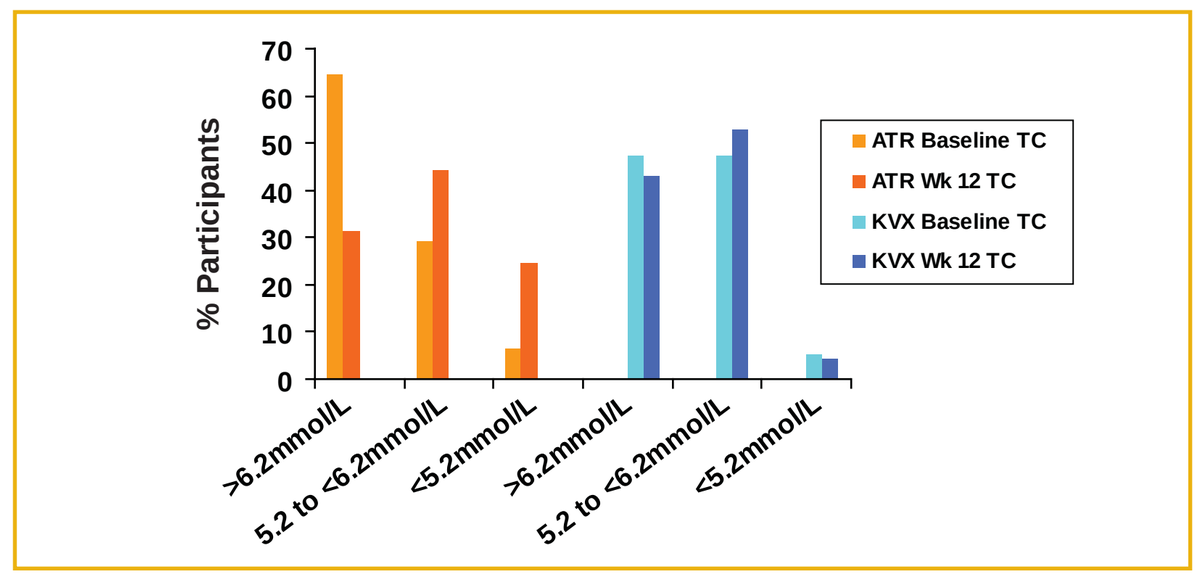
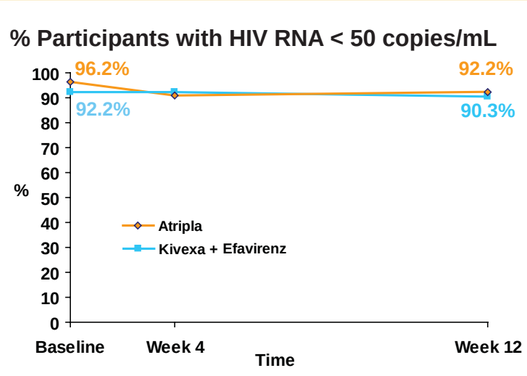


Figure 4. Viral Suppression and CD4 Wk 12 Change from Baseline

ITT Analysis Set (Missing = Excluded)

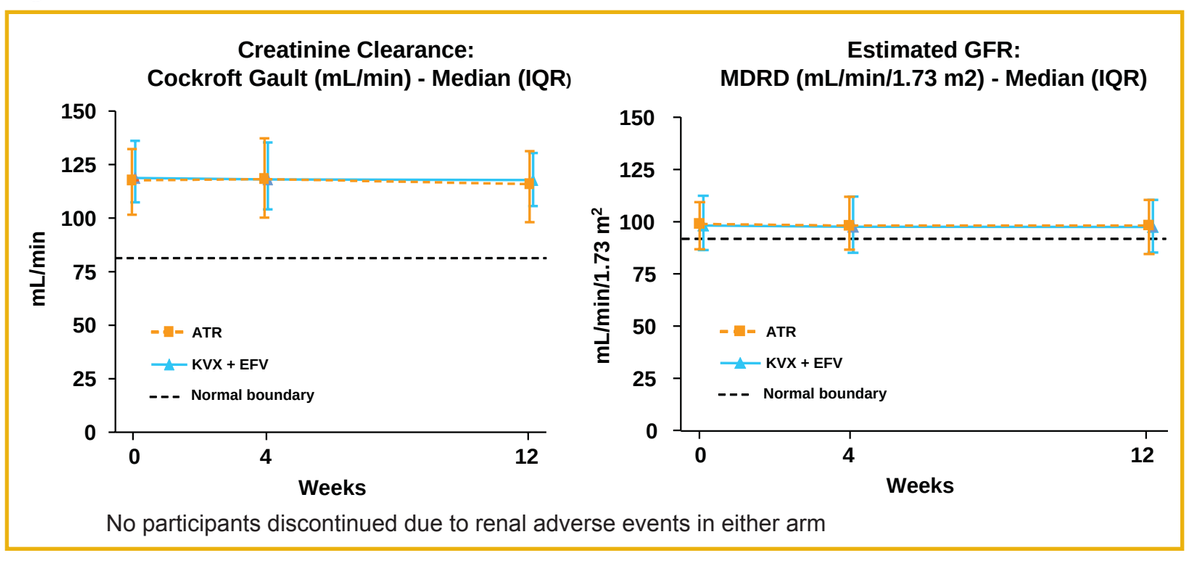


Virological failure
No participants met the criteria for virological failure in either arm (2 consecutive post-baseline value ≥ 400 copies/ml)

	Baseline		Wk 12 Change from Baseline		ATR vs KVX + EFV p-value
	ATR	KVX	ATR	KVX	
Median CD4 count (cells/mm³) (IQR)	459 (377, 604)	450 (371, 584)	-25 (-96, 49) (p =0.087)*	27 (-36, 77) (p =0.046)*	0.013†

* p-value for within treatment group comparison is from Wilcoxon Signed Rank test
† p-value for between treatment group comparison is from Wilcoxon Rank Sum test

Figure 5. Renal Function



No participants discontinued due to renal adverse events in either arm

Conclusions

- **Switching to Atripla from Kivexa +Efavirenz significantly improved atherogenic lipid parameters towards desirable levels (per NCEP guidelines)**
- **Virologic suppression was maintained**
- **Replacement of Kivexa +Efavirenz with Atripla may be part of an appropriate management approach in hypercholesterolaemic patients**

References

1. Grover, SA, et al., Am J Cardiol 2005; 95 (5): 586-591
2. Moyle, G et al., AIDS 2006; 20 (16): 2043-2050

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