Cardiovascular Biomarkers After Switching to ABC/DTG/3TC: The STRIIVING Study

660

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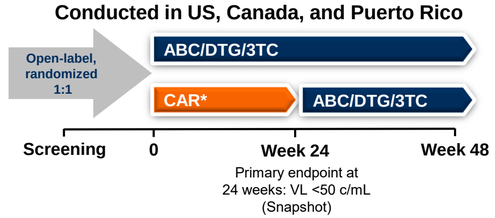
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Background

- Chronic inflammation has been associated with morbidity and mortality in treated HIV infection
- Studies have shown an improvement in inflammatory biomarker profiles in virologically suppressed patients switching from protease inhibitors (PIs) and/or non-nucleoside reverse transcriptase inhibitors (NNRTIs) to raltegravir (RAL) and elvitegravir (EVG)
- We evaluated the effects of switching to abacavir/dolutegravir/lamivudine (ABC/DTG/3TC) on markers of inflammation and immune activation in the STRIIVING study at 24 weeks

Study Design and Methods

Figure 1. STRIIVING Study Design



Inclusion criteria
- Virologically suppressed (confirmed HIV-1 RNA <50 c/mL)
- HLA-B*5701 negative

*Stable suppressive current antiretroviral therapy (CAR) with 2 NRTIs plus either a PI, an NNRTI, or an INI. ≥40% PIs, at least 25% INIs.

- C-reactive protein (hs-CRP), interleukin-6 (IL-6), D-dimer, soluble vascular cell adhesion molecule (sVCAM), soluble CD14 and CD163 (sCD14, sCD163), and intestinal fatty acid–binding protein (I-FABP) levels were measured as secondary endpoints
- Mean 24-week changes in log-transformed biomarker values were compared between patients switching to ABC/DTG/3TC and those continuing suppressive antiretroviral therapy (ART) using analysis of covariance (ANCOVA) adjusting for ART third-agent class, interaction of treatment and original ART third-agent class, sex, race (Caucasian, African American, Hispanic, or other), and baseline biomarker level
- In a post hoc sensitivity analysis, body mass index (BMI) was added to the list of original covariates listed above

Results

Baseline Characteristics

Table 1. Patient Demographics and Disease Characteristics

	ABC/DTG/3TC (n=274)	CAR (n=277)	Total (N=551)
Age (years), median	45	47	45
Female	14%	14%	14%
African American/African heritage	30%	27%	28%
HBV/HCV positive	0/8%	0/5%	0/7%
CDC class C	15%	16%	15%
CD4⁺ T (cells/mm³), median	618	597	610
<500	30%	33%	31%
≥500	70%	67%	69%
Time on ART (months), median	55	51	52
CAR at screening			
PI	43%	42%	42%
NNRTI	31%	31%	31%
INI	26%	27%	26%
TDF/FTC backbone	76%	79%	77%

- Adjusted geometric mean changes at Week 24 in hs-CRP, IL-6, D-dimer, sVCAM, and sCD163 were similar between patients switching to ABC/DTG/3TC and those on CAR; greater declines in I-FABP and sCD14 levels were observed among patients switching to ABC/DTG/3TC (P<0.05) (Figures 2 and 3)

Figure 2. sCD14 and sCD163 in Patients Switching to ABC/DTG/3TC vs CAR

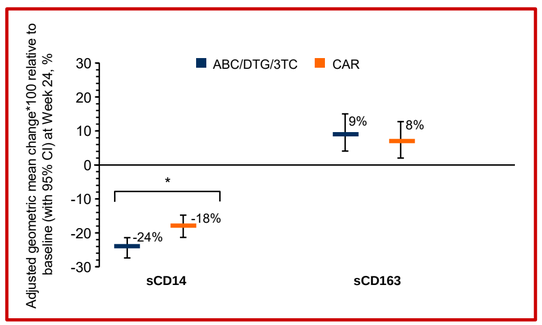
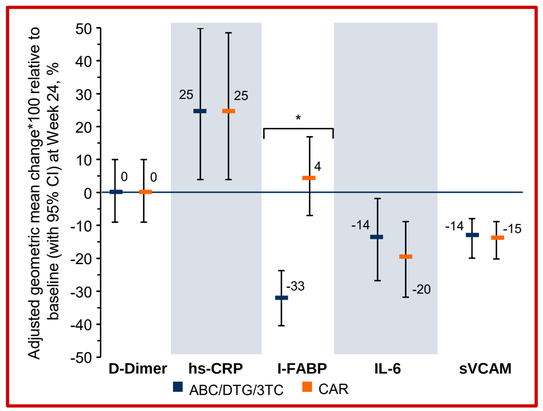


Figure 3. D-Dimer, hs-CRP, I-FABP, IL-6, and sVCAM in Patients Switching to ABC/DTG/3TC vs CAR



- Multivariate analysis of change from baseline showed statistically greater declines in sCD14 levels in men and non-white persons
- In a sensitivity analysis using a model that also adjusted for BMI, patients with BMIs ≥25 kg/m² saw slightly larger declines in sCD14 and I-FABP levels (Table 2)

Table 2. Percent Change From Baseline in I-FABP and sCD14 by BMI

Model, including baseline BMI	Adjusted geometric mean change*100 (%)	Adjusted geometric mean ratio; 95% CI for ratio	*P* value
I-FABP (ng/L)			0.078
<25 kg/m²	-10%		
≥25 kg/m²	-20%	1.12 (0.99; 1.26)	
sCD14 (ng/L)			0.031
<25 kg/m²	-19%		
≥25 kg/m²	-22%	1.05 (1.00; 1.09)	

- The treatment difference was consistent whether patients came in the study taking PIs, NNRTIs, or INIs, but patients who switched off PIs or NNRTIs had numerically larger decreases from baseline in I-FABP levels than those who switched off INIs

Table 3. Percent Change From Baseline in I-FABP Level by HIV Treatment

	Adjusted geometric mean change*100 (%)	Adjusted geometric mean ratio; 95% CI for ratio	*P* value
I-FABP (ng/L)			
PI	-22%		
INI	-6%	1.20 (1.04; 1.38)	
NNRTI	-21%	1.10 (0.88; 1.16)	0.029
Treatment by ART third agent			
I-FABP (ng/L)			
PI			
ABC/DTG/3TC	-33%	0.73 (0.61; 0.87)	
CAR	-9%		
INI			
ABC/DTG/3TC	-24%	0.66 (0.53; 0.83)	
CAR	15%		
NNRTI			
ABC/DTG/3TC	-42%	0.55 (0.45; 0.68)	
CAR	6%		

Conclusions

- Switch to ABC/DTG/3TC was associated with significantly greater declines in sCD14 and I-FABP levels compared with CAR
- No worsening of markers associated with cardiovascular disease was observed following switch to ABC/DTG/3TC as compared with CAR
- The observed declines in sCD14 and I-FABP levels may reflect improved gut barrier health and reduced microbial translocation and monocyte activation following switch to ABC/DTG/3TC. Lower sCD14 levels have also been associated with reduced mortality in HIV infection[1]
- Changes in I-FABP levels were greater for patients coming off PIs or NNRTIs than for those on other INIs, suggesting a role for the third agent in changes in I-FABP levels
- Controlling for BMI did not attenuate biomarker changes, but overweight and obese patients saw larger declines in sCD14 and I-FABP levels. As obesity may be associated with compromised gut integrity and microbial translocation, these findings also argue for a possible effect on bowel health
- Overall these data may suggest reduced microbial translocation and monocyte activation following switch to ABC/DTG/3TC, which could have important implications for morbidity and mortality

Acknowledgment

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Reference

1. Sandler NG, Wand H, Roque A, et al. Plasma levels of soluble CD14 independently predict mortality in HIV infection. *J Infect Dis.* 2011;203:780-790.