Poster Number

861

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Long-Term Efficacy and Safety of Elvitegravir/Cobicistat/Emtricitabine/Tenofovir DF Compared to Efavirenz/Emtricitabine/Tenofovir DF in HIV-1-Infected, Treatment-Naïve, Black Versus Non-Black Subjects

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ID Week (Infectious Diseases Society of America)

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Introduction

- Single-tablet regimen elvitegravir/cobicistat/emtricitabine/tenofovir DF (STB) demonstrated non-inferior efficacy to efavirenz/emtricitabine/tenofovir DF (ATR) at Week 48 (88% vs. 84%) and Week 96 (84% vs. 82%) in Study 102¹⁻²
- A meta-analysis of HIV clinical trials showed that the efficacy of antiretroviral therapy is lower in Blacks compared to other subjects³
- This subanalysis examines the efficacy and safety of STB vs. ATR through 96 weeks in Black vs. Non-Black subjects

Abbreviations: ATR, Atripla = efavirenz/emtricitabine/tenofovir DF; STB, Stribild = elvitegravir/cobicistat/emtricitabine/tenofovir DF

- Sax P. et al. Lancet 2012: 379: 2439-48
- Zolopa A, et al. JAIDS 2013; 63: 96-100 Evans et al. Poster #861. ICAAC September 9-12, 2012 in San Francisco, CA

Methods

- Efficacy and safety analyses were performed in Black and Non-Black subjects on STB or ATR using Week 96 data from Study 102
- Key endpoints:
- Efficacy
 - Percentage with HIV-1 RNA <50 copies/mL by FDA snapshot algorithm
 - Change from baseline in CD4 cell count
- Safety
- Study drug related adverse events (AEs) in \geq 5% of subjects in any treatment arm
- P-value was calculated using Fisher exact test for comparing incidence of AEs between treatment arms
- Laboratory studies
- Change from baseline in serum creatinine (SCr)
- Change from baseline in lipid parameters - P-value was calculated using 2-sided Wilcoxon rank sum test for
 - comparing continuous data between treatment arms

Study Design



Secondary Endpoints Tolerability, safety, and efficacy at Week 96

Baseline Demographics and Disease Characteristics

	Blacks	(n=197)	Non-Blacks (n=503)		
Characteristics	STB (n=106)	ATR (n=91)	STB (n=242)	ATR (n=261)	
Age (years) , mean	35	36	38	39	
Male	77%	80%	93%	93%	
Asymptomatic HIV Infection	77%	76%	86%	87%	
HIV-1 RNA (log ₁₀ c/mL), median	4.72	4.73	4.76	4.81	
>100,000 copies/mL	27%	29%	37%	34%	
CD4 count (cells/mm³), mean	384	363	394	388	
≤200 cells/mm³	16%	21%	11%	12%	
History of IV drug use	2%	5%	4%	2%	
HCV Seropositive	6%	7%	5%	3%	
Baseline eGFR (ml/min), median*	111	117	116	114	

* P > 0.05 for STB vs. ATR in Blacks and Non-Blacks



death, or discontinued drug for reasons other than AE, death, and lack/loss of efficacy with last HIV-1 RNA < 50 copies/mL. Virologic success is defined as HIV-1 RNA < 50 copies/mL at Week 48 (Study Day 309-378 inclusive) and Week 96 (Study Day 631-714 inclusive)

Non-Blacks



death, or discontinued drug for reasons other than AE, death, and lack/loss of efficacy with last HIV-1 RNA < 50 copies/mL. Virologic success is defined as HIV-1 RNA < 50 copies/mL at Week 48 (Study Day 309-378 inclusive) and Week 96 (Study Day 631-714 inclusive

Summary of Adverse Events By Race

	Blacks	(n=197)	Non-Blacks (n=503)		
Summary of adverse events (AEs) *	STB (n=106)	ATR (n=91)	STB (n=242)	ATR (n=261)	
Any grade study drug related AEs ^{a, b}	42%	67%	51%	68%	
Any grade 2-4 study drug related AEs ^{a, b}	13%	34%	13%	26%	
Serious AEs ^b	16%	14%	16%	8%	
Any AEs leading to study drug discontinuation ^a	<1%	10%	7%	6%	

* Summary of adverse events with rates that are statistically different between STB and ATR in Blacks or Non-Blacks a. P < 0.05 in Blacks for STB vs. ATR

b. P < 0.05 in Non-Blacks for STB vs. ATR

 Blacks on STB compared to ATR had statistically significant lower rates of any grade study drug related adverse events and adverse events leading to study drug discontinuation

Study Drug Related Adverse Events

STB (n=):

ATR(n=

	Black	s (n=197)	Non-Blacks (n=503		
Study drug related adverse events, n *	STB (n=106)	ATR (n=91)	STB (n=242)	ATR (n=261	
Nausea	17 (16%)	11 (12%)	40 (17%)	19 (7%	
Abnormal dreams	14 (13%)	20 (22%)	35 (14%)	73 (28%	
Diarrhea	7 (7%)	9 (10%)	32 (13%)	30 (12%	
Headache	6 (6%)	5 (5%)	19 (8%)	8 (3%)	
Dizziness	4 (4%)	17 (19%)	12 (5%)	56 (21%	
Insomnia	1 (1%)	7 (8%)	6 (2%)	22 (8%	
Rash	0	3 (3%)	5 (2%)	25 (10%	

* Frequencies of study drug related adverse events (≥ 5% in any treatment arm in Blacks or No Blacks) are based on all treatment-emergent adverse events (all grades)

Blacks on STB compared to ATR had higher rates of stud drug related nausea and lower rates of abnormal dreams diarrhea, dizziness, insomnia, and rash

Results Change From Baseline in CD4 Cell Count **Emergent Resistance Through Week 96** Change in Serum Creatinine From Baseline 0.6 ATR n = 9 n (%) W48 W48 Emergent ਫ਼ 🖯 0.4-5 (4.7%) +1 (0.9%) 3 (3.3%) +1 (1.1+%) Resistance **Primary INSTI-R** 4 (3.8%) +1 (0.9%) 3 (3.3%) +1(1.1%)or NNRTI-R P = 0.91 E92Q K103N N155H K101E/K +1 0 0 Q148R M230L 0 0 T66I 0 Y188F/H/ +1 G190A 0 V90I 0 V108I 0 P225H +1 BL 4 8 16 24 32 40 48 60 rimary NRTI-I 5 (4.7%) +1 (0.9% 24 32 40 48 60 72 84 (1.1%)STB (n=): M184V/I +1 M184V/I -5 ATR (n=): K65R +1 K65R Baseline median serum creatinine in Blacks: 0.99 mg/dL STB and 0.96 mg/dL ATR (P = 0.47) NSTI-R, integrase strand transfer inhibitor resistance

Change From Baseline in CD4 Cell Count P = 0.21



Emergent Resistance Through Week 96



Change in Serum Creatinine From Baseline 0.6 40 48 STB (n=) 224 ATR (n=)

Non-Blacks

Adverse Events Leading to Study Drug Discontinuation

Non-Blacks (n=242)

STB (n=242)

No. of subjects with AE

Leading to Drug DC

Burkitt's Lymphoma

Intentional Overdose

Completed suicide

Depression

Hepatitis C

Liver injury

Lymphoma

Nausea

Paranoia

Renal events *

Suicide behavior

Fatigue

	Non-B	Non-Blacks (n=261)					
	AT	ATR (n=261)					
16	No. of subjects with AE Leading to Drug	15					
1	DC						
1	Abnormal dreams	2	Hepatitis C				
1	Amnesia	1	Hot flush	Γ			
1	Anxiety	2	Hyperhidrosis	Γ			
1	Claustrophobia	1	Insomnia	Γ			
1	Depression	2	Intracardiac mass	Γ			
1	Drug eruptions	1	Paranoia	Γ			
1	Drug hypersensitivity	1	Presyncope	Γ			
1	Fatigue	2	Rash	Γ			
1	Feeling abnormal	1	Skin injuries				
7	Grand mal	1					

Renal Events Leading to Study Drug Discontinuation

Renal adverse	STB (n=348)				
events leading to study drug discontinuation	Blacks (n=106)		Non-Blacks (n=242)		
	W48	W96	W48	W96	
Proximal Renal Tubulopathy	0	0	4 (1.7%)	0	
Isolated rise in Serum creatinine	0	0	3 (1.2%)	0	

No renal adverse event leading to study drug discontinuation in Blacks and Non-Blacks in the ATR arm

Events	•		Blacks				
197)	Non-Blac	ks (n=503)	Blacks (n=197)				
ATR n=91)	STB (n=242)	ATR (n=261)	Adverse events leading to study drug	STB (n=106)	ATR (n=91)		
(12%)	40 (17%)	19 (7%)	discontinuation	X			
(22%)	35 (14%)	73 (28%)	leading to study drug DC	1	9		
(10%)	32 (13%)	30 (12%)	Depression	0	2		
(5%) (19%)	19 (8%) 12 (5%)	8 (3%) 56 (21%)	Dypsnea or exertional dyspnea	0	1		
(8%)	6 (2%)	22 (8%)	Metastatic neoplasm	0	1		
(3%)	5 (2%)	25 (10%)	Migraine	1	0		
≥ 5% in any treatment arm in Blacks or Non- e events (all grades) TR had higher rates of study r rates of abnormal dreams,			Nightmare	0	1		
			Pyrexia	0	1		
			Rash or rash maculo-papular	0	2		
			Sluggishness	0	1		
and ras	h		Suicide attempt	0	1		
	Note: One subject can superiorse multiple AFs loading to						

Note: One subject can experience multiple AEs leading to study drug discontinuation (DC)

* Higher level MedDRA terms included renal function analyses, nephropathies and tubular disorders nec, renal failure and impairment

convulsion



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Conclusions

- Blacks on STB compared to ATR through Week 96 Numerically higher rates of virologic success
- High and similar increases in CD4 cell count
- Low and similar rates of emergent drug resistance
- A differentiated and favorable tolerability profile
- Statistically significant lower rates of study drug related adverse events and any adverse events leading to study drug discontinuation
- Statistically significant increases in SCr that occurred as early as Week 4 and subsequently stabilized through Week 96 consistent with known cobicistat inhibition of renal tubular secretion¹
- No renal adverse event leading to study drug discontinuation
- Statistically significant smaller increases in total cholesterol and HDL

1. Lepist E-I, et al. Poster A1-1724. ICAAC September 17-20, 2011 in Chicago, IL