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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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 102[1-2]
- A meta-analysis of HIV clinical trials showed that the efficacy of antiretroviral therapy is lower in Blacks compared to other subjects[3]
- This subanalysis examines the efficacy and safety of STB vs. ATR through 96 weeks in Black vs. Non-Black subjects

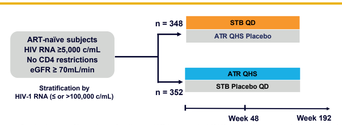
Abbreviations: ATR, Atripla = efavirenz/emtricitabine/tenofovir DF; STB, Stribild = elvitegravir/cobicistat/emtricitabine/tenofovir DF

1. Sax P, et al. Lancet 2012; 379: 2439-48
2. Zolopa A, et al. JAIDS 2013; 63: 96-100
3. 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 ≥ 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



Primary Analysis Non-inferiority efficacy (12% margin) of STB vs. ATR by proportion of subjects with HIV-1 RNA < 50 copies/mL at Week 48 by FDA snapshot algorithm

Secondary Endpoints Tolerability, safety, and efficacy at Week 96

Baseline Demographics and Disease Characteristics

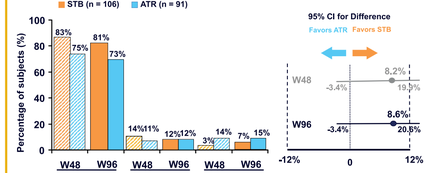
Characteristics	Blacks (n=197)		Non-Blacks (n=503)	
	STB (n=106)	ATR (n=91)	STB (n=242)	ATR (n=261)
Age (years) , mean	35	36	38	39
Male	77%	80%	93%	93%
Asymptomatic HIV Infection	77%	76%	86%	87%
HIV-1 RNA (log_{10} c/mL), median	4.72	4.73	4.76	4.81
>100,000 copies/mL	27%	29%	37%	34%
CD4 count (cells/mm³), 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

Results

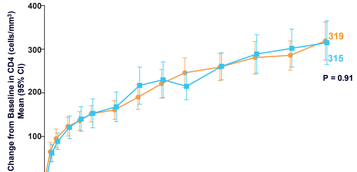
Blacks

Efficacy Endpoints: HIV-1 RNA <50 c/mL



* No virologic data in window defined as: missing HIV-1 RNA data but on study, discontinued drug due to AE or 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).

Change From Baseline in CD4 Cell Count

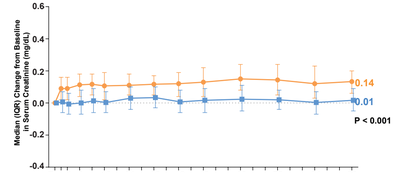


Emergent Resistance Through Week 96

n (%)	STB (n = 106)			ATR n = 91		
		W48	W96		W48	W96
Emergent Resistance		5 (4.7%)	+1 (0.9%)		3 (3.3%)	+1 (1.1+%)
Primary INSTI-R or NNRTI-R		4 (3.8%)	+1 (0.9%)		3 (3.3%)	+1 (1.1%)
	E92Q	4	0	K103N	3	+1
	N155H	1	+1	K101E/K	0	0
	Q148R	1	0	M230L	0	0
	T66I	1	0	Y188F/H/L	1	+1
				G190A	0	0
				V90I	0	0
				V108I	1	0
				P225H	0	+1
Primary NRTI-R		5 (4.7%)	+1 (0.9%)		1 (1.1%)	0
	M184V/I	5	+1	M184V/I	1	0
	K65R	1	+1	K65R	1	0

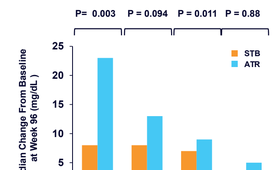
INSTI-R, integrase strand transfer inhibitor resistance

Change in Serum Creatinine From Baseline



- **Baseline median serum creatinine in Blacks: 0.99 mg/dL STB and 0.96 mg/dL ATR (P = 0.47)**

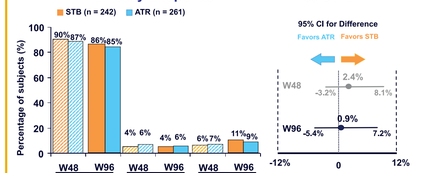
Change in Fasting Lipids From Baseline



TC - total cholesterol, LDL - low-density lipoprotein, TG - triglycerides, HDL - high-density lipoprotein

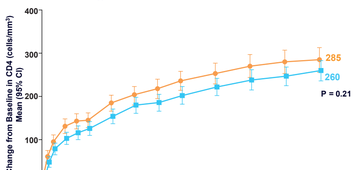
Non-Blacks

Efficacy Endpoints: HIV-1 RNA <50 c/mL



* No virologic data in window defined as: missing HIV-1 RNA data but on study, discontinued drug due to AE or 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).

Change From Baseline in CD4 Cell Count

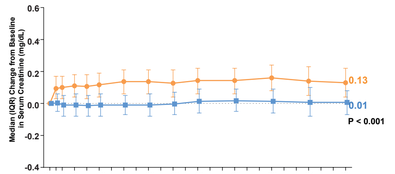


Emergent Resistance Through Week 96

n (%)	STB (n = 242)			ATR (n = 261)		
		W48	W96		W48	W96
Emergent Resistance		3 (2.8%)	+1 (0.9%)		5 (5.5%)	+1 (1.1+%)
Primary INSTI-R or NNRTI-R		3 (2.8%)	+1 (0.9%)		5 (5.5%)	+1 (1.1%)
	E92Q	3	0	K103N	4	+1
	N155H	0	+1	K101E	3	0
	Q148R	0	0	M230L	2	0
	T66I	0	0	Y188F/H/L	0	+1
				G190A	1	0
				V90I	1	0
				V108I	1	0
				P225H	1	0
Primary NRTI-R		3 (2.8%)	+1 (0.9%)		4 (4.4%)	0
	M184V/I	3	+1	M184V/I	1	+1
	K65R	2	0	K65R	1	+1

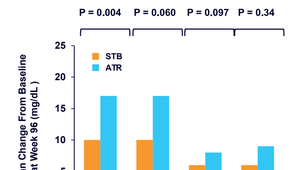
INSTI-R, integrase strand transfer inhibitor resistance

Change in Serum Creatinine From Baseline



- **Baseline median serum creatinine in Non-Blacks: 0.95 mg/dL STB and ATR (P = 0.68)**

Change in Fasting Lipids From Baseline



TC - total cholesterol, LDL - low-density lipoprotein, TG - triglycerides, HDL - high-density lipoprotein

Summary of Adverse Events By Race

Summary of adverse events (AEs) *	Blacks (n=197)		Non-Blacks (n=503)	
	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

Study drug related adverse events, n *	Blacks (n=197)		Non-Blacks (n=503)	
	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 Non-Blacks) are based on all treatment-emergent adverse events (all grades)

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

Adverse Events Leading to Study Drug Discontinuation

Blacks

Blacks (n=197)		
Adverse events leading to study drug discontinuation	STB (n=106)	ATR (n=91)
No. of subject with AE leading to study drug DC	1	9
Depression	0	2
Dypsnea or exertional dyspnea	0	1
Metastatic neoplasm	0	1
Migraine	1	0
Nightmare	0	1
Pyrexia	0	1
Rash or rash maculo-papular	0	2
Sluggishness	0	1
Suicide attempt	0	1

Non-Blacks

Non-Blacks (n=242)	
STB (n=242)	
No. of subjects with AE Leading to Drug DC	16
Burkitt's Lymphoma	1
Completed suicide	1
Depression	1
Fatigue	1
Hepatitis C	1
Intentional Overdose	1
Liver injury	1
Lymphoma	1
Nausea	1
Paranoia	1
Renal events *	7
Suicide behavior	1

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

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

Renal Events Leading to Study Drug Discontinuation

Renal adverse events leading to study drug discontinuation	STB (n=348)			
	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

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 secretion[1]**
  - **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

ClinicalTrials.gov Identifier: NCT01095796

GS-US-236-0102