



### ABOUT US

The Florida/Caribbean AIDS Education and Training Center provides state-of-the-art HIV education, consultation, and resource materials to health care providers in Florida, Puerto Rico and the US Virgin Islands.

Major funding is provided by the US Public Health Service's Health Resources Services Administration (HRSA) DHHS-HAB Grant No. H4AHA00049 through the University of South Florida Center for HIV Education and Research, Michael Knox, PhD, Director.

### EDITORS

Jeffrey Beal, MD, AAHIVS (239) 839-4645  
aetcbear@embarqmail.com  
Joanne J. Orrick, PharmD, AAHIVE (352) 273-7845  
orricj@ufl.edu

### PEDIATRIC EDITOR

Belinda Beauchamp, MD (787) 281-8501  
belinda.beauchamp@upr.edu

### MANAGING EDITOR

Kimberly Alfonso, MAcc (813) 974-4430  
alfonso@fmhi.usf.edu

## Special Bulletin: Isentress® (raltegravir) Receives FDA Approval for Treatment-Naïve Patients

Joanne J. Orrick, PharmD, AAHIVE  
Faculty, Florida/Caribbean AETC  
Clinical Assistant Professor, University of Florida, Gainesville  
Jeffrey Beal, MD, AAHIVS  
Clinical Director, Florida/Caribbean AETC

On July 9<sup>th</sup>, 2009, the FDA expanded the approval of Isentress® (raltegravir, RAL) to the use in treatment-naïve HIV-1 infected patients. RAL was previously approved only for treatment-experienced patients. The approval was based on 48-week results of the STARTMRK trial which compared tenofovir + emtricitabine + (raltegravir or efavirenz) in treatment-naïve patients. The revised product label is available online at [http://www.merck.com/product/usa/pi\\_circulars/i/isentress/isentress\\_pi.pdf](http://www.merck.com/product/usa/pi_circulars/i/isentress/isentress_pi.pdf).

### STARTMRK (Protocol 021)

- Double-blind randomized non-inferiority international study (patients from regions of Latin America, North America, Europe/Australia, Southeast Asia)
- Patients randomized to RAL 400 mg po bid (n=281) or Efavirenz (Sustiva®, EFV) 600 mg po qhs (n=282) both with Emtricitabine (Emtriva®, FTC) + Tenofovir (Viread®, TDF) (provided as Truvada®)
- Baseline characteristics between the 2 groups were similar: selected parameters in all treated patients below
  - Gender: 81% male; Age: Median 37 yrs (range 19-71)
  - Race/ethnicity: 42% White, 10% Black, 12% Asian, 23% Hispanic, 13% multi-racial
  - CD4 (cells/mm<sup>3</sup>): Median 208 (range 1-807); 47% with CD4 < 200 at baseline
  - Plasma HIV RNA (log<sub>10</sub> copies/mL): Median 5 (range 3-6) with HIV RNA (copies/mL) > 100,000 and 50,000, in 53% and 71% of patients, respectively
  - 19% of patients had non-clade B
  - Hepatitis B or C co-infected: 7%
  - Stratified by baseline HIV RNA (≤ or > 50,000 copies/mL) and hepatitis co-infection status
- Adverse Effects
  - Overall clinic adverse events with RAL vs EFV (90% vs. 96.5%, p=0.002)
  - Drug-related adverse events with RAL vs. EFV (44% vs. 77%, p<0.001)
  - Moderate to severe drug-related problems with RAL vs. EFV (32% vs. 16%, p < 0.001)
- Results-See Table 9

Table 9: Outcomes by Treatment Group through Week 48

Randomized Study Protocol 021	ISENTRESS® 400 mg Twice Daily (N = 281)	Efavirenz 600 mg At Bedtime (N = 282)	Difference (ISENTRESS® - Efavirenz) (CI) <sup>§</sup>
Outcome at Week 48			
Subjects with HIV-1 RNA less than 50 copies/mL	87%	82%	4.7% (-1.3%, 10.6%)
Subjects with HIV-1 RNA less than 400 copies/mL	91%	88%	3.6% (-1.5%, 8.7%)
Mean CD4 cell count change from baseline (cells/mm <sup>3</sup> )	176	150	25.8 (5.0, 46.5)
Virologic Failure (>50 copies/mL)	6%	7%	
Never suppressed through Week 48 and on study at Week 48	2%	3%	
Rebound	5%	5%	
Discontinued study drug	7%	10%	
Reasons for Discontinuation			
Death	<1%	0%	
Adverse experiences	2%	5%	
Other*	4%	5%	

<sup>§</sup>The 95% CI for treatment difference is adjusted by the screening HIV RNA level (≤50,000 copies/mL vs. >50,000 copies/mL) and Hepatitis B or C (negative vs. positive)  
<sup>\*</sup>Other includes lack of efficacy, loss to follow-up, consent withdrawn, protocol violation and other

- Conclusions
  - RAL is non-inferior to EFV in treatment-naïve patients

For more information,  
please visit our website:  
[www.FCAETC.org](http://www.FCAETC.org)

To request clinical consultation, please call the  
National Clinicians' Consultation Hotline:  
**1-800-933-3413**

**DOSING AND ADMINISTRATION**

- RAL 400 mg po bid with or without food (same dosing for treatment-naïve and experienced patients)
- When combined with rifampin, a potent inducer of RAL metabolism via UGT1A1, RAL 800 mg po bid
- Available in 400 mg tablets

**DRUG INTERACTIONS**

- RAL is metabolized by UGT1A1 and levels can be significantly affected by drugs that inhibit or induce this enzyme
- RAL does not inhibit or induce CYP-mediated metabolism
- Efavirenz and etravirine ↓RAL plasma concentrations. Clinical significance not yet known

**ADVERSE EFFECTS**

- Insomnia, headache, nausea, asthenia, and fatigue CPK elevations have been seen and myopathy and rhabdomyolysis have been reported but relationship to RAL is not known

**RESITANCE MUTATIONS**

- Q148H/K/R or N155H + ≥ one of the following mutations: L74M, E92Q, T97A, E138A/K, G140A/S, V151I, G163R, H183P, Y226C/D/F/H, S230R & D232N
- Y143C/H/R is another pathway to resistance. Y143R→ 10-fold increased resistance<sup>3</sup>
- GenoSure™ Integrase Resistance Test available through LabCorp test code #551871

**References**

1. ISENTRESS [package insert]. Whitehouse Station, NJ: Merck & Co., In; July 2009.  
[http://www.merck.com/product/usa/pi\\_circulars/i/isentress/isentress\\_pi.pdf](http://www.merck.com/product/usa/pi_circulars/i/isentress/isentress_pi.pdf)  
 Accessed July 14, 2009.
2. Lennox J, DeJesus E, Lazzarin A, et al. STARTMRK, a phase III study of the safety and efficacy of raltegravir-based vs efavirenz-based combination therapy in treatment-naïve HIV-infected patients. 48th Annual International Conference on Antimicrobial Agents and Chemotherapy (ICAAC). October 25-28, 2008. Washington, DC. Abstract H-896a. Summary available online at [http://www.natap.org/2008/ICAAC/ICAAC\\_07.htm](http://www.natap.org/2008/ICAAC/ICAAC_07.htm)  
 Accessed July 14, 2009.
3. [http://hivdb.stanford.edu/pages/alg/sierra\\_mutation.html](http://hivdb.stanford.edu/pages/alg/sierra_mutation.html)  
 Accessed July 14, 2009.

**Testing for Rectal and Pharyngeal Neisseria gonorrhoeae and Chlamydia trachomatis Infections by Gay-Focused Community-Based Organizations — 5 U.S. Cities, 2007**

[Included in the July 10, 2009 / 58(26); 716-719 Morbidity and Mortality Weekly Report (MMWR)]

During 2007, six gay-focused community-based organizations collected approximately 30,000 rectal and pharyngeal gonorrhea (GC) and chlamydia (CT) tests and detected approximately 1,600 infections. Nucleic acid amplification test (NAAT) positivity was:

- 5.4% for rectal GC
- 8.9% for rectal CT
- 5.3% for pharyngeal GC

**New CDC recommendation for yearly screening with NAAT for GC and CT of MSM if in prior year they have had**

- Receptive anal intercourse - screen for rectal gonorrhea and chlamydia
- Receptive oral intercourse - screen for pharyngeal gonorrhea (chlamydia not recommended)

For MSM with multiple or anonymous partners, or have sex during illicit drug use, or use methamphetamine, or have sex partners with these risk factors, screening is recommended at 3-6 mo. intervals

Although NAAT not FDA approved for rectal or pharyngeal GC or CT, establishment of performance specifications for a modification of an FDA-cleared test is straightforward

- Laboratory Corporation of America and Quest Diagnostics and the Florida Bureau of Laboratories are certified to perform this testing

**Keeping with the Pace XVIII:**  
 An HIV Update

**Wednesday, August 26th, 2009**  
 University of Florida Conference Center  
 Gainesville, Florida

**CLICK HERE TO REGISTER!**

[www.FCAETC.org/KWP](http://www.FCAETC.org/KWP)

*Intended Audience: Physicians, physician assistants, pharmacists, nurses, nurse practitioners, case managers, health educators, social workers, mental health counselors, and other health professionals.*

Presented By:

Florida/Caribbean AETC  
 Florida Department of Health  
 Southeastern National Tuberculosis Center  
 Suwannee River Area Health Education Center

**REGISTER NOW!**

Only \$50 for 5.5 CEUs and CMEs

The complete collection of previous issues of HIV CareLink are available online.

To view past issues, please visit the archives at:

**[www.FCAETC.org/Newsletter](http://www.FCAETC.org/Newsletter)**