



Florida/Caribbean AIDS Education and Training Center

HIV CareLink

A Newsletter for HIV/AIDS Primary Care Providers

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.

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FDA Approves Rilpivirine (Edurant™) for Treatment-Naïve Patients

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On May 20, 2011, the Food and Drug Administration (FDA) approved rilpivirine (Edurant™), a new non-nucleoside reverse transcriptase inhibitor (NNRTI) for the treatment of HIV in antiretroviral (ARV) naïve patients. For more information including the complete prescribing information, go to www.edurant-info.com. The approval of rilpivirine was based on 48 week safety and efficacy results from two Phase 3 randomized, double blind, active-controlled clinical trials (TMC278-C209 [ECHO] and TMC278-C215 [THRIVE]) and 96 week safety and efficacy analyses from a Phase 2b randomized, active-controlled, dose-comparison trial (TMC278-C204). All trials were in treatment-naïve subjects.

SUMMARY OF ECHO AND THRIVE TRIALS

- Both Phase 3 trials compared rilpivirine to efavirenz in ARV naïve HIV-1 infected subjects with HIV-1 RNA \geq 5000 copies/mL and no NNRTI resistance. ECHO and THRIVE were identical in design except for the background regimens. Randomization was stratified by screening viral load.

Background regimens

- ECHO - background regimen: tenofovir plus emtricitabine
- THRIVE - background regimen: 2 investigator-selected N(t)RTIs: (tenofovir plus emtricitabine) or (zidovudine plus lamivudine) or (abacavir plus lamivudine)
- Note: The background regimen in TMC278-C204 was (zidovudine plus lamivudine) or (tenofovir plus emtricitabine). See the full prescribing information for a summary of the results of this study.

Selected Baseline Characteristics and Efficacy Outcomes by Treatment Group in ECHO and THRIVE Trials

| | Rilpivirine N=686 | | | Efavirenz N=682 | | |
|---|----------------------|-------------------------------|-----------|--------------------|-------------------------------|-----------|
| | \leq 100,000 | >100,000 to \leq 500,000 | > 500,000 | \leq 100,000 | >100,000 to \leq 500,000 | > 500,000 |
| Median baseline CD4 (cells/mm ³) | 249 | | | 260 | | |
| Median plasma HIV-1 RNA (log ₁₀ copies/mL) | 5.0 | | | 5.0 | | |
| HIV-1 RNA < 50 copies/mL | 83% | | | 80% | | |
| Overall virologic failure rate | 13% | | | 9% | | |
| Discontinue due to AE/death | 2% | | | 7% | | |
| Response rate by baseline plasma HIV-1 RNA, copies/mL | 89% | 78% | 65% | 83% | 78% | 73% |
| Emergence of resistance to rilpivirine or efavirenz | 41% | | | 25% | | |
| Emergence of resistance to a background drug (emtricitabine, lamivudine, tenofovir, abacavir or zidovudine) | 48% | | | 15% | | |

- Rilpivirine was deemed to be non-inferior to efavirenz in these studies. Predicted difference in response 2.0 [95% confidence interval (-2.1;6.1)]

For more information,
please visit our website:

www.FCAETC.org

To request clinical consultation, please call the
National Clinicians' Consultation Hotline:

1-800-933-3413



IMPORTANT POINTS ABOUT RILPIVIRINE

- Virologic failure is experienced more frequently in rilpivirine-treated subjects with baseline VL >100,000 copies/mL compared to baseline VL <100,000 copies/mL.
- Higher rate of overall treatment resistance and cross-resistance to the NNRTI class with rilpivirine compared to efavirenz.
- More subjects treated with rilpivirine developed lamivudine/emtricitabine associated resistance compared to those treated with efavirenz.
- Depressive disorders reported with rilpivirine use was comparable to efavirenz use.
- Adverse reactions of GI disorders, rash, dizziness and abnormal dreams were less in the rilpivirine patients as compared to the efavirenz group.
- Lower mean lipid increases from baseline to Week 48 with rilpivirine versus efavirenz.
- Rilpivirine is primarily metabolized by the liver (cytochrome P450 3A enzymes) and has not been studied in patients with severe hepatic impairment (Child-Pugh score C). No dose adjustment for mild or moderate hepatic impairment.
- No dose adjustment for patients with mild or moderate renal impairment, but should be used cautiously in patients with severe renal impairment or end-stage renal disease.
- Rilpivirine/tenofovir/emtricitabine co-formulation is in development.

DOSING ADMINISTRATION

- Recommended adult dose of rilpivirine: one 25 mg tablet once daily taken orally with a meal. Fasting status decreases exposure to rilpivirine ~40%.
- It should be used in combination with other antiretroviral agents and only in naïve adult patients.

DRUG INTERACTIONS

The following may decrease plasma concentrations of rilpivirine due to CYP3A enzyme induction or gastric pH increase, which may result in loss of virologic response and possible resistance to rilpivirine or to the class of NNRTIs:

- Anticonvulsants: carbamazepine, oxcarbazepine, phenobarbital, phenytoin
- Antimycobacterials: rifabutin, rifampin, rifapentine
- Proton pump inhibitors: esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole
- Glucocorticoid systemic dexamethasone (more than a single dose)
- St John's wort (*Hypericum perforatum*)

The above medications are *contraindicated* with rilpivirine.

OTHER IMPORTANT DRUG INTERACTIONS

- Rilpivirine should be used with caution in patients on medications that can prolong the QTc interval since supratherapeutic doses of rilpivirine have been shown to cause QTc prolongation.
- Antacids (e.g. aluminum or magnesium hydroxide, calcium carbonate) should be taken at least 2 hours before or 4 hours after rilpivirine.
- H₂-receptor antagonists (e.g. famotidine, ranitidine) should be taken at least 12 hours before or 4 hours after rilpivirine.

ADVERSE EFFECTS

- Depression, insomnia, headache and rash

RESISTANCE MUTATIONS

The NNRTI emerging substitutions in the rilpivirine virologic failures included V90I, K101E/P/T, E138K/G, V179I/L, Y181I/C, V189I, H221Y, F227C/L and M230L. The E138K substitution emerged most frequently on rilpivirine treatment commonly in combination with the M184I substitution. The emtricitabine and lamivudine resistance-associated substitutions M184I or V and the tenofovir resistance-associated substitutions K65R or N emerged more frequently in rilpivirine virologic failures compared to efavirenz virologic failures.

- The K103N substitution did not show reduced susceptibility to rilpivirine.
- Resistance to etravirine and efavirenz in the rilpivirine failure group was 89% (n=34) while none of the efavirenz virologic failure group (n=15) showed resistance to etravirine at failure.

PREGNANCY

- Rilpivirine is Pregnancy Category B (no toxicity in animal studies, but no human data to date – use in pregnancy only if the benefit is > risk)

COST

Although retail costs vary, the average wholesale price (AWP) can be used as a method to compare relative drug costs. The AWP for a 1-month supply are as follows:

- Rilpivirine (Edurant™) 25 mg tab (#30): \$756
- Efavirenz (Sustiva®) 600 mg tab (#30): \$663

AVAILABILITY

- Rilpivirine is now available for order by pharmacies
- Rilpivirine is not yet on the Florida AIDS Drug Assistance Program (ADAP) formulary

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



EDITORIAL COMMENT:

Based on the currently available data, rilpivirine would be best used in selected treatment-naïve patients with HIV-1 RNA < 100,000 copies/mL. Patients with HIV-1 RNA > 100,000 copies/mL experienced a higher rate of failure which resulted in more resistance overall and a higher rate of NNRTI cross-resistance compared to efavirenz. The higher rate of cross-resistance to NNRTIs complicates sequencing to the 2nd generation NNRTI etravirine following treatment failure with rilpivirine. Some patients for whom there may be an advantage to using rilpivirine: patients for whom use of efavirenz has been ruled out (e.g., women of child-bearing potential who are not on adequate birth control, patients with history of psychiatric illness) and the NNRTI nevirapine cannot be used (e.g., women and men with baseline CD4 > 250 and > 400 cells/mm³, respectively) and patients who have experienced CNS-related side effects with efavirenz. Other potential benefits of rilpivirine compared to efavirenz include less increase in lipids seen in clinical trials to date and smaller pill size.

REFERENCES

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Advancing Transwomen's Health:

A Symposium to Improve Access to High Quality HIV Prevention & Care Services

Wednesday, June 29, 2011

Marriott Tampa Waterside - Tampa, FL 33602

1:00pm - 5:30 pm

(Immediately following the Ryan White Conference)

CLICK HERE FOR MORE INFORMATION

Keeping with the Pace 2011: An HIV/AIDS Update

Wednesday, August 31, 2011

12:30 PM - 4:45 PM

Check-in for on-site participants begins at
11:45 AM

**Best Western Gateway Grand
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or online via web video conferencing!

PRESENTED BY

Florida/Caribbean AIDS Education and Training Center
Florida Department of Health, HIV/AIDS Program, Alachua County
Southeastern National Tuberculosis Center
Suwannee River Area Health Education Center

Training Agenda and Registration:

www.FCAETC.org/KWP

PRE-REGISTRATION REQUIRED

DEADLINE: Monday, August 29, 2011

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

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