

# HIV CareLink

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## UPDATE ON THE 14th CONFERENCE ON RETROVIRUSES AND OPPORTUNISTIC INFECTIONS (CROI): Los Angeles, CA February 25-28, 2007

Patricia Emmanuel, MD

Associate Professor of Pediatrics  
University of South Florida College of Medicine  
Faculty, Florida/Caribbean AIDS Education and Training Center

This is an exciting time in HIV medicine with many new antiretrovirals in the pipeline. The promise of new classes of medications has arrived and several important trials of new antiretroviral therapies were presented at CROI this year.

### Abstract 104aLB and 104bLB: Efficacy and Safety of Maraviroc plus Optimized Background Therapy in Viremic ART-Experienced Patients Infected with CCR5 tropic HIV-1: 24 Week Results (MOTIVATE 1 and 2)

- Maraviroc (MVC) is one of two CCR5 inhibitors in phase III trials.
- Motivate 1 and 2 were two identical studies carried out in Europe/Australia and US/Canada respectively. Over 1,000 patients enrolled.
- Double blind, placebo controlled studies assessing the safety and efficacy of maraviroc in triple class experienced patients.
- Entry criteria: RNA > 5,000 and R5 tropic virus by tropism assay, resistant to or exposure for  $\geq 6$  mos to at least 1 agent from 3 ARV classes or at least 2 PIs.
- Patients were randomized to receive optimized background therapy (OBT) plus MVC 300 mg po QD or BID [dose changed to 150 mg po QD or BID if patient receiving any PI (except tipranavir) or the NNRTI delavirdine in the OBT].
- Baseline characteristics were equal:
  - Mean CD4 of 160 and viral load of 4.8 log<sub>10</sub>.
  - 40% of patients had enfurvitide (T-20) as part of their OBT.
- Endpoint was viral decline at 24 weeks.
- Results:
  - Mean drop in RNA of 1.9 log for treatment groups versus 1.0 log for OBT/placebo.

- 50-60 % in treatment groups at 24 weeks had RNA <400 copies/mL compared to 23% in placebo group.
  - 40-45% had <50 copies/mL at 24 weeks compared to 20% of placebo group.
  - Treatment groups experienced an average increase of 100 CD4 cells at 24 weeks compared to 50 cells in OBT alone group.
  - Adverse events were similar in all groups. There were 11 malignancies between the two studies: 5 in placebo group and 6 in MVC group.
  - There was no difference in primary endpoint for QD versus BID groups, however, subgroup analysis showed that there was a trend for those on BID MVC who had no active agents in the OBT to do better than those on QD.
  - Maraviroc is available via an expanded access program through Pfizer.  
([www.maraviroceap.com](http://www.maraviroceap.com))
- Abstract #105aLB and 105bLB: Results of Benchmark-1 and 2, a Phase III Study Evaluating the Efficacy and Safety of MK-0518, a Novel HIV-1 Integrase Inhibitor, in Patients with Triple-class Resistant Virus**
- MK-0518, now called raltegravir (RAL) is an investigational HIV-1 integrase inhibitor from Merck. Benchmark 1 and 2 were multi-center, triple-blind randomized studies, which differed only in the countries in which they were conducted.

### EDITORS

Jeffrey Beal, M.D.  
(239) 839-4645  
aetbeal@earthlink.net

Joanne Orrick, Pharm.D., B.C.P.S.  
(352) 273-6365  
orricj@nursing.usf.edu

### MANAGING EDITOR

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

### ABOUT US

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

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## Abstract #105aLB and 105bLB (continued)

- 350 patients randomized 2:1 ratio. Entry criteria: VL > 1,000 copies/mL, triple class resistant.
- Baseline characteristics were balanced:
  - Mean CD4 of 150 cells and viral load of 45,000 copies/mL.
- Raltegravir dosed at 400 mg po BID vs. placebo, each + optimized background therapy (OBT).
- Results at 16 weeks:
  - VL < 400 copies/mL: 77% RAL vs. 41% placebo.
  - VL < 50 copies/mL: 61% RAL vs. 33% placebo.
  - Increase of 80 CD4 cells in treatment group compared to 30 CD4 in placebo group.
  - No difference between AE's/SAE's between the two study groups.
  - No active agent in OBT (genotypic sensitivity score of zero) VL < 400 copies/mL: 57% RAL vs. 10% placebo.
  - One active drug in OBT VL < 400 copies/mL: 85% RAL vs. 43% placebo.
  - Further analysis showed 98% of pts receiving therapy with darunavir, enfuvirtide and raltegravir achieved VL < 400 copies/mL at 16 weeks.
- Partial analysis of resistance shows that integrase resistance can occur in two pathways N155H or Q148L/R/H.
- Longer term follow-up of this study is needed but it appears that, raltegravir will be an exciting new addition to our antiretroviral armamentarium.
- This agent is currently available via an expanded access protocol. ([www.earmrk.com](http://www.earmrk.com))

## Abstract 143 LB: The HIV Integrase Inhibitor GS-9137 Demonstrates Potent ARV Activity in Treatment-Experienced Patients

- This was a phase II, partially blinded dose finding study comparing a new Gilead integrase inhibitor, GS-9137 (elvitegravir), versus boosted PI in triple-class experienced patients.
- GS-9137 dosed at 20 mg, 50 mg or 125 mg with 100 mg of ritonavir (all po QD) vs. comparator boosted PI (CPI) each combined with optimized background therapy.
- 278 patients were enrolled in this 48 week study. Data from weeks 16 and 24 were presented.
- Results:
  - After week 8, the 20 mg dose was closed due to high rate of virologic failure.
  - GS-9137 was found to be non-inferior to CPI.
  - The 125 mg dose was superior to CPI at 16 and 24 wks.
  - There was a 1.4 to 1.7 log ↓ in VL at weeks 16-24 in the GS-9137 arm vs. 1.2 log ↓ in the CPI arm.
- In patients with no other active drug in their regimen, a prompt ↓ in VL was demonstrated but was followed by a rebound back to baseline by 24 weeks.
- There were no excess adverse events in the treatment arms.
- A phase III study is planned and the dose will be 150 mg (equivalent of the 125 mg used in this trial).

## Abstract 144 LB: 48 Week Primary Analysis of Trial TMC278-C204: TMC278 Demonstrates Potent and Sustained Efficacy in ART-naïve Patients

- TMC278 is a new non-nucleoside reverse transcriptase inhibitor (NNRTI) active against wild-type and drug-resistant HIV. It has a half life of 45 hours.
- TMC278-C204 was a randomized, active controlled, partially blinded phase IIb dose finding trial comparing three blinded QD dosages of TMC278 with open label efavirenz (EFV) each combined with lamivudine/zidovudine (Combivir®) or emtricitabine/tenofovir (Truvada®) in ART-naïve HIV-1 infected patients.
- 368 patients randomized, median baseline CD4 204 and VL 4.8 log<sub>10</sub>.
- TMC278 dosages studied were 25 mg, 75 mg and 150 mg (all po QD), and there were approximately 90 patients in each arm.
- The primary endpoint was VL < 50 copies/mL at 48 weeks.
- Results:
  - All three dose arms had equivalent viral load decline (2.6 log) and approximately 80% had viral load < 50 copies/mL. This was not different from the efavirenz arm.
  - There was a 120-140 CD4 increase at 48 weeks in all arms.
- Rash and neuropsychiatric issues were half as common in the TMC278 groups; there was also very little change in lipid levels compared with the EFV arm.
- There was a slightly increased incidence of nausea in the TMC278 groups.

## Poster Abstracts 511 and 512, CXCR4 Antagonism: Proof of Activity with AMD11070

- Up to 50% of patients with advanced disease have X4 or dual tropic viruses.
- Two posters presented early data on AMD11070, an orally bioavailable, small molecule CXCR4 antagonist.
- Both the XACT trial and ACTG 5210 evaluated 10 days of monotherapy with AMD11070.
- Patients were off therapy for at least 14 days, median CD4 was 140-190 cells and median baseline RNA was 4.5 logs. The majority of patients had dual tropic viruses.
- ≥ 1log<sub>10</sub> reduction in relative luminescence units (rlu) for X4 virus.
- With AMD11070, approximately 50% of pts had ≥ 1log<sub>10</sub> rlu reduction for X4 virus; The others did not show a significant response.
- There was no significant change in VL or CD4 from baseline.
- There were no grade three adverse events.
- In abstract 511, 3 of the 4 responders demonstrated a tropism switch to an R5 virus by the end of ten days.

This compound shows some promise against X4 viruses and will be further studied. The tropism switch seen so rapidly in these preliminary studies, does not occur as quickly with CCR5 inhibitors.

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