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UPDATE ON THE 15th CONFERENCE ON RETROVIRUSES AND OPPORTUNISTIC INFECTIONS (CROI): Boston, MA February 3-6, 2008

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The following are summaries of selected abstracts from the 15th CROI held in Boston, MA in February of this year. For more detailed information on the abstracts, go to www.clinicalcareoptions.com/HIV (conference coverage) or www.retroconference.org/2008 (program and abstracts).

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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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DATA ON RECENT MEDICATIONS

BENCHMRK-2 Phase III Study of Raltegravir (RAL)-48 Weeks.

Steigbigel R, et al., Poster 789.

- RAL 400 mg bid + OBT has > virologic and immunological efficacy compared to placebo + OBT (60% vs. 34% < 50 copies/mL, $p < 0.001$), which is sustained through week 48.
- In patients receiving new, active ARVs in OBT, up to 89% achieved HIV RNA < 50 copies/ml at week 48.
- Virologic failure associated with mutations at either Q148 or N155, in combination with ≥ 1 other mutation.
- Risk of developing malignancy is comparable between RAL and comparator groups.

TITAN Trial: Characterization of Virologic Failures on Darunavir/ritonavir.

De Meyer S, et al., Poster 874.

- TITAN is an ongoing phase III study comparing DRV/r to LPV/r in LPV-naïve, treatment-experienced patients.
- Fewer patients receiving DRV/r developed virologic failure and fewer developed primary PI mutations and NRTI RAM's compared to patients failing LPV/r-containing regimen.

- Among virologic failures, loss of susceptibility to other PIs was more frequent in patients failing LPV/r vs. DRV/r. The majority of DRV/r failures retained susceptibility to other PIs.
- Cross resistance between DRV/r and others PIs occurred less frequently in this population.

MOTIVATE Study: Maraviroc (MVC) + OBT-48 Week Results.

Hardy D, et al., Poster 792.

- Pooled 48 week results from MOTIVATE 1 (USA, Canada) and MOTIVATE 2 (Europe, Australia, USA) evaluating efficacy and safety of CCR5 inhibitor MVC in patients with R5 virus with 3-class drug-exp and/or resistance.
- > virologic suppression compared to placebo sustained at 48 weeks for MVC + OBT (45.5% <bid dose> vs. 16.7% <placebo> achieved HIV RNA < 50 copies/mL, $p < 0.0001$).
- Similar safety profile compared to placebo. More deaths reported in patients receiving MVC during the study or up to 28 days after stopping study drug; none deemed drug-related.
- MVC combined with OBT provides sustained ARV activity and tolerability through 48 weeks in treatment-exp. patients with R5 virus.

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NEW MEDICATIONS

Prevalence of Etravirine (ETR, TMC-125) Resistance Associated Mutations (RAMs).

Gaston Picchio, et al., Poster 866.

- Of 226,491 samples submitted to Virco for routine clinical resistance testing, those with ≥ 1 NNRTI IAS-USA 2006 mutation or with predicted FC in $EC_{50} >$ the vircoTYPE biological cut-off were evaluated to determine prevalence of baseline ETR RAMs.
- ETR RAMs = V90I, A98G, L100I, K101E/P, V106I, V179D/F, Y181C/I/V, G190A/S (Patients in DUET trials with ≥ 3 ETR RAMs had response comparable to placebo).
- 40% of isolates contained no ETR RAMs, 36.7%, 16%, and 7.3% contained 1, 2, or ≥ 3 ETR RAMs, respectively.
- Most prevalent ETR RAMs: Y181C and G190A
- ETR RAMs in DUET studies associated with $>$ impact on response (V179D/F, Y181V, & G190S were found at very low frequencies ($<4\%$)).
- The coexistence of ≥ 3 ETR RAMs is infrequent even in patients with baseline resistance to 1st generation NNRTIs.

Vicriviroc : VICTOR-E1 48 Week Results.

Zingman B, et al. Abst. 39LB.

- CCR5 entry inhibitor with mechanism of action similar to MVC, but with pharmacokinetic profile that allows once a day dosing when given with a RTV-boosted PI.
- VICTOR-E1: phase II double blind placebo controlled trial in patients with ≥ 3 -class ART experience.
- OBT included ≥ 2 active drugs in 43% of the cases.
- At week 48, 56% of patients receiving VCV 30 mg once daily achieved an HIV RNA <50 copies/mL compared to 14% of patients receiving placebo + OBT ($p = 0.0002$)
- No difference in Grade 3/4 adverse events.
- X4 virus emerged in 23% of VCV-treated patients vs. 9% of patients receiving placebo.

Tesamorelin (TH9507) a Growth Hormone Releasing Factor Analogue.

Falutz J, et al., Poster 943.

- Many HIV patients on ART show \uparrow visceral adipose tissue (VAT). These patients are at \uparrow risk of CVD.
- HIV patients with lipohypertrophy randomized to TH9507 (T) 2mg sq once daily or placebo (P) x 26 weeks, then randomized to continue TH9507 x 26 weeks (T-T group, n=154) or switch to placebo (T-P group, n=50) or switched to TH9507 if receiving placebo (P-T group, n=111).
- TH9507 without significant clinical effects on fasting glucose or oral glucose tolerance test.
- Significant \downarrow in VAT (trunkal fat), \uparrow in lean body mass, preservation of SQ adipose tissue and limb fat.

- TH9507 \rightarrow clinically significant \downarrow in triglycerides .
- Results suggest that TH9507 may be useful for treatment of HIV patients with lipohypertrophy.

Apricitabine (ATC)

Cahn P., et al. Abst. 793.

- ATC is a cytidine analog NRTI.
- ATC 600 or 800 mg bid + OBT vs 3TC + OBT was safe/well-tolerated, over 24 weeks in patients who failed 1st or multiple prior ARV therapy while on 3TC or FTC and with M184V mutation (n=50 patients).
- Larger phase IIb/III trials of apricitabine planned.

ADVERSE EVENTS

Abacavir (ABC) or Didanosine (ddl) and the Risk of Myocardial Infarction.

Sabin C, et al., Poster 957c and Position Statement by the D:A:D Steering Committee.

- D:A:D is a large (n=33,347) prospective observational study of 11 cohorts (Europe, US, Australia).
- ABC or ddl use within the prior 6 months was associated with \uparrow risk of MI (RR 1.90 and 1.49, respectively).
- Rates of MI/1000 person-years from patients with or without recent use of ABC was 6.1/1000 vs. 2.6/1000, respectively and ddl was 4.5 vs. 3.0, respectively.
- Cumulative use of ABC or ddl not a significant risk factor.
- \uparrow risk of MI was most pronounced in patients with high underlying CV risk, based on Framingham CHD risk assessment tool.
- D:A:D investigators could offer no potential biological mechanism to explain these findings.
- Although these findings are based on the follow-up of a large number of patients over a long period of time, they are not based on a randomized trial. It is therefore impossible to definitively exclude the possibility that the findings are explained by other factors such as channeling bias.
- The DHHS Panel is not recommending any changes to their guidelines for use of ARVs at this time. (See <http://aidsinfo.nih.gov/contentfiles/ABCComm.pdf>)



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