

# HIV CareLink

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## HIGHLIGHTS FROM THE 4<sup>TH</sup> INTERNATIONAL AIDS SOCIETY CONFERENCE ON HIV PATHOGENESIS, TREATMENT AND PREVENTION

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Part II

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The following is another installment of summaries of selected abstracts from the 4<sup>th</sup> IAS conference held in Sydney, Australia in July of this year. For more detailed information on the abstracts, go to [www.clinicalcareoptions.com/HIV](http://www.clinicalcareoptions.com/HIV) (conference summaries) or <http://www.ias2007.org/pag/> (downloadable abstracts).

### EXISTING DRUGS

**48-week efficacy and safety of darunavir/ritonavir (DRV/r, Prezista™/Norvir®) with lopinavir/ritonavir (LPV/r, Kaletra®) in LPV/r-naïve, treatment-experienced patients: (TITAN-Study).**  
Valdez-Madruga J, et al. Abstract TUAB101

- Randomized controlled, phase III trial to compare long-term efficacy and safety of DRV/r with LPV/r in patients with limited treatment experience [POWER studies demonstrated efficacy of DRV/r in heavily treatment-experienced (TRT-exp) pts]
- Study population: TRT-exp, LPV-naïve, HIV-1-infected pts (VL >1,000 copies/mL) on stable HAART for ≥ 12 wks or off-treatment for ≥ 4 wks
- Primary endpoint: non-inferiority of DRV/r to LPV/r in confirmed virologic response (VL < 400 copies/mL) at 48 wks
- 595 patients randomized to receive DRV/r 600mg/100mg bid (n=298) or LPV/r 400mg/100mg bid (n=297) plus OBR (≥ 2 NRTIs/NNRTIs)

### Results

Week 48 parameter	DRV/r bid + OBR (n=298)	LPV/r bid + OBR (n=297)	Estimated Difference DRV/r and LPV/r
VL <400 copies/mL (TLOVR), n (%)	228 (77%)	199 (67%)	10% [2%; 16%] <sup>*</sup>
VL <50 copies/mL (TLOVR), n (%)	211 (71%)	179 (60%)	11% [3%; 19%] <sup>*</sup>
Mean (±SD) log <sub>10</sub> VL change from baseline (NC=F)	-1.95±1.24	-1.72±1.34	-0.20 [-0.39; -0.004] <sup>*</sup>
Median CD4 increase, cells/mm <sup>3</sup> (LOCF)	97	102	
Incidence of serious AEs / patient discontinuations due to AEs (%)	9.4% / 6.7%	10.4% / 7.1%	
Grade 3 or 4 lab abn for total cholesterol / triglycerides (%)	8.3% / 9.0%	10.7% / 14.5%	

\* p<0.01 vs LPV/r

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### 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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- Non-inferiority criteria met [difference in response (ITT) between DRV/r and LPV/r [9% (95% CI: 2% to 16%; P < .001)]; superiority established [difference in response (ITT) between DRV/r and LPV/r 10% (95% CI 2:17) (p=0.008)]
- Rates of adverse effects generally similar between arms with exception of diarrhea occurring more frequently in LPV/r arm (14.5% vs. 7.7%) and rash occurring more frequently in DRV/r arm (3% vs. 1%)
  - Note: LPV/r-treated patients initially started on capsule formulation (approved formulation at the time) and then later switched to tablet formulation

### Conclusion

- DRV/r shown to be non-inferior to LPV/r in treatment-experienced patients; superiority also shown in this study

### Maraviroc (MVC, Selzentry™) versus efavirenz (EFV, Sustiva®)-based therapy in ARV naïve HIV-1 infected patients with R5 virus: week 48 results of the MERIT study

Saag, et al. Abstract WESS104

- Multi-center, randomized, double-blind trial of MVC (CCR5 antagonist) vs. EFV [both with Combivir® (CBV)] in ARV-naïve HIV-infected patients with R5-tropic virus
- Entry criteria: R5-tropic HIV-1, HIV RNA ≥ 2,000 copies/mL and without evidence of resistance to EFV, ZDV, or 3TC
- CBV 1 po bid + (EFV 600 mg po qd or MVC 300 mg po bid)
  - Arm containing MVC once daily was discontinued in January 2006
- Primary endpoint: % of patients with HIV-1-RNA < 400 and < 50 copies/mL at week 48; noninferiority of MVC vs EFV

### Results

- 721 patients (29% female)
  - Baseline median CD4+ count (241 and 254 cells/mm<sup>3</sup>) and mean HIV-1 RNA (4.9 and 4.9 log<sub>10</sub> copies/mL) were similar in the MVC-BID and EFV arms, respectively.

Week 48 results, As Treated	MVC BID + CBV (N=360)	EFV + CBV (N=361)	Difference* (lower bound of 1-sided 97.5% CI)
HIV RNA <400 copies/mL, %	70.6	73.1	-3.0 (-9.5)
HIV RNA <50 copies/mL, %	65.3	69.3	-4.2 (-10.9)
Mean Change from BL in CD4+ count, cells/mm <sup>3</sup>	170	143	26 (7-46†)
Patients with Category C Events	6 (1.7)	12 (3.3)	N/A

\* adjusted for randomization strata; †95% CI

- Discontinuations due to lack of efficacy: 11.9% MVC vs. 4.2% EFV
- Discontinuations due to AEs: 4.1% MVC vs. 13.6% EFV

### Conclusions

- MVC failed to meet non-inferiority endpoint vs. EFV for < 50 copies/mL
- MVC non-inferior to EFV at < 400 copies/mL
- Greater ↑ in CD4 count with MVC vs. EFV and fewer discontinuations due to AEs

### ADVERSE EFFECTS

### Renal function changes at two years in HIV-infected patients treated with tenofovir-DF (Viread®, TDF)

Javanbakht M, et al. Abstract MOPEB064

- Retrospective cohort study of patients receiving a TDF-containing ARV regimen over a 2 year period (2001-2003), using electronic medical records.
- TDF patients matched on HIV viral load and CD4 counts to subjects receiving a non-TDF regimen.
- Changes in creatinine clearance compared between groups at 6, 12 and 24 months

### Results

- n=896
- Baseline characteristics (age, gender, race/ethnicity, hypertension, diabetes, substance abuse, creatinine levels) similar between the two groups.
- A greater ↓ in CrCL was seen for those in TDF group at all time periods
- Statistically significant different at 24 months
  - ≥ 30 ml/min ↓ in CrCL: 23.2% on TDF-based regimen vs. 9.7% on a non-TDF regimen (p=0.0041)
- After adjusting for substance abuse, diabetes, hypertension and creatinine levels patients on a TDF regimen for ≥ 2 years 3.2 x more likely to have ↓ in CrCL compared to those on non-TDF regimen [odds ratio (OR)=3.2; 95% confidence interval (CI) 1.5 – 6.9].

### Conclusion

- TDF-containing ARV regimen associated with a greater ↓ in CrCL at 2 years than for non-TDF regimens. Recommendation: close monitoring of renal function in patients on TDF regimens.



## DRUG INTERACTIONS

**Pharmacokinetic interaction between the non-nucleoside reverse transcriptase inhibitor (NNRTI) TMC125 (etravirine) and atorvastatin (Lipitor®) in HIV-negative volunteers.**  
Schöller-Gyüre M, et al. Abstract WEPEA106.

- TMC 125 is an investigational NNRTI that is a substrate and inducer of CYP3A4 (atorvastatin is partially metabolized by CYP3A4)
- Open-label, randomized, 2-period crossover trial:
  - Treatment A: 40 mg atorvastatin daily for 4 days, followed by a 14 day washout period.
  - Treatment B: 800 mg TMC125 administered during Days 1-13. Atorvastatin was co-administered on Days 8-11.
- Pharmacokinetics of TMC125 assessed on Day 7 and Day 11 of Treatment B.
- Pharmacokinetics of atorvastatin and its metabolites assessed on Day 4 of Treatment A, and Day 11 of Treatment B, for 24 hours.

### Results

- Total Patients (n=16); 14 males; median age 40
- PK of TMC125 not affected by coadministration of atorvastatin.
- Coadministration with TMC125 ↓ total exposure to atorvastatin by 37% (but ↑ exposure to active atorvastatin metabolite by 27%)

### Conclusion

- TMC125 and atorvastatin can be coadministered without dose adjustment

**PK analysis of rifabutin (RBN) given with lopinavir/ritonavir (LPV/r, Kaletra®) to persons co-infected with TB and HIV.**

Boulanger C, et al. Abstract WEPEB006

- PK analysis of RBN ± lopinavir/ritonavir (LPV/r)
- Open label prospective study of HIV-infected pts in an in-patient state TB hospital in Florida (i.e. AG Holley)
- Steady state (2 weeks) serum concentrations collected at 0, 2, 4, 8, 12, 24, and 48 hours
- Analysis performed on 5 patients

### Results

- Medians RBN AUC(0-24) for both the RBN 300 mg 3 x weekly without LPV/r and RBN 150 mg 3 x weekly with LPV/r were below that associated with acquired rifamycin resistance (median 3.3 mcg•hr/ml in TBTC 23A study)
- RBN AUC(0-24) for RBN 300 mg 3 x weekly with LVP/r was closest to the value associated with cure (median 5.2 mcg•hr.mL in TBTC 23A study)
- No significant difference in toxicities amongst the groups

### Conclusions

- Suggests that RBN 300 mg 3 x weekly or RBN 150 mg 3 x weekly with LPV/r may be inadequate for some patients (Consider RBN 300 mg 3 x weekly with LPV/r)
- Consider TDM of RBN in HIV-infected TB pts, whether on HAART or not.

### TB IN HIV

**Use of QuantiFERON®-TB Gold Test to screen for tuberculosis in HIV-infected Patients.**

Aichelburg MC, et al. Abstract MOPEB021

- Longitudinal study of 701 HIV-infected patients who had had a QuantiFERON®-TB Gold Test (QFT) screen for tuberculosis
- Mean follow up time of 6 months

### Results

	Number of patients (%)	Mean CD4	Patients with Active TB
QFT reactive	39 (5.6%)	480	3
QFT indeterminate	33 (4.7%)	297	0
QFT negative	629 (89.7%)	441	0

(*p*=0.001 vs QFT reactive, *p* < 0.001 vs QFT negative)

### Demographics of Patients with Positive QFT Results (Total of 39 patients)

From High Incidence Country	23 (59.0%)
Risk Factors for acquiring TB infection (travel to high risk country, close contact with infected person)	29 (80.6%)
Systemic or Pulmonary symptoms without microbiological or radiological evidence of active TB	22 (56.4%)
Number who died during follow-up period	2 (5.1%)
Number of patients without active TB at baseline who developed active TB during follow-up	0 (0%)

- In 2 patients, a positive QFT revealed occult TB
- There was a 64% concordance between the QFT and tuberculin skin tests

### Conclusions

- QFT test is highly sensitive
- Possibly can reveal sub- or preclinical TB even in moderately immunocompromised HIV patients
- More data are needed before QFT test can be universally recommended as a screening tool for tuberculosis in HIV-infected patients