

HIV CareLink

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UPDATE ON THE 14th CONFERENCE ON RETROVIRUSES AND OPPORTUNISTIC INFECTIONS (CROI): Los Angeles, CA-Part 3 February 25-28, 2007

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The following are summaries of selected abstracts from the 14th CROI held in Los Angeles, CA in February of this year. For more detailed information on the abstracts, go to www.clinicalcareoptions.com/HIV (conference summaries) or www.retroconference.org/2007 (downloadable abstracts).

HIV-Induced Immunodeficiency Markedly Increases Risk of Fatal AIDS-Defining Malignancies (ADM)

Monforte AD, et al. Abstract 84

- Risk of ADM ↑ with immunodeficiency but risk of non-ADM unclear
- Risk factors for fatal ADM and non-ADM identified using multivariable Poisson regression analyses in D:A:D study
- D:A:D study: compilation of 11 cohorts providing data on 23,441 HIV-infected persons seen since 1999
- Causes of death classified using standardized, centralized procedure

Results

- Total deaths: 1246; 193 due to fatal non-ADM, 112 due to fatal ADM
- Most frequent non-ADM organs: lungs (n=62), GI tract (n=41), heme system (n=20), anal canal (n=20)
- Median CD4+ count: 75 cells/mL and 211 cells/mL for ADM and non-ADM, respectively
- RR of ADM or non-ADM with fatal outcome increased with lower latest CD4+ cell count
- RR not influenced by latest HIV RNA level

Latest CD4 count (uL)	Person-years (PY)	Non-AIDS defining malignancies		AIDS-defining malignancies	
		Rate (/1000py) (n)	Relative risk* (p)	Rate (/1000py) (n)	Relative risk* (p)
<50	2335	6.0 (14)	15 (<0.001)	20.1 (47)	175 (<0.001)
50-99	2295	9.6 (22)	19 (<0.001)	4.8 (11)	41 (<0.001)
100-199	8097	6.8 (55)	10 (<0.001)	2.8 (23)	24 (<0.001)
200-349	21048	2.0 (43)	3 (<0.001)	0.7 (14)	6 (<0.001)
350-499	24052	1.1 (27)	2 (0.03)	0.3 (7)	3 (0.09)
500+	46903	0.6 (27)	1 (-)	0.1 (5)	1 (-)

*adjusted for cohort, age, gender, smoking status, weight, transmission group, ethnicity, prior non-fatal non-neoplastic AIDS, HCV and HBV status, cART exposure, and latest HIV-RNA level

Conclusions

- Fatal non-ADM now more frequent than fatal ADM in pts with access to ART and is likely to continue to increase as the HIV-infected population ages

Sustained Virologic Response (SVR) in ART-Naive Patients Receiving Lopinavir/Ritonavir (LPV/r, Kaletra®)-Based HAART Does Not Differ With qd vs. bid Dosing or With Directly Observed Therapy (DOT)

Mildvan D, et al. Abstract 138

- Randomized, multicenter, 3 arm 48-week trial aimed to study use of less complicated dosing (qd vs. bid) and DOT in treatment-naïve patients initiating ART
- Study population: 402 ART-naïve patients with HIV-1 RNA ≥ 2000 copies/mL randomly stratified by HIV RNA level (> or ≤ 100,000 copies/mL) to receive LPV/r soft gel capsules:
 - 400/100 mg bid, self-administered
 - 800/200 mg qd, self-administered
 - 800/200 mg qd, DOT Monday-Friday, weeks 0-24 (self-administered qd weeks 24-48)
- LPV/r was backed with qd dosing of emtricitabine (FTC) + [stavudine (d4T XR, not commercially available) or tenofovir (TDF)]
- Primary efficacy endpoint: SVR (<200 copies/mL, intent-to-treat) at 48 weeks
- Median baseline counts: CD4+ 197 cells/mm³, HIV RNA 4.8 log₁₀ copies/mL

Results

- Overall SVR through week 48 did not differ significantly between bid and qd self-administered group
 - SVR probability difference: 0.03; 95% CI: 0.07, 0.12
- Probability of SVR through week 48 was significantly greater in bid arm in pts with HIV RNA ≥ 100,000 copies/mL
 - SVR probability difference: 0.13; 95% CI: 0.01, 0.25

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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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Results (cont)

- Probability of SVR in pts with lower HIV RNA not significantly different in bid and qd self-administered
 - SVR probability difference: -0.08; 95% CI: -0.23, 0.06
- Probability of SVR through week 24 higher for DOT than qd self-administered but difference not significant and not seen at 48 weeks; (Median DOT visit compliance 86%)

Conclusions

- No difference in SVR between bid and qd LPV/r. However, ART naïve patients with high HIV RNA may benefit from bid dosing.
- While DOT may show some promise, potential benefit is not sustained once self-administered therapy is resumed by patient

Metabolic Complications of Class-Sparing Regimens for Initial Treatment of HIV (ACTG 5142)

Haubrich RH, et al. Abstract 38

- Metabolic effects of lopinavir/ritonavir (LPV/r)- or efavirenz (EFV)-based regimens + 2 NRTIs have not been compared
- Role of NRTI-sparing regimen in preventing lipotrophy also unknown
- Open-label, randomized trial compared class-sparing regimens
- Study population: 753 ART-naïve HIV patients
 - Median CD4: 182 cells/mm³; median HIV RNA: 100,000 copies/mL, median follow-up: 112 weeks
 - [LPV/r (533/133 mg bid, dose increased from 400/100 mg bid due to interaction with EFV) + EFV (standard dose)] vs. (LPV/r + 2 NRTI) vs [EFV + 2 NRTI (all standard dose)]
 - Selected NRTI: zidovudine (AZT, 42%), stavudine (d4T XR, 24%), or tenofovir (TDF, 34%), each + lamivudine (3TC)
- Metabolic objectives evaluated at baseline and at 48 and 96 weeks
 - Changes in fat (DEXA)
 - Lipotrophy: ≥ 20% loss of limb fat from baseline
 - Fasting lipids

Results

Week 96 Result	Primary Randomized Arm					NRTI (LPV and EFV Arms)				
	N	EFV	LPV	LPV/EFV	p ≤ 0.01	N	d4T	TDF	ZDV	p ≤ 0.05
	Median value or %					Median value or %				
% Δ extremity fat	498	0.3	9.9	18	a,b,c	329	-11	17	2.0	d,e,f
% Δ trunk fat	498	12	19	17	--	329	11	23	16	d
Lipo-atrophy	498	32%	18%	8%	a,b,c	329	43%	10%	27%	d,e,f
Δ TC (mg/dL)	517	33	33	57	b,c	343	41	21	33	d
Δ HDL (mg/dl)	508	9	8	16	b,c	334	8	8	9	--
Δ non-HDL (mg/dL)	506	21	26	43	b,c	333	26	17	26	d
Δ TG (mg/dL)	518	14	47	63	a,b*,c	344	47	21	24	d

Pairwise comparisons: a = EFV vs LPV; b = LPV vs LPV/EFV; c = EFV vs LPV/EFV; d = d4T vs TDF; e = TDF vs ZDV; f = ZDV vs d4T. b = 0.025. If not listed, p > 0.05

Conclusions

- NRTI-sparing regimens ↑ lipids significantly more than NRTI-containing regimens; greater ↑ in triglycerides as well. Total cholesterol changes not significantly different.
 - LPV/r had less lipotrophy compared to EFV when given with NRTI
 - Frequency of lipotrophy lowest in NRTI-sparing and TDF-containing regimens

Safety and Efficacy of TH9507, A Growth Hormone Releasing Factor Analog, on HIV-Associated Abdominal Fat Accumulation

Falutz J, et al. Abstract 45

- HIV therapy associated metabolic complications: abdominal fat accumulation, ↑ waist circumference, dyslipidemia, insulin resistance, and others
- Currently no approved medical treatment to limit increase in visceral adipose tissue (VAT)
- In HIV-infected pts with body fat changes, growth hormone (GH) is reduced. GH supplementation may help, but causes adverse effects (e.g. ↑ glucose)
- Randomized, double-blind, placebo-controlled phase III trial to determine efficacy and safety of TH9507
- Study population: 412 HIV-infected pts with abdominal fat accumulation.
 - Baseline Characteristics (median): age 48 ± 7 years; waist-to-hip circumference: 1.1 ± 0.1; waist circumference: 104 ± 10 cm
 - 19% with Type 2 DM or glucose intolerance
- Pts randomized to receive TH9507 2 mg SC qd or placebo injection for 6 months
- Primary endpoint was % change in VAT by CT scan

Results

- At week 26, VAT ↓ significantly with TH9507 vs. placebo. Trunk fat ↓ as well. Less changes in abdominal subcutaneous adipose tissue (SAT) and limb fat
- Lipid profile also improved with significant ↓ in triglycerides and cholesterol/HDL ratio

% Change in Parameters

Treatment	VAT	Trunk Fat by DEXA	Addominal SAT	Limb Fat
TH9507	-15.2	-1	0.4	0
Placebo	5	0.4	1.8	0.2
P value	<0.001	<0.001	0.05	0.1

- Mean insulin-like growth factor (IGF-I) ↑ within physiologic range in TH9507-treated pts
- Overall treatment well tolerated (no difference in adverse effects compared to placebo)

Conclusions

- TH9507 ↓ VAT in HIV-infected patients with abdominal fat accumulation after 26 weeks of treatment
- Nominal effect on subcutaneous abdominal fat or peripheral limb fat; slight lipid profile improvement
- No adverse effects associated with GH (e.g. hyperglycemia) developed

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Improved Immunogenic Response to Hepatitis B Vaccine in HIV-infected Individuals Receiving CPG 7909 Adjuvant

Cooper C et al. Abstract 134

- Immunosuppression causes HIV patients to be hyporesponsive to vaccines, including hepatitis B (HBV)
- CPG 7909, a cytidine-phosphate-guanosine (CpG) oligodeoxynucleotide motif, activates human B cells and plasmacytoid dendritic cells via toll-like receptor 9 (TLR9)
- Randomized, double-blind, placebo-controlled trial to evaluate safety and efficacy (increased HBV immunogenicity) of CPG 7909 in HIV-infected adults (CD4+ > 200) on ART for > 6 mos (HIV VL < 50 copies/mL for ≥ 3 mos)
- HBV susceptible subjects vaccinated at 0, 1, and 2 months with double standard adult dose (40 µg/mL) of Engerix-B® ± 1 mg CPG 7909. Seroprotective titers (anti-HBs titre ≥ 10 mIU/mL) obtained every 6 months until month 60; missing values interpolated.
- Subjects immune to HBV at study entry received 1 mg CPG 7909 or placebo
- Study population: 58 HIV-infected pts 18-45 yrs of age, on ART > 6 months, and undetectable HBsAg and HBV DNA
 - 38 HBV susceptible, Median HBV titer: 0 mIU/mL
 - 19 HBV vaccine naïve
 - 19 prior HBV vaccine nonresponders
 - 20 HBV immune at baseline
 - Median HBV titer: 146 mIU/mL placebo; 1051 mIU/mL CPG 7909
- Immunogenicity analyzed at weeks 0, 2, 4, 6, 8, 10, 12, 24, 48 then q6 months thereafter, until 60 months

Results

- Mean anti-HBs titers higher in pts given HBV vaccine + CPG at all time points (p < 0.05)
- Proportion of patients retaining seroprotective titers was greater in the CPG 7909 group
- Greater proportion of CPG + HBV vaccine group achieved high-titer anti-HBs response (≥ 100 mIU/mL)

Month from initial vaccine	Proportion Retaining Seroprotective Titers (anti-HBs ≥ 10 mIU/mL)		
	CPG n (%)	Control n (%)	P value
36	17/18 (94)	10/18 (56)	0.02
42	14/16 (88)	8/17 (47)	0.03
48	11/13 (85)	8/17 (47)	0.06
54	9/11 (82)	4/13 (31)	0.02
60	6/8 (75)	3/12 (25)	0.07

Adverse effects

- Significantly more pain at injection site in CPG group
- Greater ↓ in CD4+ cell counts in CPG group
 - ~200-250 cells/mm³ ↓ in CD4 cell count seen 1 day after each vaccination in CPG group, transient and returned to baseline within 2 wks

Conclusions

- CPG 7909 increases immunogenicity of HBV vaccine in HIV-infected pts and warrants further investigation

The Florida/Caribbean AETC Welcomes
The 2007 National Conference on Latinos and AIDS
A National Forum on HIV/AIDS for Health Professionals Who Provide Care for Latinos

www.minority-healthcare.com

July 30–31st, 2007
 Miami Beach Resort & Spa - Miami, FL

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