Title: Long-Term Changes in Lipids and Glucose/Insulin Levels Among HIV-Infected Antiretroviral Naïve Persons Randomized to PI vs. NNRTI vs. PI + NNRTI-Based Antiretroviral Regimens: Results of the CPCRA 061 Metabolic Study

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Background: Long-term comparative data on metabolic effects of initiating different antiretroviral treatment (ART) strategies are limited.
Methods: Fasting triglycerides (TG), LDL-cholesterol (LDL-C), HDL-C, glucose, and insulin were measured at baseline, 1-month follow-up, and 4-month intervals among 422 antiretroviral-naïve patients randomized to 1 of 3 strategies: PI (N=141), NNRTI (N=141), or PI + NNRTI (N=140) containing regimens. The rates of change (mg/dL/month) were estimated using slopes of regression lines and overall mean changes from baseline were compared by strategy.
Results: Median age was 38 years; 22% female; 60% African-American and 10% were Latino. The mean change at 1-month, rates of change after the first follow-up, and overall mean changes (median follow-up 5 years) were:

	TG (mg/dL)			HDL-C (mg/dL)			LDL-C (mg/dL)		
Strategy	1 mo	Slope	Mean	1 mo	Slope	Mean	1 mo	Slope	Mean
PI	2.1	0.50*	15.2*	3.4*	0.01	5.6*	14.3*	-0.32*	8.5*
NNRTI	2.8	0.68*	24.9*	7.5*	-0.04	10.3*	11.6*	-0.26*	7.9*
PI + NNRTI	48.9*	-0.14	35.0*	5.1*	0.03	9.2*	25.5*	-0.42*	12.8*
Strategy differences									
NNRTI-PI	NS	NS	NS	<0.05	NS	<0.05	NS	NS	NS
PI+NNRTI-PI	<0.05	NS	<0.05	NS	NS	NS	<0.05	NS	NS
PI+NNRTI-NNRTI	<0.05	<0.05	NS	NS	NS	NS	<0.05	NS	<0.05

*P<0.05

Significant increases were seen in overall mean insulin and glucose levels which did not differ by strategy (mean insulin change: PI: 3.86mu/ml, NNRTI: 2.95mu/ml, PI + NNRTI: 2.69mu/ml, p=0.98) (mean glucose change: PI: 2.92mg/dL, NNRTI: 4.88mg/dL, PI + NNRTI: 5.21mg/dL, p=0.36). PI + NNRTI strategy required more lipid-lowering treatment, while incidence of diabetes did not differ by strategy.
Conclusions: In this prospective trial, all ART strategies had impact on lipid and glucose metabolism. Highest increase in TG and LDL was noted in PI+NNRTI containing regimens.

HDL increased the least on PI. Significant increases in insulin were seen with all strategies. These findings necessitate close monitoring of patients.