Darunavir or Atazanavir vs Raltegravir Lipid Changes Are Unlinked To Ritonavir Exposure: ACTG 5257

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Background: Lipid profiles following antiretroviral therapy (ART) vary by regimen type and by ritonavir (RTV) exposure. Changes in fasting lipid profile (FLP) were assessed after ART initiation and correlated with plasma RTV trough concentrations (C24) in the A5257 study.

Methodology: ART-naïve individuals >age 18 years with HIV-1 RNA level>1000 copies/mL were eligible. Subjects were randomized 1:1:1 to ATV (atazanavir 300 mg daily (QD)+RTV 100 mg QD), RAL (raltegravir 400mg twice daily) or DRV (darunavir 800mg QD+RTV); all subjects received emtricitabine/tenofovir 200/300 mg QD. Subjects were followed until the last enrolled reached 96 weeks. FLP was measured at weeks 0, 24, 48, 96, and 144, and steady state RTV C24 (24±2 hours post dose) was measured once for a subset of subjects on RTV tablet. Mean changes in FLP over time from baseline were plotted with 95% confidence intervals (CI), differences between ART regimens were estimated with 97.5% CI and compared using pairwise Student’s T-tests. Associations between RTV C24 and changes in FLP at 48 weeks were evaluated via Spearman correlations.

Results: A total of 1809 subjects were enrolled; 34% non-Hispanic white, 42% non-Hispanic black, 22% Hispanic, 24% were women. Subjects with confirmed baseline fasting samples were included in the analyses (n=1797). Baseline overall median HDL-cholesterol (HDL-C) 38 mg/dL, calculated LDL-cholesterol (LDL-C) 92 mg/dL, and triglycerides (TG) 103 mg/dL. LDL-C and TG levels increased with DRV and ATV but not with RAL from baseline to week 144 (Fig 1a-b). While these 2 lipid parameters were not different between DRV and ATV, each protease inhibitor (PI) arm had greater increases in these parameters compared with the RAL arm (all p≤0.001). HDL-C increased modestly with no differences between arms (all p>0.05) [Fig 1 c]. As-treated and sensitivity analyses excluding subjects on lipid-lowering agents did not change results. RTV C24 was quantified in a subset (109 on ATV and 119 on DRV) with median values of 69 ng/mL and 74 ng/mL in the ATV and DRV arms, respectively (p=0.9). No significant correlation existed between RTV C24 and changes in any of the lipid parameters (p>0.1) (Fig 1d).

Conclusions: The RAL arm produced the most favorable lipid profile. RTV C24 was not different between the 2 PI arms and had no relationship with the modest but similar increases in lipids observed with either the ATV or the DRV arm. The long-term clinical significance of the lipid changes noted in the PI arms relative to the RAL arm are unknown.

Figure 1: Panels a-c: Mean of Changes from Baseline in Fasting Lipid Profile (mg/dL) over Time; panel d: C24 (log(ng/mL)) and Fasting Triglycerides: Change from Baseline to Week 48