Darunavir or Atazanavir vs Raltegravir Lipid Changes are unlinked to Ritonavir Exposure: ACTG 5257

ABSTRACT

Darunavir (DRV) or Atazanavir (ATV) are both approved for use with ritonavir-boosted protease inhibitors (PIs) to treat HIV-1 infection. The impact of these PIs on lipids is unclear.

METHODS

A5257 trial evaluated the virologic efficacy and tolerability of RAL and 2 RTV boosted PIs (ATV and DRV) co-administered with FTC/TDF in treatment naïve HIV-infected individuals. A5257 was a phase III, prospective, randomized, open-label trial comparing 3 non-nucleoside reverse transcriptase inhibitors (NRTIs): 400 mg/d RAL, 100 mg/d RTV (co-administered with 100 mg/d FTC), and 800 mg/d DRV (co-administered with 100 mg/d FTC). All subjects received FTC/TDF at 200 mg/d. Subjects were randomized to receive either: (1) ATV/RTV 400/100 mg QD; (2) DRV/RTV 800/100 mg QD; (3) RAL 400 mg QD + FTC/TDF 200 mg/200 mg QD. Subjects received the above RTV-boosted regimens for 48 weeks for virologic and safety evaluation. Blood samples were collected at enrollment, 24, 48, and 96 weeks for lipid analysis. The primary endpoint of the trial was change in TC measured at week 48 from baseline. Secondary endpoints included DRV vs. ATV change in triglycerides (TG), TC, HDL-C, LDL-C, and non-HDL-C, ATV vs. RAL change in TG, TC, HDL-C, LDL-C, and non-HDL-C, DRV vs. RAL change in TG, TC, HDL-C, LDL-C, and non-HDL-C, and all changes in lipids are reported as the mean difference from baseline.

RESULTS

Baseline demographic characteristics for the 595 subjects who completed the trial are presented in Table 1. The baseline demographics and viral loads were comparable between the 3 ART arms.

Of the 595 subjects evaluated in A5257, 197 with confirmed baseline fasting samples were included in the PK-PD analysis. Baseline demographic, characteristics and metabolic profiles were similar across arms and are summarized in Table 1.

ATV vs. RTV: DRV/RTV vs. ATV

No significant differences were observed in Fasting TG, Fasting TC, Fasting HDL-C, and Fasting LDL-C between the ATV/RTV and DRV/RTV treatments. The median change in TC, HDL-C, and LDL-C with ATV/RTV were similar to that of DRV/RTV.

The change in triglycerides (TG) with ATV/RTV was similar to that of DRV/RTV. With RAL 400 mg/d, an increase of 41 mg/dL was observed in Fasting TG compared with ATV/RTV.

CONCLUSIONS

Individuals on RTV boosted PI regimens maintain stable lipids over time. Differences in lipids observed with other ART regimens were apparent. With the exception of HDL-C levels, at study entry the majority of this change resulted from exposure to ART and was not different between ATV and DRV.

REFERENCE