Clinical course of increased LFTs and hepatic events associated with ritonavir (RTV)-boosted tipranavir (TPV/r) based therapy in the RESIST trials

Abstract
Baseline characteristics of RESIST 1 and 2 patients

Methods
The RESIST 1 and 2 studies were pragmatic, open-label, community-based Phase III studies of TPV/r (800/100 mg) or CPI/r (1000 mg) in treatment-naive and treatment-experienced HIV-infected patients. At entry, all patients were taking stable antiretroviral regimens, including two nucleoside reverse transcriptase inhibitors (NRTIs, NNRTIs, PIs) and at least one protease inhibitor (PI) [2-5]. RESIST 1 is taking place in North America and Australia; RESIST 2 in Europe. 1486 patients received TPV/r or CPI/r plus OBR. Baseline characteristics were similar in both studies and both treatment arms (Table 1).

Results
Baseline characteristics

Conclusion
The analyses have been updated to reflect the completion of 48 weeks of follow-up. During the first 48 weeks of RESIST, 76/749 (10.1%) TPV/r patients developed Grade 3/4 ALT and/or AST. Of these 76 pts, 71 had Grade 3/4 ALT and 45 had grade 3/4 AST. Tables 2 presents the number of RESIST patients with Grade 3/4 ALT or AST levels, and by end of follow-up (Table 4).

Incidence of Grade 3 or greater transaminase elevations during week 48 of the RESIST studies. Cox multivariate regression analysis of time to Grade 3 or greater transaminase elevation was performed. Baseline ALT or AST levels, race, and gender, showed that TPV/r treatment (HR=2.77, 95% CI 1.85-4.17, p=0.0001) and an initial grade 3 or higher ALT/AST level at baseline (HR=2.09, 95% CI 1.47-3.33, p=0.0004) were independent risk factors for development of Grade 3/4 ALT/AST (Table 4). Baseline ALT/AST were also a risk factor for both treatment arms (RR=2.03, 95% CI 1.40-3.02, p<0.0001). Male gender (HR=1.16, 95% CI 0.63-2.15, p=0.636) and race (HR=1.32, 95% CI 0.66-2.65, p=0.88-4.70) but did not reach significance (p=0.10).

Risk Factors
Table 3: Potential risk factors for the occurrence of Grade 3/4 ALT/AST elevations during week 48 of RESIST studies. Cox multivariate regression analysis of time to Grade 3 or greater transaminase elevation was performed. Baseline CD4+ cell count, race, and gender, showed that TPV/r treatment (HR=2.77, 95% CI 1.85-4.17, p=0.0001) and an initial grade 3 or higher ALT/AST level at baseline (HR=2.09, 95% CI 1.47-3.33, p=0.0004) were independent risk factors for development of Grade 3/4 ALT/AST. Baseline ALT/AST were also a risk factor for both treatment arms (RR=2.03, 95% CI 1.40-3.02, p<0.0001). Male gender (HR=1.16, 95% CI 0.63-2.15, p=0.636) and race (HR=1.32, 95% CI 0.66-2.65, p=0.88-4.70) but did not reach significance (p=0.10).

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