Letters to the Editor

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The Use of Darunavir/Ritonavir as Intensification in Low Viremic HIV-Infected Patients Treated With Boosted Protease Inhibitor-Containing Regimens

To the Editor:

Persistent low-level viremia is a precursor to the development of resistant mutations leading to overt treatment failure.[1] Hence, the most updated US Department of Health and Human Services (DHHS) guidelines recommend that the goal of human immunodeficiency virus (HIV) treatment is to suppress HIV-RNA levels maximally and prevent further selection of resistance mutations, if possible.[2] Trials of newer antiretroviral (ARV) agents have shown that it is possible to achieve plasma HIV-1 RNA levels below 50 copies/mL even in highly treatment-experienced patients.[3] Darunavir (DRV) is an example of a newer ARV agent belonging to the class of protease inhibitors (PIs) with potent antiviral effect on wild type and resistant HIV virus. We hypothesize that patients with a low-level viremia while treated with ritonavir-boosted PI (PI/r), in the absence of genotypic mutations, will be able to achieve complete viral suppression with DRV/r.

Patients were selected if they had been on a stable PI/r-containing regimen for at least 12 months and had >95% adherence by self-report and physician evaluation. Low viremia was defined as having HIV-RNA level >50 but <2000 copies/mL on 2 consecutive occasions within last 3 months before enrollment and no evidence of DRV genotypic mutations. DRV/r was added in place of PI/r without changing other agents.

A total of 14 patients met these selection criteria. The median age was 55 years (range: 38-62) with 93% being male (n = 13). The PI/r consisted of lopinavir/r in 6 patients, fosamprenavir/r in 4, atazanavir/r in 2, and lopinavir/saquinavir/r in 2. Ten patients were also receiving tenofovir and emtricitabine and 4 abacavir (ABC) and lamivudine (3TC). Genotypic testing in all patients did not disclose any resistant conferring mutation to DRV or other PIs. The median baseline CD4 count and HIV-RNA levels were, respectively, 345 cells/mm^3 (7-586) and 774 copies/mL (2.9 $\log_{10}$; 139-1450). At week 12, the median CD4 count was increased by +42 cells/mm^3 and 93% of patients were <400 copies/mL (n = 13). At week 24, the median CD4 count was 412 cells/mm^3 (+69 from baseline; 29-837) with 100% of patients <400 copies/mL and 93% of patients <50 copies/mL (n = 13; <50-250). Total cholesterol and triglycerides were 162 mg/dL (119-218) and 200 mg/dL (79-416) at baseline; 155 mg/dL (101-268) and 120 mg/dL (72-280), respectively, at week 24. All patients tolerated DRV/r well and there were no ≥grade 2 adverse events.

Previous studies have shown the impact of mutational patterns in the presence of low-level viral replication. One such retrospective study was the continuous treatment with Trizivir (the fixed-dosed combination of ABC, 3TC, and zidovudine) in the presence of viral replication, which resulted in a stepwise accumulation of resistance mutations.[4] Lafeuillade et al performed 2 genotypic tests on 22 HIV-positive patients while they were receiving a stable regimen of ARV drugs and maintaining viral loads between 50 and 1000 copies/mL.[5] Almost 70% of the patients developed new mutations over a median of 28 months. In another retrospective analysis, the EuroSIDA cohort focused on 110 patients with HIV-RNA >400 copies/mL who continued on failing regimens for a median of 6 months.[6] Overall, 77% of patients acquired 1 or more mutations over the study period. Although our study does not address the etiology of low-level viremia, it demonstrates that intensification with a potent agent is able to reduce detectable viremia, in all but one, indicating that this approach could be a viable option.

In summary, our findings suggest that DRV/r is a viable alternative in allowing HIV-RNA suppression to undetectable levels in patients with low-level viremia treated with a boosted PI. In addition, DRV/r seems to be associated with improvement in triglyceride parameters. The newer ARV agents with increased potency (ie, DRV/r) and/or newer viral targets (ie, HIV integrase inhibitors) may be of help. Further studies are needed.

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