Correspondence

Class of Antiretroviral Therapy and CD4+ T Cell Count Recovery: Independence Questioned

To the Editor—I would like to congratulate Khanna et al. [1] for their study, which investigated risk factors associated with poor increases in the CD4+ T cell count in a Swiss cohort of HIV-1–infected patients. A priori knowledge of these factors would be very useful in clinical practice to aid in the selection of the combination antiretroviral therapy (ART) regimen that is most likely to optimize immunologic recovery.

In terms of increases in the CD4+ T cell count, however, Khanna et al. [1] reported “similar” (nonsignificant) effects for boosted protease inhibitors (PIs; 452 recipients; median increase, 343 cells/μL), nonnucleoside reverse-transcriptase inhibitors (NNRTIs; 251 recipients; median increase, 255 cells/μL), and nonboosted PIs (2590 recipients; median increase, 310 cells/μL). In contrast, a large, systematic review [2] reported significant differences in CD4+ T cell count among recipients of these ART classes after 48 weeks of treatment: for boosted PIs (1002 recipients), the increase was 200 cells/μL; for NNRTIs (6705 recipients), the increase was 173 cells/μL; and for PIs (4602 recipients), the increase was 179 cells/μL. Importantly, the superior and statistically significant effect on the CD4+ T cell count associated with boosted PI ART was also noted in multivariate analysis [2]. It remains uncertain whether the discordant conclusions of these 2 studies resulted from differences in statistical power, from the statistical model used (Cox vs. linear regression), or from bias adjustment.

I would also like to point out that, in the 2 studies cited in the Discussion section to support the absence of a statistically significant difference in effect between boosted PIs and NNRTIs, the one randomized study [3] included atazanavir—without ritonavir—that is, a nonboosted PI.

In my opinion, the results reported by Khanna et al. [1] should not undermine the fact that PIs [4], but not NNRTIs, modulate activation of peripheral blood CD4+ T cells and decrease their susceptibility to apoptosis, both in vitro and in vivo. This occurs independently of HIV replication inhibition [5]. Of note, low doses of ritonavir increase PI exposure to these cells, without additional hepatic toxicity, compared with administration of nonboosted PIs [6].

Of interest, the authors reported that hepatitis C virus (HCV)–coinfected individuals were significantly less likely to have an increase in the CD4+ T cell count. They speculated, “Whether co-infection with HCV or a poorer adherence to ART in this group of primarily injection drug users is responsible for this observation remains to be shown” [1, p. 1099]. Of note, this group of patients was also significantly less likely to be prescribed boosted-PI ART (21% were HIV-HCV coinfected, compared with 35% of patients in the nonboosted PI group). Arguably, you cannot adhere to a regimen that your physician did not prescribe to you. It would be interesting to know whether HCV infection status remained significant in the subgroup of patients who had access to more-potent boosted PIs.

In conclusion, the superior effect of commencing of an ART regimen that includes boosted PIs should be considered in the context of risk factors for poor likelihood of recovery of the CD4+ T cell count, including among HIV-HCV–coinfected persons.

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Reply to Parienti

To the Editor—Parienti [1] highlights important study results and findings regarding the effect of different combined...