Therapeutic Response of HIV-1 Subtype C in African Patients

To the Editor—The pioneering work of Cassol et al. on the treatment of HIV-1–coinfected patients in Africa [1] is to be commended, but some important information seems to have been left out. There was no mention of toxicities or the development of an immune-reconstitution inflammatory syndrome (IRIS) in any of the patients. If IRIS develops in a significant number of patients being treated for HIV-1–tuberculosis coinfections, this would have a significant impact on the already limited resources of Africa. Perhaps new ways to diagnose IRIS would have to be developed, rather than the extensive studies done here in the developed world. Since the patients in their study had relatively high CD4+ T cell counts, perhaps no IRIS developed. Could the authors please clarify this?

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Reference

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Reply to Tayloe

To the Editor—Don Tayloe [1] raises some important and fundamental questions related to the complexity of antiretroviral treatment in Africa, especially in the setting of dual infections, and to the coadministration of highly active antiretroviral therapy (HAART) and tuberculosis (TB) or HAART and Kaposi sarcoma (KS) medications. Issues relating to drug-drug interactions, toxicity, and the risk of immune-reconstitution events are all concerns that warrant investigation. Although large, randomized trials will be needed to adequately address these issues, our studies have generated a limited amount of data on short-term toxicity and adverse events. Our study recently published in the Journal of Infectious Diseases focuses primarily on the kinetics of viral clearance and CD4+ restoration after the initiation of antiretroviral therapy, whereas some of the more clinical aspects of our work that relate to compliance and toxicity have been presented at scientific meetings and in recent publications [2, 3, 4].

In both patient cohorts, the medications were well tolerated, and there were relatively few treatment interruptions. In the initial (pilot) study of 20 patients coinfected with HIV-1 and TB, only 3 patients withdrew from the study: 1 as a result of a combination of adverse drug effects (loss of appetite, vomiting, abdominal pain, nightmares, and dizziness) and social issues and 2 as a result of social and environmental factors. Other adverse effects were transient, were mainly grade 1 and 2 (insomnia and dizziness), and were associated with the neuropsychological effects of efavirenz (EFV). No immune-reconstitution events were identified. One patient who failed to respond and showed rapid clinical deterioration was, on retrospective analysis, found to be infected with a multidrug-resistant strain of Mycobacterium tuberculosis. The same treatment strategy—didanosine, lamivudine (3TC), and EFV—administered concomitantly with standard TB therapy has now been extended to an additional 70 patients living in a rural community of northern KwaZulu-Natal. Again, tolerance has been excellent, and toxicities have been minimal (results to be presented at the International AIDS Society Conference in Rio de Janeiro, Brazil, in July 2005).

In the cohort of patients coinfected with HIV-1 and KS, patients received generic fixed-dose nevirapine (NVP), stavudine, and 3TC. Once again, adherence was excellent, and toxicities were minimal, with no immune-reconstitution events being detected. Two patients developed a grade 1 NVP-related rash that resolved during further treatment. Another 2 patients, with baseline CD4+ T cell counts of 130 and 373 cells/μL, developed NVP-associated hepatitis requiring discontinuation of treatment. Both patients recovered fully when NVP was replaced with EFV. Four additional patients, 2 of whom were found to be positive for hepatitis B surface antigen, developed transient hepatitis due to concomitant alcohol abuse and/or the use of herbal medications. All other adverse effects were minimal (grade 1 peripheral neuropathy, fatigue, and increased appetite) and did not require discontinuation of treatment.

Although promising, these studies are still limited by the small sample size and the relatively short duration of follow-up (12–18 months). There is an urgent need to confirm and extend this work to other sites and other population groups, especially in the setting of dual (or multiple) infections.

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