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## Reply to Torre and Pugliese

SIR—The letter by Torre and Pugliese [1] questions whether all patients with pulmonary hypertension related to HIV (PAHRH) should be treated with HAART, as we suggested on the basis of the results of our recent study [2]. Because PAHRH is a serious complication that, if untreated, has a high mortality rate, treatments that are targeted to reduce mortality are clearly indicated. In the era of HAART, pulmonary hypertension and its progression, more than the HIV infection itself, will determine the patient's prognosis. However, in the pre-HAART era, approximately half of all patients with PAHRH died of HIV-related causes [3]. Treatment with intravenous epoprostenol, inhaled iloprost, and, more recently, oral bosentan have been shown to significantly decrease the right ventricular systolic pressure over right atrial pressure gradient in patients with PAHRH. Although not always proven, because of the lack of a control group, the magnitude of the decrease in pressure gradient achieved with these drugs is likely to have a positive impact on overall survival rates.

To our knowledge, our study [2] is the only one that has systematically evaluated the time course of the pressure gradient as a function of antiretroviral therapy in a larger patient population. In the study

by Pugliese et al. [4], a difference in PAHRH frequency from 0.7% to 2.0% was reported between patients treated with 1 or 2 nucleoside analogues and patients treated with HAART during a later time period. Because the authors do not report the overall number of HIV-infected patients in their cohort, a calculation of incidence is not possible, and the data cannot be interpreted as showing an increase in PAHRH frequency due to HAART. The unusually high frequency of 2.0% suggests that a bias has affected the data; possibly there were more patients with PAHRH receiving HAART than patients not receiving antiretroviral therapy. More importantly, neither the definition of pulmonary hypertension nor the pressure gradient values nor their time course are mentioned in the article [4].

Current treatment recommendations for HAART only consider whether the CD4 cell count is  $>350$  cells/mm<sup>3</sup> if a patient is asymptomatic. However, we consider PAHRH to be a symptom of HIV infection, because it is epidemiologically linked to HIV infection, and, possibly, is associated with human herpesvirus 8 coinfection; pathological immune activation due to HIV; genetic factors; or other, yet unknown, factors. Although we agree that starting HAART at a CD4 cell count of  $>350$  cells/mm<sup>3</sup> is not warranted for the broad population of asymptomatic patients, HAART does lead to a decrease in immune activation, irrespective of the CD4 cell count. This effect may have indirectly contributed to the improved hemodynamics seen in our study. In the face of the rare occurrence—but high mortality—of PAHRH, we believe that every step should be taken to improve the prognosis of patients with PAHRH. On the basis of our data, we believe that HAART should always be initiated, because it stabilizes or decreases the pulmonary hypertension and prolongs survival [2]. Additional treatments that improve the hemodynamics should be started if a patient is moderately to severely symptomatic.

Among patients who are moderately symptomatic, the endothelin receptor antagonist bosentan seems to be the drug of choice, because of the availability of the drug in an oral formulation and because of its proven efficacy [5].

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