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LETTER TO THE EDITORS

Reply

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TO THE EDITORS:

We are grateful to Dr. Teicher and Dr. Duclos-Vallée for their interest in our article.[1] Although our sample is small and the difference in the incidence of opportunistic infections between the French and Spanish cohorts is not statistically significant, a trend toward a higher incidence of opportunistic infections can be observed in our cohort. We agree with Teicher and Duclos-Vallée's rationale, and we would like to comment on their observations:

1. In our cohort, we diagnosed 2 cases of zygomycosis, an aggressive fungal infection that is not typical in human immunodeficiency virus (HIV)–infected patients. The main risk factors for this complication are neutropenia and immunosuppressive therapy. In one case, the infection developed very early after transplantation (14 days), and the site of the infection was the surgical wound; this indicated a possible infection during surgery. In the other case, the patient had a CD^{4+} T cell count greater than 200/mm^3; therefore, immunosuppression seems to be the main risk factor for the development of zygomycosis.
2. We had 2 cases of late-onset tuberculosis, but there was only 1 case of tuberculosis in the study by Teicher and Duclos-Vallée. The incidence of tuberculosis is higher in Spain versus France (16 versus 9.3 cases per 100,000 inhabitants[2,3]). This could explain, at least in part, the different numbers of patients with posttransplant tuberculosis in the 2 cohorts.
3. The patient with *Pneumocystis jirovecii* pneumonia developed this complication on the sixth day after surgery before prophylaxis with cotrimoxazole was started. On combined antiretroviral therapy, this patient had a $CD4^+$ T cell count of 240 cells/mm^3 (13%) and an undetectable plasma HIV-1 RNA viral load immediately before surgery.
4. Another important issue is the fact that Teicher and Duclos-Vallée's series was from a single center, whereas our cohort was based on data from 17 transplant centers throughout Spain. Consequently, the incidence of opportunistic infections varied widely among the centers. In fact, 11 opportunistic infections occurred in patients from only 7 of these 17 centers; the remaining 10 centers did not report any opportunistic infections.

HIV/hepatitis C virus (HCV)-coinfected patients should be monitored closely because their probability of developing opportunistic infections is higher than that of non–HIV-infected patients. A pretransplant evaluation is essential because HIV/HCV-infected patients with cirrhosis are potential carriers of opportunistic infections at the time of transplantation. Patients with latent tuberculosis should be treated while they are on the waiting list.[4] Environmental factors increase the risk of fungal infections, and although the number of cases is low, HIV-infected patients seem to have more predisposing factors and a higher risk for this complication. For typical opportunistic infections such as cytomegalovirus disease and candidiasis, we believe that the general guidelines on prevention and treatment for solid organ transplant recipients should be followed for HIV/HCV-coinfected patients.[5,6]

In our series, we observed a 38% rejection rate, which falls within the range of 30% to 40% reported by other authors,[7-9] yet it is higher than the current incidence of rejection (15%-25%) reported for HIV-negative recipients.[10] This high rate of rejection among our HIV-infected patients, which possibly resulted from difficulties in achieving stable trough levels of calcineurin inhibitors due to pharmacological interactions with antiretroviral drugs, argues against the possibility of overimmunosuppression suggested by Teicher and Duclos-Vallée. The establishment of optimal immunosuppressive and antiretroviral regimens remains a key area for improvement, and we agree with most comments by Teicher and Duclos-Vallée on this point.

In conclusion, although the incidence of opportunistic infections can vary with the country and the experience of the transplantation center, HIV/HCV-coinfected patients may be at higher risk for opportunistic infections in comparison with other liver transplant recipients, and in many cases, this may be a result of host characteristics. We agree that optimal strategies

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for combined antiretroviral therapy and immunosuppressive regimens have yet to be developed. Information based on larger cohorts is warranted.

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