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Rapamycin and HIV Replication in Liver Transplant Recipients

We appreciate the concerns from Baccarani et al. regarding the active replication of HIV among our series of patients in calcineurin inhibitor immunosuppressive treatment after liver transplantation (LT). To better understand the experience of Baccarani et al., it would be necessary to have more detailed data, such as antiretroviral (ARV) therapy adopted, HIV viral load (VL) at different time points from transplantation to the last check, and HIV VL of all patients of their series. An important difference between our experience and the experience of Baccarani et al. seems to be the switch time from calcineurin inhibitor to rapamycin. Indeed, the median time of immunosuppression switch in the patient cohort of Baccarani et al. was significantly longer than in our experience.

HIV VL control is mandatory for the success of patient and organ survival postorthotopic liver transplantation, and this is a matter of the choice of the best ARV therapy available independently of the type of antirejection treatment. In this perspective, we also discourage LT in patients with no effective ARV option post-LT. Never the less the questions “when” and “what to start” ARV post-LT are still open and our experience meant to underline that rapamycin ability to inhibit HIV replication needs to be considered while tailoring ARV post-LT.

In our series, most patients had undetectable HIV VL after transplantation; however, two patients developed HIV reactivation, although they were on a triple

ARV therapy. Instead, HIV replication did not occur among the rapamycin group. However, based on the experiences reported in the literature (1–5), nobody could know whether rapamycin is really effective in HIV replication control among liver transplant recipients. Since the study by Heredia et al. (4), our impression, from a preliminary analysis of a set of liver transplant HIV+ recipients, is that rapamycin may allow a better control of HIV replication. We hypothesized that rapamycin contributed to a more rapid ability to obtain VL undetectable in patients with VL rebound secondary to ARV interruption in the early postorthotopic liver transplantation period.

To definitively establish a baseline on this topic, a prospective study with a larger patient cohort and with more appropriate clinical tests (such as CCR5 count on the lymphocyte surface) is necessary. We also believe that future studies may be able to specifically investigate the potential advantage of rapamycin in HIV VL kinetics, in reducing HIV residual viremia in patients with undetectable VL, and in the reduction of hepatitis C virus recurrence.

Fabrizio Di Benedetto¹
Stefano Di Sandro¹
Roberto Ballarin¹
Giovanni Guaraldi²
Giorgio E. Gerunda¹

¹ Liver and Multivisceral Transplant Center
University of Modena and Reggio Emilia
Modena, Italy

² Department of Medicine and Medical
Specialties
Infectious Diseases Clinic
University of Modena and Reggio Emilia
Modena, Italy

Address correspondence to: Fabrizio Di Benedetto, M.D., Ph.D., Liver and Multivisceral Transplant Center, University of Modena and Reggio Emilia, Via del Pozzo 71, 41100 Modena, Italy.

E-mail: f.diben@virgilio.it

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The Spleen as a Site for Hematopoiesis

We read with interest the recent article by Tan and O'Neill in *Transplantation* (1). On the basis of a spleen transplant experiment in allotype-distinct

recipient mice, they describe the role of this organ as a site for endogenous myelopoiesis. Although the role of the spleen as an extramedullary site

of hematopoiesis is well established in this species, it has remained uncertain whether this can be extrapolated to humans.