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LETTER TO THE EDITORS

Does MMF really slow down fibrosis of HCV recurrence in liver transplant recipients?

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We read with interest the study by Manzia *et al.* [1] on the effect of maintenance of mycophenolate mofetil (MMF) monotherapy on progression of recurrent hepatitis C virus (HCV) after liver transplantation.

The authors concluded: MMF ''monotherapy may currently represent the preferred immunosuppressive alternative for the long-term management of liver transplant recipients with HCV infection''. However, we believe that they should exert great caution in coming to this conclusion, as their results [1] have not been properly evaluated within the context of the complete picture of the published literature on the subject.

Our group recently published a review on the role of MMF and azathioprine in liver transplantation with regard to acute rejection, renal dysfunction and HCV recurrence [2]. Considering HCV recurrence, we showed that between 2001 and 2007, 17 studies evaluated MMF and HCV recurrence; among these, only two studies [3,4] found a decreased severity of HCV recurrence with MMF and one of these had no multivariate analysis [3] – cited by Manzia *et al.* Nine studies (reported in reference 2) documented similar severity of HCV recurrence; however, six studies [5–10] showed increased severity of HCV recurrence, but only one of these [10] was cited by Manzia *et al.*

Therefore, the study by Manzia *et al.* [1] represents only the third study out of 18 (17%) showing a beneficial therapeutic effect of MMF on HCV progression after liver transplantation, whereas 33% shows a deleterious effect. For this reason, in omitting to cite this literature, Mania *et al.* have gone against the available evidence in stating that MMF is the preferred immunosuppressive alternative for long-term regimen in patients transplanted for HCV-related cirrhosis.

Moreover, although Manzia *et al.* [1] showed in their patient cohort a positive association between a favorable effect of MMF monotherapy on the progression of hepatic fibrosis in HCV liver transplant patients, there are several methodological issues. There was no multivariate analysis evaluating MMF with respect to fibrosis progression. This is especially important, as the study was retrospective and nonrandomized and with only 15 patients per arm. Although other studies have also been retrospective and nonrandomized [2], several have included multivariate analyses.

Thus, overall, the current published evidence for MMF with respect to the severity of fibrosis and HCV recurrence does not suggest a beneficial effect. If anything, a potential adverse effect is shown as we pointed out in our review [2], although we acknowledged then, and now that the evidence is weak.

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Conflicts of Interest

None.

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