Letter: calcineurin inhibitor level reduction during treatment with sofosbuvir in liver transplanted patients

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SIRS, In liver transplant, during anti-viral therapy for hepatitis C virus (HCV) recurrence, the immunosuppressant levels should be monitored to prevent both toxicity and rejection.

Sofosbuvir (SOF) has been used within compassionate programs for HCV recurrence and, according to pharmacokinetic analyses, is not supposed to have significant pharmacological interactions with tacrolimus (Tac) or ciclosporin.[1] This was reported in the review article by Koff recently published.[2] We treated eight transplant recipients with SOF/ribavirin (RBV) for a severe HCV recurrence, and observed unexpected Tac/ciclosporin reduction during SOF.

The patients' mean age was 48.1 years. They were all men and had mean time from liver transplant 4.2 years, mean MELD-score 13.4 (range, 7–22), mean Child-Turcotte-Pugh score 8 (6–11). There were six (75%) genotype 1, one (12.5%) was genotype 3, and one (12.5%) was genotype 4.

All patients were on a stable Tac regimen except one who was on ciclosporin. Treatment with oral daily doses of SOF 400 mg + RBV (range, 200–1000 mg) was started after the SOF compassionate use approval by the Ethics Committee.

Initial Tac/ciclosporin dose was not modified at the beginning of anti-viral treatment. The Tac/ciclosporin levels were monitored weekly (Figure 1). At week 4, mean Tac/ciclosporin reduction was 40.2% (range, 21.4–72.1%). Daily Tac/ciclosporin doses were increased in all, except one patient who had renal failure and was also receiving mycophenolate mofetil. All patients except one reached undetectable HCV-RNA at week 4. The mean CTP reduced from 8 at baseline to 6 at week 4.

Currently available data report no significant reciprocal influence of absorption, distribution, metabolism or excretion of Tac/ciclosporin and SOF. No dose adjustment is recommended for immunosuppressants during SOF, as indicated in the recent review article (2). Nonetheless, this information arises from a single-dose study, while our data reveal a reduction in immunosuppressant levels. This might be a consequence of an improvement of liver function, even if a drug–drug interactions cannot be *a priori* excluded.

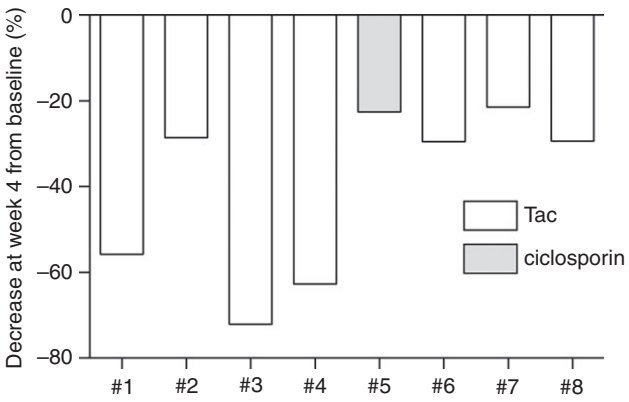

Figure 1 | Percentage decrease of Tac/ciclosporin in 8 liver transplanted patients after 4 weeks of SOF/RBV.

Regardless of the underlying mechanism, our report is aimed to raise awareness to hepatologists who are familiarising themselves with SOF in the post-transplant HCV-recurrence setting as we are now moving towards SOF global availability.

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