

replaced by parenteral drug addiction or sexual transmission.<sup>4,5</sup> It is not surprising that prevention is the most adequate and cost-effective control measure for these patients.

Treating chronic HCV before kidney transplantation is currently not an essential criteria for including HCV-positive patients on the transplant waiting list. However, risk of post-transplant chronic hepatitis C and the difficulty to treat it at this stage of the chronic kidney disease have been reported.<sup>6-11</sup>

Pegylated interferon and interferon + ribavirin are better than conventional interferon, according to clinical trials. However, the differences are small. Combining ribavirin and pegylated interferon requires close follow-up during haemodialysis given the severity of the secondary effects. It has increased the sustained viral response, although it is still less in the population without chronic kidney disease.<sup>12</sup> This, along with the difficulty of treating patients with stages 4 and 5 chronic kidney disease in predialysis, highlights the importance of resolving the infection at early kidney disease stages.

Transjugular liver biopsy reduces the risks of bleeding associated with this procedure and the kidney patient, although there is little evidence in the literature.<sup>13,14</sup> This technique also allows the hepatic venous pressure gradient to be measured, providing diagnostic and prognostic data.

Studies that determine whether the association of protease inhibitors (telaprevir, boceprevir) with interferon and ribavirin is safe for kidney patients and may increase viral response rates.

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## Cyclophosphamide-induced lupus flare?: the role of C4 and interferon-gamma in lupus flare

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**To the Editor,**

We read with great interest the contribution by Heras, et al.<sup>1</sup>. They reported a significant case that seemed not to respond to intravenous (IV) cyclophosphamide (CPM) induction treatment at 1 g but to respond to increased CPM dose to 1.5 g. Reading the case report, we wondered whether CPM certainly induced the lupus flare or other mechanisms were involved in the pathogenesis. They speculated

that the lupus flare might have been due to the initial underdosing of cyclophosphamide. This explanation is plausible, but we would like to say that lupus flares can occur during or after stopping CPM treatment, suggesting the possible pathomechanisms of lupus flare.

In the immunological test after the first treatment of IV CPM, the patient had increased C3 level, but C4 was decreased. According to a previous study by Ho, et al.<sup>2</sup>, a decrease in C4 was associated with a concurrent increase in renal disease activity ( $p = 0.02$ ). A decrease in C4 was especially associated with concurrent decreases in the hematocrit levels ( $p = 0.009$ ), and previous increases in C3 were also associated with a higher frequency of decrease in platelet counts ( $p = 0.02$ ). These data show that the renal and hematologic systemic lupus erythematosus (SLE) activity and flares are strongly associated with decreased C4.

Recently, Finke, et al.<sup>3</sup> demonstrated that complement C4-deficient mice result in elevated intravascular levels of apoptotic DNA, targeted to the splenic marginal zone where it accumulates and induces type I interferon-gamma (IFN- $\gamma$ ). Type I IFN- $\gamma$  is important for the initiation and potentiation of SLE activity and correlated with the renal disease and the presence of cutaneous manifestations<sup>4</sup>.

Therefore, we suggest that CPM is not an inducer but an inhibitor of lupus flare, and decreases in C4 and increased type I IFN- $\gamma$  might play the central role in the development of lupus activity and flares. However, further studies are necessary to elucidate the exact molecular roles of complement deficiency and elevated levels of IFN- $\gamma$ . The potential therapeutic antibodies directed to either type I IFN- $\gamma$  or IFN  $\alpha$  chain of the receptor 1 (IFNAR1)/IFNAR2 should also be further evaluated in the future.

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## Flare lupic during induction with cyclophosphamide therapy in diffuse proliferative lupus nephropathy

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### To the Editor,

With regards our scientific letter, "Cyclophosphamide-induced lupus flare in diffuse proliferative lupus nephropathy"<sup>1</sup> we would like to thank

Park at al for their contribution, and their suggestions of the possible immunological mechanisms involved in a lupus flare. Although they question whether cyclophosphamide really induces the flare or whether other mechanisms are involved, we would like to clarify that the title of the English version "Cyclophosphamide-induced lupus flare" could lead readers to believe that we consider that treatment with cyclophosphamide induced the flare, however, we wanted to communicate exactly the opposite. Indeed, as was reflected in the "Discussion" section, cyclophosphamide treatment is the best immunosuppressive agent, with the best results in inducing remission in severe forms of lupus nephropathy (LN).<sup>2</sup> As Park at al have pointed out in their letter, the lupus flare may or may not occur after cyclophosphamide treatment. In our case, it was during the cyclophosphamide induction period (less than 15 days). The flare was confirmed following the first phosphamide dose. Therefore, after having dismissed several causes (renal vein thrombosis, infection, etc.), we brought another cyclophosphamide dose forward (the second dose was 1.5g), which caused clinical and biochemical improvements, and the patient went into remission. To date, the patient has not had any further flares. We would like to emphasise the importance of the cyclophosphamide administered: we used the Euro-Lupus Nephritis Trial regime, 500mg every 15 days.<sup>3</sup> In this patient the flare would have been earlier, since the relapse occurred less than 15 days with 1g of the first dose of cyclophosphamide. For that reason, before considering cyclophosphamide treatment to be ineffective, it is important to bear in mind the dose that has been administered. Finally, we must highlight that we did not consider for one moment that cyclophosphamide induced the lupus flare. Given an error in the English version, the English title should have been: *Flare lupic during induction with cyclophosphamide therapy in diffuse proliferative lupus nephropathy*.