

Is sirolimus a treatment option for patients with systemic lupus erythematosus?

Sirs,

There has been interest in sirolimus as a rejection preventing agent in kidney transplants and in autoimmune diseases including ankylosing spondylitis, psoriatic arthritis, systemic sclerosis and systemic lupus erythematosus (SLE). The recently reported favourable results with sirolimus in SLE need further discussion. Lai *et al.* reported favourable results with sirolimus in patients with SLE who are refractory or intolerant to conventional therapy in a single-arm, open-label, phase 1/2 trial (1). Although activation of mechanistic target of rapamycin may have a role in the pathogenesis of SLE, we have some doubts whether sirolimus could be a plausible immune-modulator agent. As mentioned briefly by Lai *et al.*, sirolimus had been mostly tried as a rejection prevention treatment in renal transplant recipients for some years. However, what is rather less mentioned is that it showed no superiority or was indeed inferior to calcineurin inhibitors or anti-metabolites including mycophenolate mofetil and azathioprine. Moreover, it was associated with significant side effects including dyslipidemia, proteinuria and bone marrow suppression in this patient population (2-4). Finally a sys-

tematic review of 21 randomised trials of sirolimus in renal transplant recipients showed that sirolimus was associated with an increased risk of death (HR: 1.43, 95% CI 1.21–1.71) (5).

Another important issue is that the definition of the inclusion criteria in the SLE study at hand is problematic. According to Table I in the manuscript, 27/43 (63%) were not using prednisone at their initial visit. This is simply curious. It further weakens the validity of the consideration that sirolimus might work as a glucocorticoid sparing agent proposed in the accompanying article (6). In brief, we need a much more strict description of the inclusion criteria for this study before we can generalise its findings.

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