



## **Reply to letter by Efe et al.**

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We thank Dr Efe and colleagues<sup>1</sup> for their interest in our review article regarding the modern management of autoimmune hepatitis (AIH).<sup>2</sup> Tumour necrosis factor (TNF)-alpha, clearly plays a major role in promulgating autoimmune processes and, indeed, has been implicated in the pathogenesis of AIH.<sup>3</sup> In addition, an association has been identified between genetic polymorphisms in the TNF promoter region and type I AIH which, significantly, was also associated with higher rates of cirrhosis and poorer responses to corticosteroids.<sup>4,5</sup> However, in respect of the management of AIH, we feel it is important to proceed with caution in respect of agents that block TNF-alpha for the following reasons.

Firstly, the evidence for their use comes from very few, single case reports,<sup>6,7</sup> with therapy in one report instituted for non AIH indications.<sup>5</sup> Secondly, these agents appear to be potentially hepatotoxic, which is clearly undesirable in a hepatic disease process such as AIH.<sup>8</sup> Indeed, AIH has actually been shown to be precipitated by TNF-alpha therapy.<sup>9</sup> Finally, there remains the concern surrounding the risk of opportunistic infection. Indeed, in the case report cited by Dr Efe and colleagues<sup>6</sup>, the patient suffered 2 infection related complications necessitating withdrawal of therapy. Interestingly this patient was not managed with either tacrolimus or cyclosporine.

Consequently we believe the vast majority of AIH patients non responsive to standard therapy can be successfully managed through better implementation of longer established, non-hepatotoxic immunosuppressive therapies (MMF, tacrolimus, ciclosporin) whose side effect profile is well understood. Whilst it is accepted that, conceptually at least, TNF-alpha therapies may be novel agents in difficult to treat AIH, their use is little studied in this context with particular concerns existing over their safety. For these reasons their utility was not expanded upon in this review and their future use should be limited to clinical trials.

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