

Reply to comment on: Clinical efficacy of oral alendronate in ankylosing spondylitis: a randomised placebo-controlled trial

Sirs,

We thank Giollo and colleagues for their comment. They suggest that our placebo controlled trial (1) on oral alendronate was not effective in the treatment of ankylosing spondylitis (AS) in contrast to the open label studies using intravenous bisphosphonates, since the dose delivered with intravenous bisphosphonate is far greater than can be achieved with once weekly oral dosing. Whilst we accept that the oral dose of alendronate in any month would be lower than that given through the intravenous route, the problem with the intravenous bisphosphonate studies has been that they have been open label and not placebo-controlled, giving rise to conflicting results (2, 3). Our interpretation of these open label trials is that they have not proven that intravenous bisphosphonates are effective in reducing the clinical burden of disease in AS and this can only be established if they are conducted as placebo controlled trials. We accept that such a trial may prove difficult due to the occurrence of an acute phase response with the intravenous amino bisphosphonates, but it is only after such a trial has proven to be effective that we can then

speculate on the possible mechanisms of action of bisphosphonates on the immune system or on immune cells. The authors have suggested one possible mechanism through a reduction in circulating levels of $\gamma\delta$ T cells, which are expanded in patients with AS (4).

The results of our study show that oral bisphosphonates are ineffective in modifying the clinical presentation of ankylosing spondylitis. Whether intravenous bisphosphonates behave differently will need to be demonstrated in a proper placebo controlled trial with adequate numbers of patients.

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