Correspondence on 'Efficacy and safety of brodalumab, an anti-IL17RA monoclonal antibody, in patients with axial spondyloarthritis: 16-week results from a randomized, placebo-controlled, phase 3 trial'

We read with great interest the article 'Efficacy and safety of brodalumab, an anti-IL17RA monoclonal antibody, in patients with axial spondyloarthritis: 16-week results from a randomised, placebo-controlled, phase 3 trial' by Wei *et al*.[1] As the first multicentre randomised controlled trial in patients with axial spondyloarthritis (axSpA) of brodalumab, it makes a remarkable contribution to treatment of this novel interleukin-17 (IL-17) inhibitor in two disease subtypes, which shows a great remission rate and short-term safety. However, there are some aspects that need to be discussed.

First, regarding the study design, it was mentioned that the dose of 210 mg is based on the therapeutic dose of psoriasis. However, in clinical trials of psoriasis, the drug dose is usually 210 mg every 2 weeks from the beginning to the end,[2] instead of once in the first week and the second week, also known as load treatment, the latter has been administered in this study. The rapid ASAS 40/20 response at as early as week 2 in this study might be due to the load treatment at baseline.

Second, for the safety aspects, in the past two phase III clinical trials of brodalumab in patients with plaque psoriasis, one case of depression[3] and one case of suicide attempt[4] were reported, which also led to the termination of both studies. Therefore, it is a breakthrough to add Columbia-Suicide Severity Rating Scale and Patient Health Questionnaire-8 in this study to comprehensively assess the suicidal tendency and depression of patients with axSpA. So far, there is no evidence whether depression or suicidal tendency is caused by brodalumab. In this study, including depression in the exclusion criteria will miss the chance of probing whether these two conditions and brodalumab are indeed related.

Third, there are inconsistent results among clinical trials of different IL-17 inhibitors. Liver injury cases can be seen in the long-term safety studies of ixekizumab[5 6] and brodalumab,[7] but not in the long-term safety studies of secukinumab.[8 9] Studies have shown that IL-17 blockade can protect from liver injury, whereas its administration increases liver damage in mouse models.[10] Furthermore, in this article, there were four (5%) treatment-emergent adverse event (TEAE) cases of inflammatory bowel disease in the brodalumab treatment group, which were not seen in previous studies of brodalumab. We suggest that authors discuss on both TEAEs, and more studies of underlying mechanism are required.

Finally, although the ASAS 40 response at week 16 observed in this article is similar to the result of previous clinical trials of secukinumab[8] and ixekizumab,[11] as the author mentioned in the limitation, the number of participants should generally be greater than 300[5 6 12] to provide more credible evidence. We look forward to large-scale trials involving more regions and races, and head-to-head trials among brodalumab and other IL-17 blockers in the future.

We appreciate the work of Wei *et al* for proving the effectiveness and safety of brodalumab in patients with axSpA. We believe this comprehensive study will give clinicians one more choice when giving treatment options to patients with axSpA in the future.

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