

LETTER TO THE EDITOR

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New insights from a systematic review and meta-analysis on the treatment of difficult-to-treat rheumatoid arthritis

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Dear Editors,

The recently published article by Qin-Yi Su et al. systematically reviewed and analyzed the efficacy and safety of various therapies for difficult-to-treat rheumatoid arthritis (D2T RA) [1]. This study offers evidence-based guidance on the most effective and safest treatments for patients with D2T RA, holding particular value for the healthcare field in the context of an aging population. However, I would like to offer a few constructive suggestions that could further enhance the impact of this excellent article.

Firstly, it is essential to consider the potential impact of the study period on the research findings. The authors included articles published between 2013 and 2024, a period during which treatment approaches and guidelines for Rheumatoid Arthritis (RA) may have evolved. Such changes could influence the frequency or dosage of certain medications, potentially affecting the validity of the study findings and their current clinical applicability. Although the authors analyzed the main existing therapies and mentioned some newer biologics and targeted synthetic DMARDs. However, there was a lack of detailed discussion on the potential of new therapies or

innovative drugs currently in development, which may limit the study's ability to provide a forward-looking perspective on future treatment options [2].

Secondly, although the authors conducted subgroup analyses based on prior treatment failures, further studies are needed to refine these conclusions. Some researchers have found that baseline disease activity can help verify the efficacy and safety of various drugs in patients with mild, moderate, and severe disease [3]. Further subgroup analyses could better enhance the clinical applicability and broad relevance of personalized treatment strategies. However, it is undeniable that the duration of D2T RA is often long, and some individual factors (such as genetic background, mental health, lifestyle, and concomitant medications) may lead to different therapeutic responses or increased risk of adverse events. Moreover, due to limitations such as sample size and heterogeneity, there may be some bias in the statistical results. In the future, increasing sample sizes and conducting multicenter randomized controlled trials could improve the statistical significance of the findings. We can also ensure the robustness of the results through multivariable adjustment and sensitivity analyses.

Finally, this study primarily focused on the short-term efficacy and safety of treatments. In contrast, D2T RA is a chronic condition requiring long-term management. The lack of sufficient long-term follow-up data may limit the comprehensive evaluation of safety and efficacy of the drugs [4]. Therefore, we should incorporate long-term safety monitoring of the drugs through research process in order to detect potential delayed adverse effects. For D2T RA patients, long-term treatment must consider not only efficacy but also the potential for long-term side

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effects and economic burden. Based on this, we advocate for the following in future work: (1) Preventing the progression of RA to a difficult-to-treat stage; (2) Optimizing treatment strategies for D2T RA to slow disease progression or reduce the incidence of complications; (3) Improving the quality of life for D2T RA patients so as to reduce the disease burden.

In conclusion, this article provides a systematic evaluation of the efficacy and safety of various drugs in the treatment of D2T RA. It also recommends the optimal therapeutic dosages to guide the best treatment strategies, aiming to improve clinical outcomes for patients. Our suggestions are intended to further refine an already perfect study, and we hope to see more healthcare professionals, social workers, and others join in the research on D2T RA in the future, bringing hope to patients suffering from this chronic disease.

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