

Peer-review Coments and Responses

Reviewer 1

1. *There are some opportunities for improvement. On page 2, 3rd paragraph: " Infiximab and etanercept are monoclonal antibodies with diverse underlying mechanisms of action". Please review that sentence. Etanercept is not a monoclonal antibody, it is an anti-TNF o TNF blocker. It has molecular differences and a different mechanism of action than monoclonal antibodies. On page 3 publication publication is duplicated in the 3rd paragraph. I think is a good article that can be improved.*

Dear Reviewer, thank you for pointing this out. We have, accordingly, modified the second paragraph of the introduction (page 2) to emphasize the different mechanisms of etanercept and infliximab. Also, we removed the duplicated word on page 3. Thanks for your comments.

Reviewer 2

2. *Clarity and presentation: It is really difficult to understand author's main point's and their flow of ideas. Their paper could be better organized, specially their introduction. I had to read the paper three times to understand what their research question was, their research gap and what had they done. My main suggestion at this time is to make introduction more concise, and written in a way it naturally leads to an understanding of the gap. For example, author's first line is: "Rheumatoid arthritis (RA) is an inflammatory disease that manifests with articular or extra-articular symptoms (Chaurasia et al., 2020). This is certainly not the most important information to start with. Also, the following paragraph breaks the readers flow thoughts: "Infiximab and etanercept are monoclonal antibodies with diverse underlying mechanisms of action. Infiximab neutralizes TNF- α by binding and impairing the monomeric and trimeric forms of this cytokine, thus causing apoptosis of activated T cells and lamina propria lymphocytes. Etanercept is a recombinant version of the soluble p75 of TNF- α that competes with soluble TNF- α for binding to TNF- α receptors (Ehlers, 2005). Thus, it is plausible that these drugs mediate different effects on the reactivation of latent or active TB." My suggestions are: start with RA being important; prevalence or burden of disease; some severe cases need TNF-blocking; TNF- α blocking may lead to latent TB reactivation; different TNF- α inhibitors might display different; your gap: last meta-analysis on the topic was published many years ago, and our goal at this time is to pool data from studies published since then. Also, please, look carefully for grammar and spelling. For example: " In addition, due to the difference in costs of these drugs, the cost-benefit of each of them should be consider."*

Dear Reviewer, we agree with your suggestions, and we have incorporated them in the introduction. We have reorganized the paragraphs in order to make the reading more smooth and easier to understand.

3. *Scientific methods: Methods are well written and performed. Please, cite the PRISMA 2020 guideline, and please, double-check guideline compliance. Refer to their check-list available on: <https://pubmed.ncbi.nlm.nih.gov/33782057/>. I suggest to include "systematic review and meta-analysis" on your title, in accordance to the PRISMA 2020 guidelines.*

Dear Reviewer, thank you for your suggestion. We included the “systematic review and meta-analysis” in our title, as well as we referred to the PRISMA 202 guideline in the first paragraph on page 3.

4. *Tables and figures: On Figure 3, having actual drug names "etanercept" and "infliximab" would be easier to read and understand.*

Dear Reviewer, thank you for your suggestion. We adjusted Figure 3 as per your suggestion.

5. *Results: Authors report pooled information on TB screening. However, it is unclear what they want to address with that information. This could be interesting information, but what is the gap? I suggest to either remove it, or further explain it.*

Dear Reviewer, thank you for your suggestion. You have raised an important point here. The American College of Rheumatology and the World Health Organization Guidelines recommend TB screening before the use of biologic drugs, in order to define the need for Latent Tuberculosis Infection prophylaxis or active tuberculosis treatment. In our review, we wanted to evaluate if all the included articles performed the screening, and if the screening had some impact on the risk of TB. We have elaborated the fifth paragraph of the discussion on page 6 for better understanding.

In addition to the above comments, all spelling and grammatical errors pointed out by the reviewers have been corrected.