Efficacy And Safety Of Biological Therapy For Treatment Of Adults With Moderate-severe Crohn's Disease: A Systematic Review And Network Meta-analysis

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INTRODUCTION

The initial therapeutic approach for Crohn's, a chronic inflammatory bowel disease, involves immunosuppressants, aminosalicylates, corticosteroids.

However, about 30 to 45% of patients are resistant to this first-line approach, thus, requiring biological drugs[1,2].

OBJECTIVE

We aimed at synthesizing the evidence on the effects (efficacy and safety) of biologic drugs for treating moderate-severe Crohn's disease in adults.

METHOD

A systematic review was performed with searches in PubMed, Scopus, Web of Science (February-2024). Randomized controlled trials evaluating biological drugs for the induction of remission in adult patients with moderate-severe Crohn's disease were included. For each outcome of interest [remission, serious adverse events (SAE)], data were pooled using network meta-analysis p-score analysis. The results were presented as risk ratio (RR) with 95% confidence intervals (NMAStudio, R/RStudio).

RESULTS

Overall, 39 trials (n=10,561) (1997-2023) assessing 23 biologic drugs across 79 different dosages were included **(Figures 1 and 2)**.

Alongside infliximab 5mg/kg (p-score probabilities of 95%) and 10mg/kg (85%), recently approved drugs such as mirikizumab 600mg (90%) and guselkumab 200mg (87%) and 600mg (86%) presented higher probabilities of disease remission. Adalimumab 160mg/80mg (81%), vedolizumab 300mg (72%) and ustekizumab 6mg/kg (69%) presented an intermediate effect. Certolizumab 200mg (25%) and 400mg (44%), and fontolizumab 0.1mg/kg (11%) ranked last for this outcome **(Figure 3)**.

Certolizumab also presented a worse safety profile, with high probabilities of leading to SAE (200mg-77%; 400mg-66%), while mirikizumab 600mg (45%) and guselkumab 200mg (41%) and 600mg (51%) were considered safer alternatives. Vedolizumab 300mg (53%) and ustekizumab 6 mg/kg (45%) presented moderate rates of SAE **(Figure 3)**.

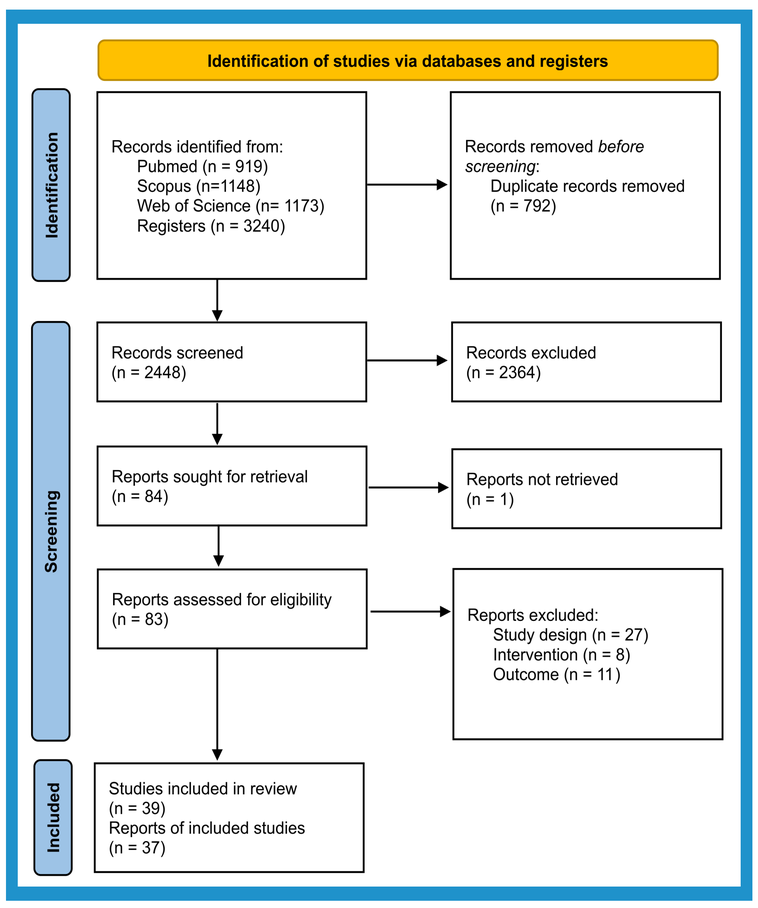

Figure 1. PRISMA 2020 flow diagram

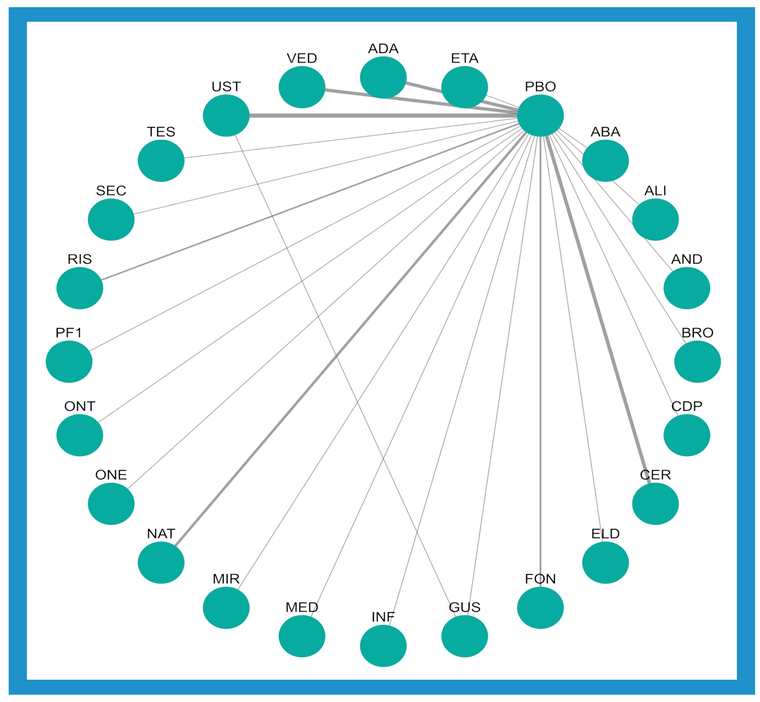

Figure 2. Overall network plot of treatment comparisons

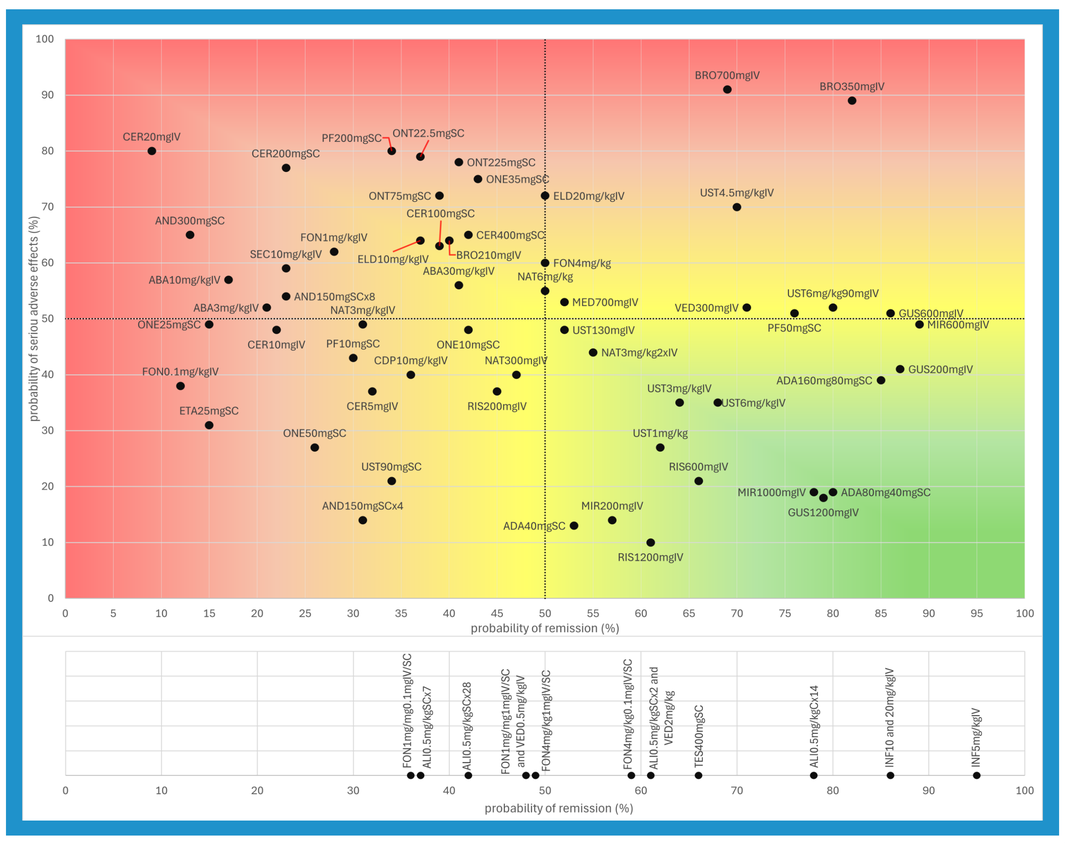

Figure 3. Comparison of clinical remission and SAE probability rates.
Data based on p-score from network meta-analysis.
Drugs outside of the main graph: SAE data unavailable

Abbreviations
ABA: abatacept; ALI: alicaforsen; AND:andecaliximab; BRO: brodalumab; CDP: CDP571; CER: certolizumab pegol; ELD: eldelumab; ETA: etanercept FON: fontolizumab; GUS: guselkumab; INF: infliximab; MED: MEDI2070; MIR: mirikizumab; NAT: natalizumab; ONE: onecerpt; ONT: ontamalimab; PF1: PF-0423921; RIS: risankizumab; SEC: secukinumab; TES: tesnatilimab; UST:Ustekinumab; VED: vedolizumab

CONCLUSIONS

Inhibitors of interleukin-23 (mirikizumab, guselkumab) appear to be promising alternatives for the treatment of moderate-severe Crohn's disease. Given their safety profile, some anti-TNF drugs should be avoided in practice. Other important factors, such as drugs' access and costs, should be considered for this decision.

REFERENCES

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