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Topic: Psoriasis

Efficacy and Safety of IL-12, IL-17, IL-12/23, and IL-23 Inhibitors for Moderate-to-Severe Psoriasis: A Systematic Review and Bayesian Network Meta-Analysis

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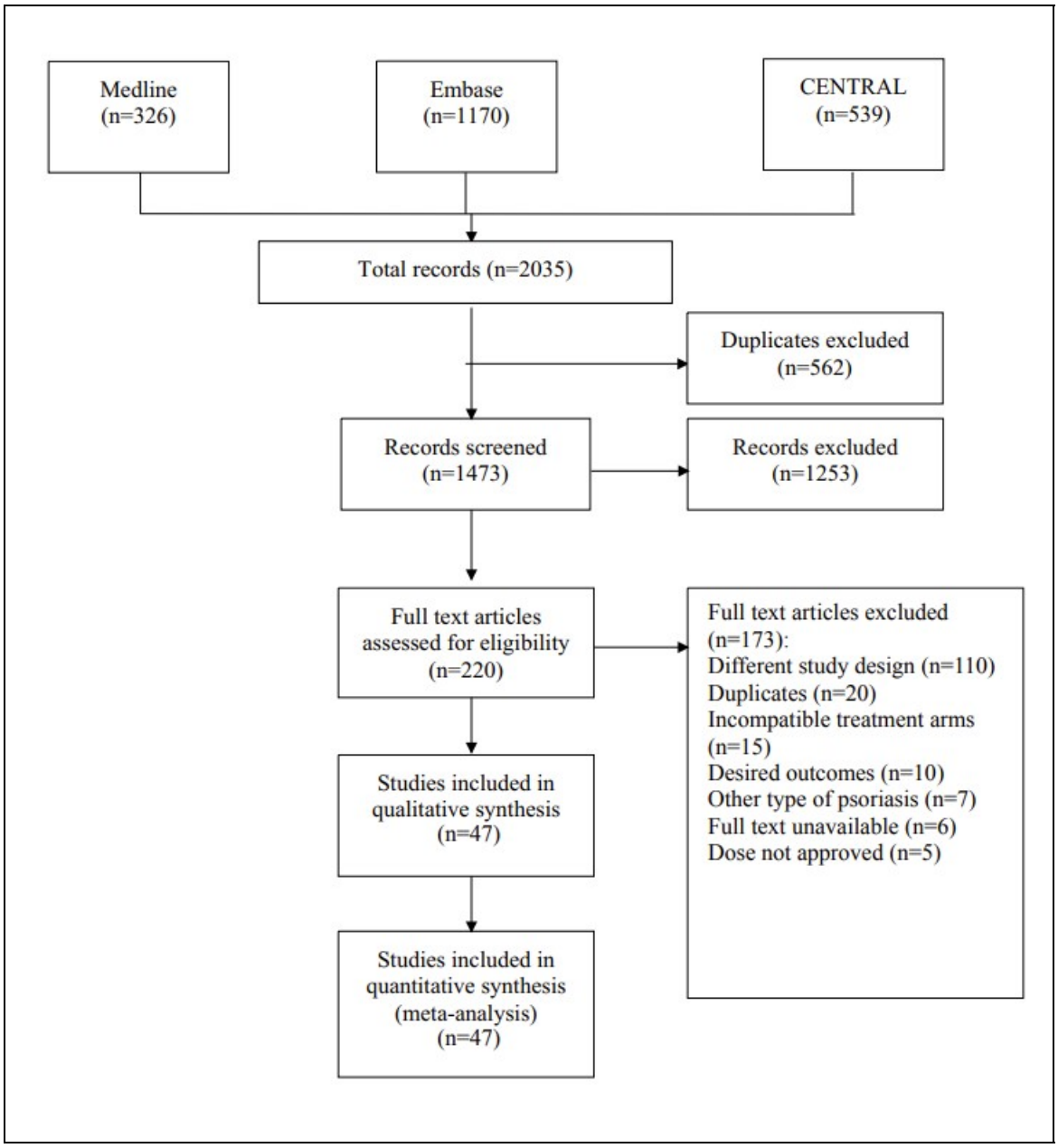
Introduction

Plaque psoriasis is an inflammatory skin disease that classically present as erythematous plaques with thick scales affecting the extensor surfaces, trunk, and scalp (1).The estimated prevalence of psoriasis in adults ranges from 0.51% to 11.43% worldwide, while the prevalence in children is approximately 1.37% (2). Several biologic agents targeting these cytokine pathways are available, however, differences in their efficacy, safety profiles, and long-term outcomes can make treatment selection challenging. In addition, there are limited direct head-to-head clinical trials comparing these agents. Thus, network meta-analysis is important to provide indirect comparisons for a better understanding of their relative effectiveness and safety in patients with moderate to severe plaque psoriasis.

Materials and Methods

A systematic literature search was conducted using MEDLINE, Embase and Cochrane Central Register of Controlled Trials (CENTRAL). The references and citations of the included trials were also reviewed for relevant studies. This systematic review and network meta-analysis protocol was registered at PROSPERO (CRD420251045626). Eligible studies were randomized controlled trials (RCTs) published in English only that compared biologic interventions targeting interleukin (IL) pathways, specifically IL-12, IL-17, IL-12/23, or IL-23 inhibitors, with placebo or with another biologic within the same classes. The population of interest consisted of adults (≥18 years of age) with moderate-to-severe plaque psoriasis. Studies must report at least one desired efficacy and/or safety outcome. In addition, only approved doses by either the Food and Drug Administration (FDA) or the European Medicines Agency (EMA) were included.



Results

Out of the 47 included RCTs, 18 had an overall low risk of bias, 17 had some concern, and 12 had an overall high risk. A total of 19,683 participants were included). The majority were male (n = 13,656; 69.38%), while 6,027 participants (30.62%) were female. The mean age of participants receiving interventions was 45.45 (±12.99) and for placebo group 45.34 (±13.09). For PASI75, ixekizumab 80 mg demonstrated the highest response in the main analysis, followed by ustekinumab 90mg. However, a sensitivity analysis was done due to substantial heterogeneity by removing high risk and some concern included studies, which shifted the results toward brodalumab 210 mg achieving the highest response in PASI75 followed by bimekizumab 320 mg. Brodalumab 210 mg was the most effective treatment for achieving PASI90, followed by ixekizumab 80 mg. Similarly to PASI75, sensitivity analysis was done and demonstrated brodalumab 210 mg as the most effective for PASI90 followed by bimekizumab 320 mg. Regarding safety, Tildrakizumab 200 mg was associated with the lowest risk of adverse events, whereas bimekizumab 320 mg had the highest based on SUCRA

Conclusions

This network meta-analysis comprehensively evaluated the efficacy and safety of IL-12, IL-17, IL-12/23, and IL-23 inhibitors in adults with moderate-to-severe plaque psoriasis. The results demonstrated that IL- 17 inhibitors, particularly ixekizumab and brodalumab, were associated with the highest efficacy in achieving skin clearance, while IL-23 inhibitors, especially tildrakizumab, exhibited the most favorable safety profile. These results reinforce the role of Interleukin targeting biologics as cornerstone therapies for plaque psoriasis and provide valuable evidence to guide individualized treatment selection based on efficacy expectations and safety considerations. Further head-to-head and

real-world comparative studies are needed to validate our findings and to better inform long term therapeutic decision making in clinical practice.

References:

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