

NOVAS PERSPECTIVAS TERAPÊUTICAS E ALVOS MOLECULARES EMERGENTES NA PSORÍASE

New Therapeutic Perspectives and Emerging Molecular Targets in Psoriasis

João Cardoso Faccio¹, Charlene Kruhs Picolotto²

1.Professor do Curso de Medicina Afya Centro Universitário de Pato Branco - Pr¹,
2.Acadêmica do Curso de Medicina da Afya Centro Universitário de Pato Branco – Pr²,
charlenepicolotto@gmail.com

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RESUMO

Introdução: A psoríase é uma doença inflamatória imunomediada, crônica e recorrente, decorrente da hiperproliferação e diferenciação anormal dos queratinócitos concomitantemente à ativação do sistema imunológico. O avanço dos tratamentos direcionados a diferentes alvos moleculares tem elevado as oportunidades de terapêuticas tanto para as formas de psoríase moderada, grave e pustulosa. **Objetivo:** Este estudo pretende avaliar a eficácia e segurança do uso de imunossuppressores e imunomoduladores no tratamento da psoríase, enfatizando as terapias direcionadas e seus respectivos alvos moleculares. **Método:** Para tal estudo, foi realizado uma revisão bibliográfica descritiva, de caráter integrativo, mediante busca de artigos nas bases PubMed e Scielo, priorizando publicações entre 2022 e 2025, enriquecidas por evidências clínicas e diretrizes vigentes. Também foram analisados, estudos de revisão sistemática, meta-análises e evidências clínicas relacionadas as intervenções específicas. **Resultados:** A elevada eficácia dos tratamentos biológicos direcionados, especialmente os que atuam nas vias de interleucina 17 e da interleucina 23, foi demonstrado nos resultados. Houve destaque também para o uso de bimequimabe, ixekizumabe e risankizumabe, além do infliximabe, e agente anti-fator de necrose tumoral alfa. As possibilidades terapêuticas pelo bloqueio da tirosina quinase 2 pelo deucravacitinibe e do receptor da interleucina 36 pelo spesolimabe é ampliada nas diferentes formas clínicas da doença. **Conclusão:** Conclui-se que o uso de terapias direcionadas apresenta expressivos resultados de eficácia e diferentes perfis de segurança, favorecendo uma dinâmica de tratamento individualizado em pacientes que possuem psoríase.

Palavras-chave: Psoríase; Terapias direcionadas; Alvos moleculares; Imunobiológicos; IL-17.

ABSTRACT

Introduction: Psoriasis is a chronic, recurring, immune-mediated inflammatory disease resulting from the hyperproliferation and abnormal differentiation of keratinocytes, along with the activation of the immune system. The advancement of treatments targeting different molecular targets has increased therapeutic opportunities for moderate, severe, and pustular forms of psoriasis. **Objective:** This study aims to evaluate the efficacy and safety of using immunosuppressants and immunomodulators in the treatment of psoriasis, emphasizing targeted therapies and their respective molecular targets. **Method:** For this study, a descriptive bibliographic review with an integrative approach was conducted, searching for articles in the PubMed and Scielo databases, prioritizing publications from 2022 to 2025, enriched with clinical evidence and current guidelines. Systematic review studies, meta-analyses, and clinical evidence related to specific interventions were also analyzed. **Results:** The high effectiveness of targeted biological treatments, especially those acting on the interleukin 17 and interleukin 23 pathways, was shown in the results. There was also emphasis on the use of bimekizumab, ixekizumab, and risankizumab, in addition to infliximab, an anti-tumor necrosis factor alpha agent. Therapeutic possibilities through blocking tyrosine kinase 2 with deucravacitinib and the interleukin 36 receptor with spesolimab are expanded across the different clinical forms of the disease. **Conclusion:** It is concluded that the use of targeted therapies shows significant efficacy results and different safety profiles, supporting a personalized treatment approach for patients with psoriasis.

Keywords: Psoriasis; Targeted therapies; Molecular targets; Biologics; IL-17.

INTRODUCTION

Psoriasis is a chronic, recurrent, immune-mediated inflammatory disease that affects approximately 1.3% of the Brazilian population. It appears as erythematous, scaly lesions affecting both men and women, can occur at any age, and can involve any anatomical site. This condition is characterized by skin inflammation resulting from immune system activation, associated with abnormal keratinocyte hyperproliferation and differentiation, manifesting in various parts of the body such as skin, scalp, nails, and genital and intertriginous areas. Joint involvement occurs beyond the skin manifestation, potentially leading to disability and deformities that interfere with a person's personal and social life, although not all individuals with the condition are affected. According to the new Brazilian Psoriasis Consensus, some targeted therapies, like spesolimab which acts on the IL-36 receptor, used for generalized pustular psoriasis². Other treatments like agents that modulate the IL-17, IL-23 pathways and TYK2-mediated signaling such as bimekizumab, brodalumab, tildrakizumab, ixekizumab, risankizumab, and deucravacitinib are treatment alternatives by modulating the classic axis and interfering with different molecular pathways. These treatments still follow the rule of having side effects like any other treatment. But they have high therapeutic selectivity and different efficacy and safety profiles. Understanding the pathophysiology of psoriasis is extremely important to guide future treatments with greater potential to control the disease, impacting patients' quality of life as well as prognosis and therapy individualization^{2,3}. Well, besides seriously impacting an individual's quality of life, the disease becomes a systemic risk factor for the occurrence and development of other cardiovascular diseases, especially in young people³. Considering the range of therapies and different molecular targets involved in the treatment of psoriasis, it is essential to compare the available evidence on the efficacy and safety of these treatments, taking into account the different forms of the disease^{1,2}. Reviewing this evidence is important to clarify the understanding of new therapeutic approaches and to choose treatment in an individualized way². This study aimed to evaluate the scientific evidence on the efficacy and safety of targeted therapies in the treatment of moderate, severe, and pustular psoriasis.

METHOD

A descriptive, integrative literature review was carried out by searching for articles in the PubMed and SciELO databases. Systematic review studies, meta-analyses and new

findings with therapeutic approaches and molecular targets in the treatment of psoriasis. Publications between 2022 and 2025 were prioritized for this study, complemented by robust clinical evidence and previous guidelines when necessary for therapeutic approaches. We used terms related to psoriasis, biological therapies, targeted therapies, and molecular targets, including IL-17, IL-23, TYK2, and IL-36 pathways. Studies addressing targeted therapies, effectiveness, safety, and new therapy strategies in the treatment of psoriasis were listed, except for topics unrelated to the study's objective. The analysis was qualitative, with a compilation of records related to the effectiveness of targeted therapies and their respective molecular targets.

RESULTS

The real clinical benefit validated by the research body regarding the effectiveness of targeted therapies used in the treatment of psoriasis shows a significant clinical response, even though response rates vary depending on the drug, the molecular target, the outcome evaluated, and the follow-up period. IL-17 and IL-23 pathway inhibitors, as well as the selective TYK2 inhibitor, are part of the targeted therapies that showed relevant measures of therapeutic success, particularly for PASI 75 and PASI 90 outcomes. A systematic review with network meta-analysis, involving 204 studies and 67,889 participants, showed that biological treatments targeting IL-17, IL-12/23, IL-23, and TNF- α had higher response rates, achieving PASI 90 compared to non-targeted systemic therapies. Among the most effective drugs, infliximab, ixekizumab, bimekizumab, ixekizumab, and risankizumab stood out. Ixekizumab is an anti-IL-17A monoclonal antibody, standing out among the most effective treatments in this analysis. Some of the main targeted therapies, their respective molecular targets, and efficacy results are shown in Table 1.

Table 1 – Some of the targeted therapies, molecular targets, and efficacy results in psoriasis.

Medicine	Molecular target	Main efficacy result	Study
Bimekizumab	IL-17A/IL-17F	PASI 90: 85,0% ; PASI 100: 58,6% , week 16	BE VIVID [4]
Brodalumab	IL-17RA	PASI 90: 86% ; PASI 100: 74% , week 120	AMAGINE-2/3 [5]
Tildrakizumab	IL-23p19	PASI 90: 70,8–73,1% ; PASI 100: 28,6–36,6% , week 28*	reSURFACE [6]
Deucravacitinib	TYK2	PASI 75: 53,0–58,4% ; PASI 90: 27,0–35,5% , week 16	POETYK PSO-1/2 [7]
Certolizumab pegol	TNF- α	PASI 75: 76,7–82,0% ; PASI 90: 53,0–58,4% , week 16	CIMPASI-1/2 [8]

		PASI 90: 45,9–52,2% , week 16	
Espesolimab	IL-36R	Absence of pustules:54% vs. 6% placebo, week 1	Effisayil 1 [9]
Xeligekimabe	IL-17A	PASI 90 — among the most effective treatments in network analysis	Sbidian et al. [1]

Note: The rates reported for the drug Tildrakizumab reflect the response (PASI 90 and PASI 100) exclusively of the subgroup of responding patients who continued in the extension study, and not of the total number of patients initially randomized at week 28.

The compiled data shows that different classes of biological therapies offer significant clinical efficacy in treating psoriasis, varying according to the molecular target, the drug used, the outcome assessed, and the follow-up time of these patients. Above all, alternatives aimed at blocking IL-17 resulted in high skin clearance rates. Bimekizumab (an IL-17A and IL-17F inhibitor) reached PASI 90 responses in 85% of individuals and PASI 100 in 58.6% by week 16 (BE VIVID trial). Meanwhile, brodalumab (an IL-17RA receptor antagonist) stood out for maintaining long-term response, achieving PASI 90 in 86% and PASI 100 in 74% of patients at follow-up, results coming from a follow-up period different from that used in the other studies presented. Tildrakizumab, an IL-23 inhibitor, showed sustained high responses among individuals who responded to treatment in the reSURFACE studies. On the other hand, deucravacitinib, which is a TYK2 blocker, had a different therapeutic strategy, with PASI 75 of 58.4% and 53.0% in the POETYK PSO-1 and PSO-2 studies, respectively, at week 167. Certolizumab pegol, an anti-TNF- α agent, showed significant results, with PASI 75 of 76.7% and 82.0% and PASI 90 of 45.9% and 52.2% at doses of 200 mg and 400 mg, respectively, at week 168. The IL-36 receptor blocker spesolimab offers a distinct molecular approach to generalized pustular psoriasis. In the EFFISAVIL study, 1.54% of treated patients had no pustules by week 1, compared to 6% in the placebo group, showing a quick clinical response.

CONCLUSION

The available evidence shows high effectiveness of targeted therapies, especially agents that act on the IL-17 and IL-23 pathways, with notable use of bimekizumab, ixekizumab, and risankizumab, as well as infliximab, an important anti-TNF- α agent. The progress in using therapies aimed at different molecular targets, like TYK2 and IL-36R, expands treatment options and allows for a personalized approach based on the clinical form of the disease.

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