



BIOLOGIC THERAPIES FOR PSORIASIS

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ABSTRACT

Psoriasis, a chronic immune-mediated inflammatory skin disorder, has witnessed transformative advancements in treatment with the advent of biologic therapies. These agents target specific cytokines and immune pathways, including TNF- α , IL-17, IL-23, and IL-36, offering improved efficacy and safety compared to traditional systemic therapies. This review examines the molecular mechanisms of biologic agents, evaluates their clinical performance in plaque psoriasis and rare subtypes (e.g., generalized pustular psoriasis), and addresses challenges such as treatment resistance, paradoxical reactions, and long-term safety. By synthesizing recent clinical trials and mechanistic studies, this review underscores the importance of tailoring biologic therapies to individual patient profiles to optimize outcomes.

Keywords: Biologics, psoriasis, IL-17 inhibitors, IL-23 inhibitors, IL-36 inhibitors, TNF- α inhibitors, treatment resistance

INTRODUCTION

Psoriasis is a chronic, immune-mediated skin disease. In clinical management, although topical therapies such as topical medications and phototherapy are commonly used to alleviate symptoms, these methods often have limited efficacy. Currently, targeted therapies, including biologic agents, offer new treatment options for these patients¹. This review explores the mechanisms, clinical efficacy, and limitations of biologic agents, focusing on TNF- α , IL-17, IL-23, and IL-36 inhibitors, while highlighting future directions in precision medicine.

DISCUSSION

Psoriasis affects approximately 2–3% of the global population, characterized by hyperproliferation of keratinocytes, immune dysregulation, and systemic inflammation. Psoriasis, a chronic immune-mediated inflammatory skin disorder, has witnessed transformative advancements in treatment with the advent of biologic therapies.

TNF- α Inhibitors are impeding the interaction between TNF- α and its receptors, thereby mitigating systemic inflammation². In the context of psoriatic arthritis, these TNF- α inhibitors have demonstrated effectiveness. They can alleviate joint pain, swelling, and stiffness, and also slow down the progression of joint damage. This is likely due to their ability to modulate the inflammatory environment within the joints, reducing the infiltration of inflammatory cells and the production of other pro-inflammatory mediators³.

IL-17 inhibitors, such as secukinumab and ixekizumab, play a pivotal role in the treatment of psoriasis. IL-17A is known to be a key mediator in the activation of keratinocytes, which are the primary cells of the epidermis. In psoriasis, the over-activation of keratinocytes leads to abnormal skin proliferation and scaling. Additionally, IL-17A is responsible for the recruitment of neutrophils into the skin. The influx of neutrophils further contributes to the inflammatory process in psoriatic lesions. One of the most remarkable features of IL-17 inhibitors is their ability to induce rapid and high-rate responses in patients with psoriasis⁴. Specifically, a significant proportion of patients, more than 70% to be precise, achieve a Psoriasis Area and Severity Index (PASI) 90 or PASI 100 response. A PASI 90 response indicates a 90% improvement in the psoriasis area and severity, while a PASI 100 response means complete clearance of the psoriasis symptoms³. This makes them an essential part of the therapeutic arsenal available to dermatologists when dealing with this common yet often challenging skin condition.

IL-23 is a cytokine that plays a central and multifaceted role in the complex immune-mediated pathogenesis of psoriasis. IL-23 inhibitors, including guselkumab and risankizumab, By blocking IL-23 prevent the differentiation of Th17 cells. There are potential advantages in selective blockade of the IL-23-specific p19 subunit with respect to distal blockade of IL-17A or its receptor. Acting upstream in the IL-23/IL-17 cytokine pathway is likely to reduce the expression of multiple pro-inflammatory cytokines acting on keratinocytes⁵. Therefore, some studies have found that in the treatment of moderate to severe psoriasis, compared with secukinumab, guselkumab demonstrates more superior long-term efficacy in terms of

achieving a Psoriasis Area and Severity Index (PASI) 90 improvement at week 48⁶.

Generalized pustular psoriasis (GPP) is a severe and rare form of inflammatory skin disease characterized by widespread, rapidly appearing sterile pustules on the skin, accompanied by systemic symptoms such as fever and malaise. The pathogenesis of GPP involves a complex interplay of immune dysregulation, and emerging evidence has identified interleukin-36 receptor (IL-36R) as a pivotal driver in this process. In recent clinical trials, medications designed to specifically block IL-36R have demonstrated remarkable efficacy. One of the most striking outcomes is the rapid clearance of pustules, which typically occurs within just a few days of initiating treatment⁷. The success of IL-36R-targeted therapies has far-reaching implications, potentially paving the way for the development of more targeted treatments for other inflammatory skin diseases and even systemic autoimmune disorders.

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The long-term use of biologic agents for the treatment of psoriasis may be associated with several hazards and potential risks, which deserve careful consideration and monitoring in clinical practice. One of the most prominent concerns is the elevated risk of infections. Also, some studies suggest that immune suppression caused by biologics might interfere with the body's ability to detect and eliminate cancerous cells. The use of biologics may also trigger the development of autoimmune diseases. Moreover, by altering the normal balance of the immune system, these medications can sometimes lead to the production of autoantibodies and the activation of autoreactive immune cells. Finally, long-term exposure to biologics can lead to the development of drug resistance and a decline in treatment efficacy.

CONCLUSION

Biologic therapies have redefined psoriasis treatment by targeting key inflammatory pathways with precision. While IL-17 and IL-23 inhibitors dominate current practice for plaque psoriasis, IL-36 inhibitors fill a critical niche in GPP management. Challenges such as treatment resistance, paradoxical reactions, and cost barriers persist, necessitating innovative approaches like biosimilars, combination therapies, and biomarker-driven regimens. Future research should prioritize large-scale real-world studies and mechanistic investigations to refine therapeutic algorithms and improve patient outcomes.

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