OPEN ACCESS Freely available online

Journal of Clinical & Experimental Dermatology Research

Research Article

Paradoxical Responses in Biologic Therapy for Psoriasis: Unraveling Mechanisms and Optimizing Treatment Strategies

Jingyan Kong[1], Minghui Zhao[2], Xiaoyu Ma[2*], Fan Yang[1*], Hongxiao Gao[2]

[1]Department of Chinese Medicine and Cosmetology, Tianjin University of Traditional Chinese Medicine, Tianjin, China; [2]Department of Basic Teaching and Research in Traditional Chinese Medicine, Tianjin University of Traditional Chinese Medicine, Tianjin, China

ABSTRACT

This review article comprehensively investigates the paradoxical reactions provoked by biologics in the treatment of psoriasis, examining the role of chemokines, inflammatory mediators, oxidative stress responses, as well as genetic and environmental factors. Biologics, whilst offering significant relief to psoriasis symptoms, can in some cases exacerbate the condition through the induction of other chemokines and inflammatory mediators, or by disrupting intracellular antioxidant mechanisms. Additionally, the presence of gene polymorphisms in psoriasis patients may influence the sensitivity to biologics, with specific polymorphisms in the *HLA-Cw6*, *IL23R*, and *IL12B* genes possibly impacting the reactivity to TNF-α and IL-23 inhibitors. Environmental factors, such as infections, lifestyle, and psychological stress, can also affect the occurrence of paradoxical reactions, with smoking, alcohol consumption, and infections potentially impacting the efficacy and safety of biologics. This review underscores the importance of a holistic understanding of the role of these factors in paradoxical reactions for optimizing psoriasis treatment plans.

Keywords: Psoriasis; Biologics; Immune system; Paradoxical reactions; Treatment optimization

INTRODUCTION

Psoriasis is a common chronic skin disease, primarily characterized by local skin redness, scales, and itching [1]. The prevalence of psoriasis varies among different regions and populations, but it maintains a certain level of prevalence worldwide [2]. The etiology of psoriasis is not entirely understood, but research indicates that it's associated with aberrant activation of the immune system, genetic factors, and environmental influences [3]. Moreover, the incidence of psoriasis can increase with age, and there are gender differences, with varying rates between men and women [4].

Biologics refer to drugs with specific biological activities produced through genetic engineering. They can interfere with specific cytokines and signaling pathways in the immune system, thereby achieving therapeutic effects in psoriasis [5]. Currently, biologics have become an important treatment choice, especially for patients who are resistant or intolerant to traditional therapies. The use of biologics can significantly improve patients' symptoms and quality of life, reduce the area and severity of skin lesions, and maintain long-term efficacy [6-8]. Despite the notable efficacy of biologics in the treatment of psoriasis, paradoxical reactions occur. For instance, the long-term use of biologics may lead to the suppression of immune function, increasing the risk of opportunistic infections [9,10]. Therefore, understanding the mechanisms of paradoxical reactions in biologic treatment is important for optimizing treatment plans and reducing treatment risks. Current studies have found that altering the dosage and administration of biologics, and the combined use of other drugs may help reduce the occurrence of paradoxical reactions [7,11].

Correspondence to: Fan Yang, Department of Chinese Medicine and Cosmetology, Tianjin University of Traditional Chinese Medicine, Tianjin, China, E-mail: yang_fan1981@sina.com

Xiaoyu Ma, Department of Basic Teaching and Research in Traditional Chinese Medicine, Tianjin University of Traditional Chinese Medicine, Tianjin, China, E-mail: 1067650789@qq.com

Received: 23-Oct-2023, Manuscript No. JCEDR-23-27970; **Editor assigned:** 25-Oct-2023, Pre QC No. JCEDR-23-27970 (PQ); **Reviewed:** 10-Nov-2023, QC No. JCEDR-23-27970; **Revised:** 17-Nov-2023, Manuscript No. JCEDR-23-27970 (R); **Published:** 24-Nov-2023, DOI: 10.35841/2329-9509.23.14.651.

Citation: Kong J, Zhao M, Ma X, Yang F, Gao H (2023) Paradoxical Responses in Biologic Therapy for Psoriasis: Unraveling Mechanisms and Optimizing Treatment Strategies. J Clin Exp Dermatol Res. 14:651.

The aim of this review is to provide a comprehensive analysis and summary of the importance and current status of biologic treatment for psoriasis, as well as the mechanisms of paradoxical reactions. Through this comprehensive analysis, we hope to provide a reference for optimizing the biologic treatment of psoriasis.

LITERATURE REVIEW

Common types of biologic agents used for treating psoriasis

Biologics, innovative medications with broad applications in various diseases, have proven significantly effective in the field of dermatology, especially in treating psoriasis. Currently, the biologics commonly used in dermatology for psoriasis treatment internationally include:

Tumor Necrosis Factor (TNF: Inhibitors are a class of drugs that counteract the activity of TNF. This class of biologics includes Etanercept, Infliximab, Adalimumab, golimumab, and certolizumab, among others. They inhibit TNF activity, reducing inflammation and thus alleviating the symptoms of psoriasis [12-18].

Cell inhibitors: Common drugs include Rituximab and Omalizumab. These medications inhibit the activity of B cells, reducing the production of inflammatory factors and autoantigens, thus modulating the function of the immune system and relieving the inflammatory response in psoriasis [19-21].

IL-12/23 inhibitors: Such as Ustekinumab and Briakinumab, primarily inhibit IL-12 and IL-23 to suppress the activation of Th1 and Th17 cells, thus alleviating inflammation [22,23].

Interleukin-17A (IL-17A: Inhibitors mainly include secukinumab, ixekizumab, and brodalumab. These drugs moderate the immune system by inhibiting the function of IL-17A, thereby reducing psoriasis symptoms and the inflammatory response [24,25].

IL-1 antagonists: Include, but are not limited to, Anakinra, Canakinumab, and Gevokizumab. These medications modulate the function of the immune system, alleviating inflammation and thus improving symptoms in psoriasis patients. Anakinra, a human recombinant IL-1Ra antagonist, can inhibit IL-1α and IL-β and has shown results in the treatment of Generalized Pustular Psoriasis (GPP) and patients with IL-1 receptor antagonist deficiency [26,27]. Canakinumab, an anti-IL-1β antibody, has shown benefits in the treatment of GPP [28,30]. As a novel anti-IL-1β antibody, Gevokizumab can also be used in the treatment of GPP patients [31,32].

IL-23 inhibitors: These are drugs that inhibit the cytokine IL-23, an important immune-mediated factor closely associated with the pathogenesis of psoriasis. Several specific drugs have been developed, including ustekinumab, guselkumab, tildrakizumab, and risankizumb. By interfering with the signaling pathway of IL-23 and inhibiting its activation effect on the immune system, these drugs achieve their therapeutic effect in psoriasis [22,33-38] (Figure 1).

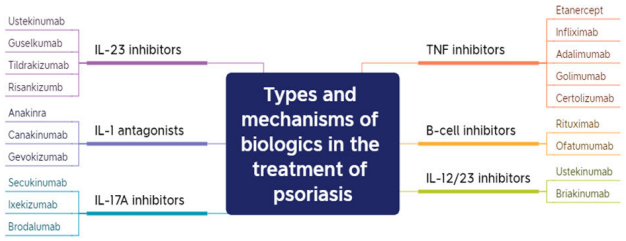

Figure 1: Types and mechanisms of biologics in the treatment of psoriasis.

Mechanism of action and efficacy evaluation of biologics

The mechanism of action of biologics in psoriasis treatment primarily involves suppressing the inflammatory response, blocking T-cell activation, and inhibiting B-cell function [13]. Regarding efficacy evaluation, the Psoriasis Area and Severity Index (PASI) scoring is commonly employed to assess treatment outcomes [39,40]. Research indicates that, in the treatment of psoriasis, optimal results from biologics are generally achieved after 4-6 weeks of continuous therapy [41,42]. Despite the significant efficacy of biologics in psoriasis treatment, certain adverse reactions are associated with their use. Common side effects include infections [43], headaches [44], gastrointestinal discomfort, and allergic reactions [45-47]. Moreover, some biologics, such as Infliximab and Adalimumab, may pose a risk of malignant tumors during use [48-51]. Therefore, regular checks for complete blood count and liver and kidney function assessments are necessary during the course of psoriasis treatment with biologics to monitor potential adverse reactions.

The manifestation of paradoxical reactions in psoriasis treatment with biologics

A paradoxical reaction refers to an unexpected response that contradicts the theoretical mechanism of a drug during treatment [52]. They can be categorized into mild, moderate, and severe, based on their nature and intensity. Mild reactions may only present as transient discomfort, moderate reactions may lead to decreased treatment efficacy, and severe reactions may threaten the patient's life [53,54]. Biologics primarily work by blocking the biological activity of inflammatory factors, thereby suppressing inflammatory responses and alleviating psoriatic lesions. However, paradoxical reactions can occur during this treatment process, such as a worsening of psoriasis or the emergence of new skin lesions, particularly common when using anti-TNF drugs [55-57]. Here is a detailed overview of various commonly used biologics:

Tumor Necrosis Factor (TNF) inhibitors: Infliximab, Etanercept, and Adalimumab have been proven effective in treating diseases such as psoriasis and psoriatic arthritis. However, some studies have pointed out potential paradoxical reactions associated with the use of TNF inhibitors, including the emergence of new or worsening psoriatic rash; gastrointestinal discomfort; increased risk of infections such as tuberculosis, fungal infections, and bacterial infections; and

potential disease rebound after discontinuation of TNF inhibitors [46,58-62].

B cell inhibitors: Like Rituximab, primarily used to treat autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus, it achieves disease control by selectively eliminating CD20 positive B cells. However, some studies have found that new or worsening psoriasis may occur during treatment with B cell inhibitors, posing an increased risk of certain infections such as fungal and bacterial infections, and potential disease rebound after discontinuation [63-67].

IL-12/23 inhibitors: Like Ustekinumab, a biologic used to treat moderate to severe psoriasis, it works by inhibiting the activation and proliferation of Th1 and Th17 cells. However, some studies have found paradoxical reactions may occur during treatment with IL-12/23 inhibitors, such as atypical psoriasis responses like collagenosis or psoriatic arthritis, increased risk of bacterial and viral infections, and potential triggering or worsening of some immune-mediated diseases like Crohn's disease and ulcerative colitis, as well as headaches, upper respiratory infections, and skin irritation. [68-73].

IL-1 antagonists: Like Anakinra, used to treat some inflammatory diseases, including psoriasis. However, some studies have shown that paradoxical reactions may occur during treatment with IL-1 antagonists, manifesting as rashes, including psoriatic-like rash, reversible after discontinuation of the drug, increased risk of bacterial and viral infections, and potential triggering or worsening of some immune-mediated diseases like Cohn's disease and ulcerative colitis [74-78].

IL-23 inhibitors: IL-23 inhibitors achieve therapeutic effects by suppressing immune responses, which could potentially suppress the patient's immune system, thereby increasing the risk of infectious diseases [79]. Some studies have indicated that the treatment of psoriasis with IL-23 inhibitors could lead to a rebound of rash [80]. IL-23 inhibitors may also affect the efficacy of vaccines [81-84].

IL-17A inhibitors: Some studies have found that IL-17A inhibitors may lead to the occurrence of novel diseases during the treatment of psoriasis, and the use of IL-17A inhibitors may increase the risk of inflammatory bowel diseases (such as Cohn's disease and ulcerative colitis) [85]. Some research also indicates that some patients may experience disease rebound, worsening condition after discontinuation of IL-17A inhibitors [86]. Additionally, some patients may develop resistance to these drugs, leading to a gradual decline in treatment efficacy (Figure 2).

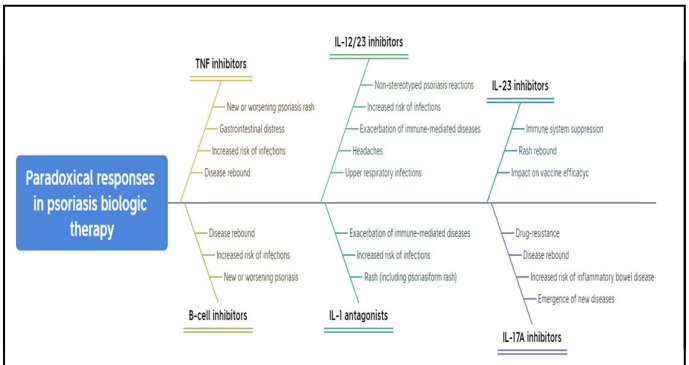

Figure 2: Paradoxical responses in psoriasis biologic therapy.

Impact of paradoxical reactions on treatment efficacy and quality of life

Paradoxical reactions can potentially affect the treatment outcome, prolonging or exacerbating the course of psoriasis, thereby impacting patients' quality of life. These reactions may also instill fear and resistance towards the medication in patients, lowering their adherence to the treatment, and thus influencing the overall treatment efficacy. During the administration of biologics, it is important to regularly conduct safety assessments, closely monitor the emergence of paradoxical reactions, and if severe reactions occur, the use of the drug should be immediately discontinued and alternative treatment options should be sought.

The treatment efficacy of biologics can be assessed through a variety of indices, including the Psoriasis Area and Severity Index (PASI), Patient Global Assessment (PGA) [87] and the Health-Related Quality of Life (HRQoL) [88]. The degree of improvement in these indices post-biologic treatment can reflect the efficacy of the medication. Furthermore, long-term follow-up of patients is necessary to monitor the durability of treatment effects and the occurrence of paradoxical reactions. Hence, paradoxical reactions in the treatment of psoriasis with biologics not only concern the selection and usage of drugs but also involve a comprehensive evaluation of treatment efficacy and safety, requiring the joint attention and handling of both physicians and patients.

Mechanisms underlying paradoxical reactions

The role and regulatory mechanisms of the immune system in the treatment of psoriasis with biologics: The development and progression of psoriasis are associated with immune system abnormalities [89]. Biologics treat psoriasis by modulating the immune system to suppress inflammatory responses. Studies have shown that biologics can effectively control the development of psoriasis by regulating the balance of cytokines such as Th1, Th2, and Th17 [90,91], as well as by modulating the functions of antigen presentation, phagocytosis, and natural killer cells [92,93]. Additionally, biologics can activate anti-inflammatory signaling pathways, such as NF-kB inhibitors and STAT3 inhibitors, to alleviate skin inflammation [94-97] (Figure 3).

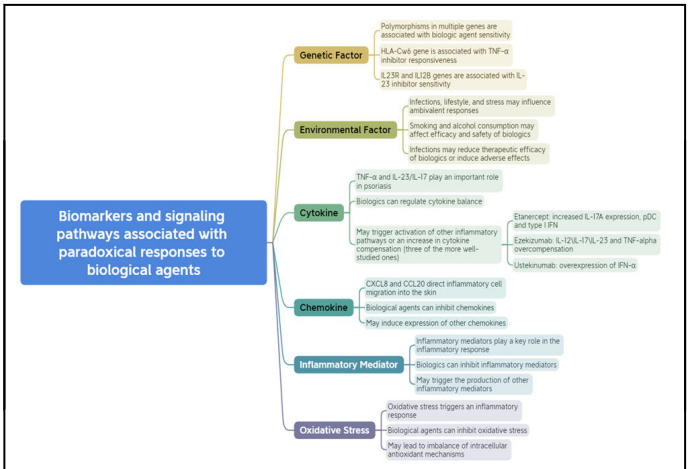

Figure 3: Biomarkers and signaling pathways associated with paradoxical responses to biological agents.

Biomarkers and signaling pathways associated with paradoxical reactions to biologics

Paradoxical reactions, characterized by a worsening or relapse of symptoms after the use of biologics, is a common phenomenon in the treatment of psoriasis [7,98,99]. The mechanisms underlying these reactions are not fully understood but may be related to the immunoregulatory effects of biologics, individual differences, and environmental factors [100,101]. Certain biomarkers and signaling pathways, such as cytokines, chemokines, inflammatory mediators, and oxidative stress responses, may play key roles in paradoxical reactions. Monitoring these biomarkers and signaling pathway alterations can help in early identification and prevention of paradoxical reactions [100,102-104]. Psoriasis is a complex inflammatory disease whose pathophysiology involves numerous signaling pathways and cell types, including T cells, keratinocytes, dendritic cells, and myriad cytokines like Tumor Necrosis Factor (TNF) and Interleukins (ILs) [105-108]. Biologics target these signaling pathways and cytokines to treat psoriasis, but sometimes they may trigger paradoxical reactions.

Cytokines: Cytokines like TNF-α and the IL-23/IL-17 axis play an important roles in psoriasis. Biologics such as TNF-α inhibitors and IL-17 inhibitors can effectively alleviate symptoms. However, some patients may experience worsening of their condition after using these agents, possibly due to the activation of other inflammatory pathways or compensatory increase in cytokines [75,109-111].

Chemokines: Chemokines such as CXCL8 and CCL20 can guide inflammatory cells to the skin, exacerbating inflammation. Biologics can mitigate symptoms by inhibiting these chemokines, but in some cases, they may induce the expression of other chemokines, exacerbating the condition [112-116].

Inflammatory mediators: Inflammatory mediators, including various prostaglandins and leukotrienes, play a key role in inflammatory responses. Biologics can alleviate symptoms by inhibiting these mediators, but in some instances, they may trigger the production of other inflammatory mediators, worsening the condition [117-122].

Oxidative stress responses: Oxidative stress responses can trigger inflammatory reactions and exacerbate skin lesions. Biologics can improve the condition by inhibiting oxidative stress responses, but in certain cases, they may disrupt the intracellular antioxidant mechanisms, worsening the condition [123-126].

Genetic and environmental factors in paradoxical reactions

Genetic and environmental factors play critical roles not only in the pathogenesis of psoriasis but also in the occurrence of paradoxical reactions. Studies have shown the presence of polymorphisms in multiple genes in patients with psoriasis, which may be related to the sensitivity of psoriasis to biologics [127]. Polymorphism in the *HLA-Cw6* gene has been found to be associated with the reactivity of psoriasis to TNF-α inhibitors [128]. Another study found that polymorphisms in *IL23R* and *IL12B* genes might influence the sensitivity of psoriasis patients to IL-23 inhibitors [129]. Environmental factors such as infections, lifestyle, and psychological stress could also affect the occurrence of paradoxical reactions [130-132]. Smoking and alcohol consumption could potentially impact the efficacy and safety of biologics [133]. Furthermore, infections may lead to a decrease in the therapeutic effect of biologics and even trigger severe adverse reactions [134]. Therefore, a comprehensive understanding of the role of genetic and environmental factors in paradoxical reactions is vital for optimizing psoriasis treatment plans.

Strategies for managing and preventing paradoxical reactions

Firstly, for the identification and assessment of paradoxical reactions, careful observation of symptom changes and adverse reactions during the treatment process is necessary. Simultaneously, a holistic evaluation should be conducted in conjunction with individual differences and specific disease characteristics. Necessary information could be gathered through medical history inquiries, physical examinations, and relevant laboratory tests to promptly identify and assess the occurrence and severity of paradoxical reactions. Secondly, various strategies can be employed in managing and treating paradoxical reactions. On one hand, the drug dosage and frequency of use could be reduced or adjusted to minimize the occurrence and severity of adverse reactions [8,135,136]. On the other hand, adjunctive treatment measures, such as local care, physiotherapy, and traditional Chinese medicine, could be used to alleviate adverse reactions and promote disease improvement [137-140]. Lastly, for the prevention of paradoxical reactions and personalized treatment strategies, a multi-faceted approach is needed. Firstly, patients should be guided to adopt good lifestyle habits, including regular sleep and meal schedules, balanced diet, and moderate exercise, to enhance immune resistance [141]. Psychological regulation is also vital to maintain a positive mental and emotional state, which could be achieved through psychological counseling and support. Moreover, personalized treatment is of paramount importance. Treatment plans should be customized based on the patient's disease characteristics and individual differences to achieve optimal therapeutic outcomes [142].

Psoriasis is a chronic inflammatory skin condition characterized primarily by patchy red skin covered with white scales. Patients often experience symptoms such as itching and dryness, which tend to worsen during the winter and lighten during the summer [3].Currently, significant progress has been made in the treatment of psoriasis using biologics. These biologics work by modulating the immune system functions, reducing the inflammatory response, and thus improving patient symptoms. However, a number of paradoxical reactions may occur during the biologic treatment of psoriasis, including immune suppression, infection, and diminished vaccine response. The mechanisms of biologic treatment primarily function by inhibiting inflammatory mediators and regulating immune cell

functions [143-145]. However, the specific mechanisms warrant further exploration and research. In terms of future research prospects and recommendations, current studies are primarily focused on clinical observations and case studies. Future research could delve deeper into the pathogenesis of psoriasis, mechanisms of biologic therapy, and the occurrence mechanisms of paradoxical reactions. Moreover, multi-center and large-scale clinical studies can be conducted to more comprehensively and objectively assess the efficacy and safety of biologic treatments [146,147]. In conclusion, biologic treatment for psoriasis is currently an effective therapeutic approach, albeit potential paradoxical reactions may occur during the treatment process. Future research can further explore the treatment mechanisms and conduct more extensive and in-depth clinical studies.

CONCLUSION

In conclusion, the management and prevention of paradoxical reactions in psoriasis can be effectively addressed through identification and assessment, management and treatment, as well as prevention strategies and personalized treatment approaches. The implementation of these strategies requires considering the patient's disease characteristics and individual differences to enhance treatment outcomes and improve the patients' quality of life.

REFERENCES

1. Armstrong AW, Read C. Pathophysiology, clinical presentation, and treatment of psoriasis: A review. JAMA. 2020;323(19):1945-1960.
2. Parisi R, Iskandar IY, Kontopantelis E, Augustin M, Griffiths CE, Ashcroft DM. National, regional, and worldwide epidemiology of psoriasis: Systematic analysis and modelling study. BMJ. 2020;369.
3. Griffiths CEM, Armstrong AW, Gudjonsson JE, Barker JNWN. Psoriasis. Lancet. 2021; 397(10281): 1301-1315.
4. Ding J, Joseph M, Chawla S, Yau N, Khosa Z, Khawaja F, et al. Disparities in psoriasis clinical trials: A cross-sectional analysis. J Am Acad Dermatol. 2022;87(6):1386-1389.
5. Xiao Q, Li X, Li Y, Wu Z, Xu C, Chen Z, et al. Biological drug and drug delivery-mediated immunotherapy. Acta Pharm Sin B. 2021;11(4):941-960.
6. Egeberg A, Ottosen MB, Gniadecki R, Broesby-Olsen S, Dam TN, Bryld LE, et al. Safety, efficacy and drug survival of biologics and biosimilars for moderate-to-severe plaque psoriasis. Br J Dermatol. 2018;178(2):509-519.
7. Ortiz AJ, Fernández-Freire RL, Rodríguez HJC, NeilaB R, Romero DAJ. Efficacy and safety of biological therapy in patients with psoriasis and recent neoplasia: Experience in real single-center clinical practice. Arch Dermatol Re. 2023;315(4):1045-1048.
8. Ribero S, Ortoncelli M, Mastorino L, Quaglino P, Dapavo P. Reduced doses of biological therapies in psoriasis: A new potentially "sustainable" frontier of psoriasis treatment. Expert Opin Biol Ther. 2023;23(9):867-868.
9. Murphy MJ, Cohen JM, Vesely MD, Damsky W. Paradoxical eruptions to targeted therapies in dermatology: A systematic review and analysis. J Am Acad Dermatol. 2022;86(5):1080-1091.
10. Lu RM, Hwang YC, Liu IJ, Lee CC, Tsai HZ, Li HJ, et al. Development of therapeutic antibodies for the treatment of diseases. J Biomed Sci. 2020;27(1):1-30.
11. Lozano CR. Safety of biological therapies: New data from BIOBADASER. Reumatol Clin. 2011;6:S1-S6. [Crossref] [Google Scholar] [PubMed]
12. Chédotal H, Narayanan D, Povlsen K, Gotfredsen CH, Brambilla R, Gajhede M, et al. Small-molecule modulators of tumor necrosis factor signaling. Drug Discov Today. 2023:103575.
13. Leone GM, Mangano K, Petralia MC, Nicoletti F, Fagone P. Past, present and (foreseeable) future of biological anti-tnf alpha therapy. J Clin Med. 2023;12(4):1630.
14. Ducharme E, Weinberg JM. Etanercept. Expert Opin Biol Ther. 2008;8(4):491-502.
15. Li S, Li G, Li X, Wu F, Li L. Etanercept ameliorates psoriasis progression through regulating high mobility group box 1 pathway. Skin Res Technol. 2023;29(4):e13329.
16. Kishimoto M, Komine M, Kamiya K, Sugai J, Kuwahara A, Mieno M, et al. Drug survival of tumor necrosis factor-alpha inhibitors and switched subsequent biologic agents in patients with psoriasis: A retrospective study. Dermatol Ther (Heidelb). 2023:1-4.
17. Onsun N, Güneş B, Kaya G, Güçkan Işık B, Yabacı Tak A. Comparison of survival and retention rates between infliximab and adalimumab for psoriasis: 10-year experience at a single tertiary center. Dermatology. 2023;239(3):355-361.
18. Hagino T, Saeki H, Kanda N. Biomarkers and predictive factors for treatment response to tumor necrosis factor- ff inhibitors in patients with psoriasis. J Clin Med, 2023, 12(3):974.
19. Fetter T, Niebel D, Braegelmann C, Wenzel J. Skin-associated B cells in the pathogenesis of cutaneous autoimmune diseases-implications for therapeutic approaches. Cells. 2020;9(12):2627.
20. Kim DW, Park SK, Woo SH, Yun SK, Kim HU, Park J. New-onset psoriasis induced by rituximab therapy for non-Hodgkin lymphoma in a child. Eur J Dermatol. 2016;26(2):190-191.
21. Abdelmaksoud A, Temiz SA, Daye M, Yavuz S, Wollina U, Lotti T, et al. Response of chronic refractory psoriasis vulgaris with urticaria to combined secukinumab and omalizumab: A case report and review of the literature. J Cosmet Dermatol. 2023;22(4):1416-1418.
22. Gönülal M, Balcı DD, Öztürk A, Doğan S. Effectiveness and safety of ustekinumab for the treatment of psoriasis; six years of clinical experience. J Dermatolog Treat. 2023;34(1):2241941.
23. Schurich A, Raine C, Morris V, Ciurtin C. The role of IL-12/23 in T cell-related chronic inflammation: Implications of immunodeficiency and therapeutic blockade. Rheumatology (Oxford). 2018;57(2):246-254.
24. Vsn M, Mothe RK, Hyderboini RK, Likhar N, Ganji K, Singuru S, et al. Ssystematic review and meta-analysis of briakinumab, a fully human interleukin 12/23 monoclonal antibody, for the treatment of moderate to severe chronic plaque psoriasis. Value in Health. 2016;19(3):A123.
25. Wang C, Torisu-Itakura H, Hanada T, Matsuo T, Cai Z, Osaga S, et al. Treatment persistence of interleukin-17 inhibitor class drugs among patients with psoriasis in Japan: A retrospective database study. J Dermatolog Treat. 2023;34(1):2229465.
26. Dastoli S, Passante M, Loconsole F, Mortato E, Balato A, Piccolo V, et al. Long-term efficacy and safety of secukinumab in real life: A 240 weeks multicenter study from Southern Italy. J Dermatolog Treat. 2023;34(1):2200868.
27. Naik HB, Pichard DC, Schwartz DM, O'Brien M, Masciocchi M, Thompson J, et al. Anakinra for refractory pustular psoriasis: A phase II, open-label, dose-escalation trial. J Am Acad Dermatol. 2022;87(6):1380-1383.
28. Macca L, Pomi FL, Ingrasciotta Y, Morrone P, Trifirò G, Guarneri C. Hidradenitis suppurativa and psoriasis: The odd couple. Front Med (Lausanne). 2023;10.

29. Skendros P, Papagoras C, Lefaki I, Giatromanolaki A, Kotsianidis I, Speletas M, et al. Successful response in a case of severe pustular psoriasis after interleukin1β inhibition. Br J Dermatol. 2017;176(1): 212-215.
30. Mansouri B, Richards L, Menter A. Treatment of two patients with generalized pustular psoriasis with the interleukin-1β inhibitor gevokizumab. Br J Dermatol. 2015;173(1):239-241.
31. Moreau A, Le Vée M, Jouan E, Denizot C, Parmentier Y, Fardel O. Effect of gevokizumab on interleukin-1β-mediated cytochrome P450 3A4 and drug transporter repression in cultured human hepatocytes. Eur J Drug Metab Pharmacokinet. 2017;42:871-878.
32. Kong L, huang DW, Lu JJ, Zhang Y, Li Y, Yi X, et al. Development of bullous pemphigoid during treatment of psoriasis with ustekinumab: A case report and literature review. Front Med (Lausanne). 2023;10 :1171802.
33. Bartholomew E, Chung BY, Davis M, Yeroushalmi S, Chung M, Hakimi M, et al. Rapid Remission of Sunburn-Induced Guttate Psoriasis with Guselkumab. Dermatol Ther (Heidelb). 2023:1-6.
34. Gerdes S, Hoffmann M, Asadullah K, Korge B, Mortazawi D, Krüger N, et al. Effectiveness, safety and quality of life effects of guselkumab and ustekinumab in patients with psoriasis: Week 104 results from the non-interventional, prospective, German multicentre PERSIST study. J Eur Acad Dermatol Venereol. 2023.
35. Egeberg A, Jullien D, Gaarn Du Jardin K, Thaçi D. Five-year safety of tildrakizumab in patients with moderate-to-severe psoriasis from two phase 3 trials (reSURFACE 1 and reSURFACE 2): Number needed to harm for occurrence of adverse events of special interest. J Dermatolog Treat. 2023;34(1):2220447.
36. Ruggiero A, Fabbrocicni G, Cacciapuoti S, Potestio L, Gallo L, Megna M. Tildrakizumab for the treatment of moderate-to-severe psoriasis: Results from 52 weeks real-life retrospective study. Clin Cosmet Investig Dermatol. 2023:529-536.
37. Huang K, Wu X, Li Y, Lv C, Yan Y, Wu Z, et al. Artificial intelligence–based psoriasis severity assessment: Real-world study and application. J Med Internet Res. 2023;25:e44932.
38. Maravilla-Herrera P, Merino M, Alfonso Zamora S, Balea Filgueiras J, Carrascosa Carrillo JM, Delgado Sánchez O, et al. The social value of a PASI 90 or PASI 100 response in patients with moderate-to-severe plaque psoriasis in Spain. Front Public Health. 2023;11:1000776.
39. Papp KA, Weinberg MA, Morris A, Reich K. IL17A/F nanobody sonelokimab in patients with plaque psoriasis: A multicentre, randomised, placebo-controlled, phase 2b study. Lancet. 2021;397(10284):1564-1575.
40. Puig L, Bakulev AL, Kokhan MM, Samtsov AV, Khairutdinov VR, Morozova MA, et al. Efficacy and safety of netakimab, a novel anti-IL-17 monoclonal antibody, in patients with moderate to severe plaque psoriasis. Results of a 54-week randomized double-blind placebo-controlled PLANETA clinical trial. Dermatol Ther (Heidelb). 2021;11(4):1319-1332.
41. Gambra MP, Montesinos JJ, Valenzuela MT, Cárcamo ME. Risk of infections associated with the use of biological medications; a review. Rev Med Chil. 2020;148(8):1155-1170.
42. Carrascosa JM, Del-Alcazar E. Apremilast for psoriasis treatment. G Ital Dermatol Venereol. 2020;155(4): 421-433.
43. AbuHilal MD, Walsh S, Shear N. Use of apremilast in combination with other therapies for treatment of chronic plaque psoriasis: A retrospective study. Cutan Med Surg. 2016;20(4):313-316.
44. Jiraskova Zakostelska Z, Reiss Z, Tlaskalova-Hogenova H, Rob F. Paradoxical reactions to anti-TNFα and anti-IL-17 treatment in psoriasis patients: Are skin and/or gut microbiota involved?. Dermatol Ther. 2023;13(4):911-933.
45. Thomaidou E, Ramot Y. Injection site reactions with the use of biological agents. Dermatol Ther. 2019;32(2):e12817.
46. Chen Y, Friedman M, Liu G, Deodhar A, Chu CQ. Do tumor necrosis factor inhibitors increase cancer risk in patients with chronic immune-mediated inflammatory disorders?. Cytokine. 2018;101:78-88.
47. Fuxench ZC, Shin DB, Beatty AO, Gelfand JM. The risk of cancer in patients with psoriasis: A population-based cohort study in the health improvement network. JAMA Dermatol. 2016;152(3): 282-290.
48. Langley RG, Strober BE, Gu Y, Rozzo SJ, Okun MM. Benefit-risk assessment of tumour necrosis factor antagonists in the treatment of psoriasis. Br J Dermatol. 2010;162(6):1349-1358.
49. Semaka A, Salopek TG. Risk of developing melanoma with systemic agents used to treat psoriasis: A review of the literature. J Cutan Med Surg. 2022;26(1):87-92.
50. Miyagawa F. Pathogenesis of paradoxical reactions associated with targeted biologic agents for inflammatory skin diseases. Biomedicines. 2022;10(7):1485.
51. Kremenevski I, Sander O, Sticherling M, Raithel M. Paradoxical reactions to biologicals in chronic inflammatory systemic diseases. Dtsch Arztebl Int. 2022;119(6):88.
52. Yagiz B, Lermi N, Coskun BN, Dalkilic E, Kiraz S, Erden A, et al. The predictors of paradoxical reactions, especially psoriasis, to biologic therapy—findings from the TReasure database: A 5-year follow-up study. Rheumatology. 2023:kead318.
53. Bataille P, Layese R, Claudepierre P, Paris N, Dubiel J, Amiot A, et al. Paradoxical reactions and biologic agents: A French cohort study of 9303 patients. Br J Dermatol. 2022;187(5):676-683.
54. Ancor SG, Reolid A, Fisas LH, Munoz-Aceituno E, Llamas-Velasco M, Sahuquillo-Torralba A, et al. DNA copy number variation associated with anti-tumour necrosis factor drug response and paradoxical psoriasiform reactions in patients with moderate-to-severe psoriasis. Acta Derm Venereol. 2021;101(5).
55. Su HJ, Chan YP, Shen PC, Ku CL, Ng CY. Anti-IL-17A antibody-associated de novo vitiligo: Case report and review of literature. Frontiers in Immunology. 2023;13:1077681.
56. Kim HW, Kim EH, Lee M, Jung I, Ahn SS. Risk of cancer, tuberculosis and serious infections in patients with ankylosing spondylitis, psoriatic arthritis and psoriasis treated with IL-17 and TNF-α inhibitors: A nationwide nested case-control analysis. Clin Exp Rheumatol. 2023;41:1491-1499.
57. Li M, You R, Su Y, Zhou H, Gong S. Characteristic analysis of adverse reactions of five anti-TNFα agents: A descriptive analysis from WHO-VigiAccess. Front Pharmacol. 2023;14.
58. Pauline O, Robert M, Bernardeau C, Hlavaty A, Fusaroli M, Roustit M, et al. Assessment of reported adverse events after interchanging between tnf-α inhibitor biosimilars in the who pharmacovigilance database. BioDrugs. 2023:1-9.
59. Zhou X, Mubanga D, Chen Z, Bi X. Secondary generalized cutaneous mucinosis developed during etanercept treatment in a patient with psoriasis. Clin Cosmet Investig Dermatol. 2022:987-992.
60. Coşkunol İ, Turan O, Baysak A, Solmaz D, Can G. Frequency of latent tuberculosis in patients receiving anti-TNF-alpha therapy. Afr Health Sci. 2023;23(2):128-132.
61. Berger JR, Houff SA, Major EO. Monoclonal antibodies and progressive multifocal leukoencephalopathy. MAbs. 2009;1(6): 583-589.
62. Fagni F, Simon D, Tascilar K, Schoenau V, Sticherling M, Neurath MF, et al. COVID-19 and immune-mediated inflammatory diseases: Effect of disease and treatment on COVID-19 outcomes and vaccine responses. Lancet Rheumatol. 2021;3(10):e724-e736.

63. Kovarik J. From immunosuppression to immunomodulation: Current principles and future strategies. Pathobiology. 2013;80(6):275-281.
64. Guidelli GM, Fioravanti A, Rubegni P, Feci L. Induced psoriasis after rituximab therapy for rheumatoid arthritis: A case report and review of the literature. Rheumatol Int. 2013;33:2927-2930.
65. Seror R, Sordet C, Guillevin L, Hachulla E, Masson C, Ittah M, et al. Tolerance and efficacy of rituximab and changes in serum B cell biomarkers in patients with systemic complications of primary Sjögren's syndrome. Ann Rheum Dis. 2007;66(3):351-357.
66. Puzenat E, Bronsard V, Prey S, Gourraud PA, Aractingi S, Bagot M, et al. What are the best outcome measures for assessing plaque psoriasis severity? A systematic review of the literature. J Eur Acad Dermatol Venereol. 2010;24:10-16.
67. Reich K, Langley RG, Papp KA, Ortonne JP, Unnebrink K, Kaul M, et al. A 52-week trial comparing briakinumab with methotrexate in patients with psoriasis. N Engl J Med. 2011;365(17):1586-1596.
68. Patel BM, Ramos Rivers C, Koutroumpakis F, Ahsan M, Dueker J, Hashash J, et al. Ustekinumab-induced remission of two cases of refractory cutaneous crohn's disease. Inflammatory Bowel Diseases. 2021;27(10):e124.
69. Toussirot É, Michel F, Béreau M, Binda D. Ustekinumab in chronic immune-mediated diseases: A review of long term safety and patient improvement. Patient preference and adherence. 2013:369-377.
70. Xu X, Qin G, Meng Z, Pei D. Body mass index, disease duration and tumor necrosis factor inhibitor history predict reduced ustekinumab response in Chinese psoriasis patients: A real-world study. Indian J Dermato. 2021;66(5):574.]
71. Davidson L, van den Reek JM, van Hunsel F, de Jong EM, Kullberg BJ. Global risk of bacterial skin infections and herpesviridae infections with ustekinumab, secukinumab, and tumour necrosis factor-alpha inhibitors: Spontaneous reports of adverse drug reactions from the world health organization pharmacovigilance center. Acta Dermato-Venereologica. 2022;102.
72. López GMA, Taboada MVM, Vela GMC, Llaca FH, Bernal VJF. New onset psoriasis following treatment with the interleukin1 receptor antagonist anakinra. Br J Dermatol. 2008;158(5): 1146-1148.
73. Karamanakos A, Vergou T, Panopoulos S, Tektonidou MG, Stratigos AJ, Sfikakis PP. Psoriasis as an adverse reaction to biologic agents beyond anti-TNF-α therapy. Eur J Dermatol. 2021;31(3): 307-317.
74. Tauber M, Viguier M, Alimova E, Petit A, Lioté F, Smahi A, et al. Partial clinical response to anakinra in severe palmoplantar pustular psoriasis. Br J Dermatol. 2014;171(3):646-649.
75. Viguier M, Guigue P, Pagès C, Smahi A, Bachelez H. Successful treatment of generalized pustular psoriasis with the interleukin-1-receptor antagonist Anakinra: Lack of correlation with IL1RN mutations. Ann Intern Med. 2010;153(1):66-67.
76. Fleischmann RM, Tesser J, Schiff MH, Schechtman J, Burmester GR, Bennett R, et al. Safety of extended treatment with anakinra in patients with rheumatoid arthritis. Ann Rheum Dis. 2006;65(8): 1006-1012.
77. Reich K, Armstrong AW, Foley P, Song M, Wasfi Y, Randazzo B, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the treatment of patients with moderate to severe psoriasis with randomized withdrawal and retreatment: Results from the phase III, double-blind, placebo-and active comparator–controlled VOYAGE 2 trial. J Am Acad Dermatol. 2017;76(3):418-431.
78. Gordon KB, Strober B, Lebwohl M, Augustin M, Blauvelt A, Poulin Y, et al. Efficacy and safety of risankizumab in moderate-to-severe plaque psoriasis (UltIMMa-1 and UltIMMa-2): Results from two double-blind, randomised, placebo-controlled and ustekinumab-controlled phase 3 trials. Lancet. 2018;392(10148):650-661.
79. Abdo AI, Tye GJ. Interleukin 23 and autoimmune diseases: Current and possible future therapies. Inflamm Res. 2020;69(5):463-480.
80. Nogueira M, Warren RB, Torres T. Risk of tuberculosis reactivation with interleukin (IL)-17 and IL-23 inhibitors in psoriasis–time for a paradigm change. J Eur Acad Dermatol Venereol. 2021;35(4): 824-834.
81. Palakornkitti P, Nimmannitya K, Rattanakaemakorn P. Biological therapy in Psoriasis: An emphasis on its dermatologic adverse events. Asian Pac J Allergy Immunol. 2021;39(4):215-230.
82. Winthrop KL, Silverfield J, Racewicz A, Neal J, Lee EB, Hrycaj P, et al. The effect of tofacitinib on pneumococcal and influenza vaccine responses in rheumatoid arthritis. Ann Rheum Dis. 2016;75(4): 687-695.
83. Mehta P, Lawrence A, Aggarwal A. Paradoxical gastrointestinal effects of interleukin-17 blockers. Ann Rheum Dis.2023;82(6):e152.
84. Thaçi D, Blauvelt A, Reich K, Tsai TF, Vanaclocha F, Kingo K, et al. Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe plaque psoriasis: CLEAR, a randomized controlled trial. J Am Acad Dermatol. 2015;73(3): 400-409.
85. Langley RG, Ellis CN. Evaluating psoriasis with psoriasis area and severity index, psoriasis global assessment, and lattice system physician's global assessment. J Am Acad Dermatol. 2004;51(4): 563-569.
86. Kasiem FR, Kok MR, Luime JJ, Tchetverikov I, Wervers K, Korswagen LAet al. The burden of psoriasis in patients with early psoriatic arthritis. Rheumatology. 2022;61(4):1570-1578.
87. Zhang Y, Xu X, Cheng H, Zhou F. AIM2 and Psoriasis. Front Immunol. 2023;14:1085448.
88. Park J, Son MJ, Ho CC, Lee SH, Kim Y, An J, et al. Transcriptional inhibition of STAT1 functions in the nucleus alleviates Th1 and Th17 cell-mediated inflammatory diseases. Front Immunol. 2022;13:1054472.
89. Yan K, Zhang F, Ren J, Huang Q, Yawalkar N, Han L. MicroRNA-125a-5p regulates the effect of Tregs on Th1 and Th17 through targeting ETS-1/STAT3 in psoriasis. J Transl Med. 2023;21(1):678.
90. Babaie F, Omraninava M, Gorabi AM, Khosrojerdi A, Aslani S, Yazdchi A, et al. Etiopathogenesis of psoriasis from genetic perspective: An updated review. Curr Genomics. 2022;23(3):163.
91. Marusina AI, Ji-Xu A, Le ST, Toussi A, Tsoi LC, Li Q, et al. Cell-Specific and Variant-Linked Alterations in Expression of ERAP1, ERAP2, and LNPEP Aminopeptidases in Psoriasis. J Invest Dermatol. 2023;143(7):1157-1167.
92. Jia HY, Qiu HY, Zhang MD, Hou JJ, Zhou ML, Wu Y. Lenalidomide attenuates IMQ-induced inflammation in a mouse model of psoriasis. Biomed Pharmacother. 2022;156:113883.
93. Srivastava AK, Srivastava S, Kumar V, Ghosh S, Yadav S, Malik R, et al. Identification and mechanistic exploration of structural and conformational dynamics of NF-kB inhibitors: Rationale insights from *in silico* and *in vitro* studies. J Biomol Struct Dyn. 2023:1-21.
94. Lu H, Gong H, Du J, Gao W, Xu J, Cai X, et al. Piperine ameliorates psoriatic skin inflammation by inhibiting the phosphorylation of STAT3. Int Immunopharmacol. 2023;119:110221.
95. Ravipati A, Nolan S, Alphonse M, Dikeman D, Youn C, Wang Y, et al. IL-6R/signal transducer and activator of transcription 3 signaling in keratinocytes rather than in T cells induces psoriasis-like dermatitis in mice. J Invest Dermatol. 2022;142(4):1126-1135.

96. Camela E, Potestio L, Fabbrocini G, Megna M. Paradoxical reactions to biologicals for psoriasis. Expert Opin Biol Ther. 2022;22(12):1435-1437.

97. Fisher S, Ziv M. Skin and soft tissue infections in biological therapy for psoriasis-A case report and systematic review of the literature. Int J Dermatol. 2021;60(11):1429-1434.

98. Krušič M, Jezernik G, Potočnik U. Gene ontology analysis highlights biological processes influencing responsiveness to biological therapy in psoriasis. Pharmaceutics. 2023;15(8):2024.

99. Singh R, Koppu S, Perche PO, Feldman SR. The cytokine mediated molecular pathophysiology of psoriasis and its clinical implications. Int J Mol Sci. 2021;22(23):12793.

100. Ceccarelli M, Rullo VE, Berretta M, Cacopardo B, Pellicano GF. New generation biologics for the treatment of psoriasis and psoriatic arthritis. State of the art and considerations about the risk of infection. Dermatol Ther. 2021;34(1):e14660.

101. Chen J, Li C, Li H, Yu H, Zhang X, Yan M, et al. Identification of a TH2-high psoriasis cluster based on skin biomarker analysis in a Chinese psoriasis population. J Eur Acad Dermatol Venereol. 2021;35(1):150-158.

102. Solberg SM, Aarebrot AK, Sarkar I, Petrovic A, Sandvik LF, Bergum B, et al. Mass cytometry analysis of blood immune cells from psoriasis patients on biological therapy. Eur J Immunol. 2021;51(3): 694-6702.

103. Contassot E, French LE. Killing two birds with one stone: TNF antagonists downregulate systemic IL-1β in Psoriasis. J Invest Dermatol. 2021;141(3):476-478.

104. Xiang R, Hu L, Li S, Wei Z, Song Z, Chen Z, et al. Tiamulin inhibits TNF-α and alleviates psoriasis-like dermatitis. J Dermatol Sci. 2022;107(1):32-40.

105. Avallone G, Maronese CA, Murgia G, Carrera CG, Mastorino L, Roccuzzo G, et al. Interleukin-17 *vs.* Interleukin-23 Inhibitors in Pustular and Erythrodermic Psoriasis: A retrospective, multicentre cohort study. J Clin Med. 2023;12(4):1662.

106. Zhu C, Ren Y, Yao H, Feng B, Liu L, Zheng M. Heparanase contributes to psoriatic lesions through crosstalk with IL-17 pathway. Indian J Dermatol. 2023;68(1):59-66.

107. Carrasquillo OY, Pabón-Cartagena G, Barrera-Llaurador J, Colón-Fontanez F, Martín-García RF. Psoriatic alopecia in a patient with Crohn Disease: An uncommon manifestation of tumor necrosis factor α inhibitors. Cutis. 2021;107(4):E48-E55.

108. Ho CH, Silva AA, Tomita B, Weng HY, Ho IC. Differential impacts of TNFα inhibitors on the transcriptome of Th cells. Arthritis Res Ther. 2021;23:1-3.

109. Ożóg MK, Grabarek BO, Wierzbik-Strońska M, Świder M. Neurological complications of biological treatment of psoriasis. Life. 2022;12(1):118.

110. Choudhary S, Anand R, Pradhan D, Bastia B, Kumar SN, Singh H, et al. Transcriptomic landscaping of core genes and pathways of mild and severe psoriasis vulgaris. Int J Mol Med. 2021;47(1): 219-231.

111. Furue K, Ito T, Tanaka Y, Yumine A, Hashimoto-Hachiya A, Takemura M, et al. Cyto/chemokine profile of *in vitro* scratched keratinocyte model: Implications of significant upregulation of CCL20, CXCL8 and IL36G in Koebner phenomenon. J Dermatol Sci. 2019;94(1):244-251.

112. Kanda N, Hau CS, Tada Y, Tatsuta A, Sato S, Watanabe S. Visfatin enhances CXCL8, CXCL10, and CCL20 production in human keratinocytes. Endocrinology. 2011;152(8):3155-3164.

113. Yang Y, Xie S, Jiang W, Tang S, Shi Y. Discovering novel biomarkers associated with the pathogenesis of psoriasis: Evidence from bioinformatic analysis. Int J Gen Med. 2022:2817-2833.

114. Abdallah BH, Seeler S, Bregnhøj A, Ghatnekar G, Kristensen LS, Iversen L. et al. Heat shock protein 90 inhibitor RGRN-305 potently attenuates skin inflammation. Front Immunol. 2023;14:1128897.

115. Gomes L, Santos A, Gil Â, Filipe P, Quinhones-Levy P, Bicho M. 309 interleukin-1β, cyclooxygenase-2 and prostaglandin E2 receptor 4 genetic polymorphisms may modulate inflammation influencing the severity of psoriasis. J Invest Dermatol. 2022;142(12):S233.

116. Morin S, Tremblay A, Dumais E, Julien P, Flamand N, Pouliot R. Eicosapentaenoic acid influences the lipid profile of an *in vitro* psoriatic skin model produced with T cells. Biomolecules. 2023;13(9):1413.

117. Wadi JS, Dunya AD, Jabir M, Najim MA, Jawad SF, Hamzah SS, et al. Exploring the interaction between 3-D structure of TLR 9 and prostaglandin analogues. Arab J Chem. 2023;16(5):104692.

118. Paine A, Brookes PS, Bhattacharya S, Li D, de La Luz Garcia Hernandez M, Tausk F, et al. Dysregulation of bile acids, lipids, and nucleotides in psoriatic arthritis revealed by unbiased profiling of serum metabolites. Arthritis Rheumatol. 2023;75(1):53-63.

119. Tsukayama I, Kawakami Y, Tamenobu A, Toda K, Maruoka S, Nagasaki Y, et al. Malabaricone C derived from nutmeg inhibits arachidonate 5-lipoxygenase activity and ameliorates psoriasis-like skin inflammation in mice. Free Radic Biol Med. 2022;193(1):1-8.

120. Yokomizo T, Shimizu T. The leukotriene B4 receptors BLT1 and BLT2 as potential therapeutic targets. Immunol Rev. 2023;317(1): 30-41.

121. Blagov A, Sukhorukov V, Guo S, Zhang D, Eremin I, Orekhov A. The role of oxidative stress in the induction and development of psoriasis. Front Biosci. 2023;28(6):118.

122. Dobrică EC, Cozma MA, Găman MA, Voiculescu VM, Găman AM. The involvement of oxidative stress in psoriasis: A systematic review. Antioxidants. 2022;11(2):282.

123. Salahuddin Z, Rafi A, Muhammad H, Aftab U, Akhtar T, Zafar MS, et al. Revolutionalizing the age old conventional treatment of psoriasis: An animal based comparative study between methylprednisolone and different doses of a novel anti-oxidant humanin analogue (HNG). Int Immunopharmacol. 2022;110:108990.

124. Zhang Z, Tang S, Jiang Y, Long F, He F, Liu J, et al. Oxidative stress induces meiotic defects of oocytes in a mouse psoriasis model. Cell Death Dis. 2022;13(5):474.

125. Al-Janabi A, Eyre S, Foulkes AC, Khan AR, Dand N, Burova E, et al. Atopic polygenic risk score is associated with paradoxical eczema developing in patients with psoriasis treated with biologics. J Invest Dermatol. 2023;143(8):1470-1478.

126. Talamonti M, Botti E, Galluzzo M, Teoli M, Spallone G, Bavetta M, et al. Pharmacogenetics of psoriasis: HLA Cw6 but not LCE3B/3C deletion nor TNFAIP3 polymorphism predisposes to clinical response to interleukin 12/23 blocker ustekinumab. Br J Dermatol. 2013;169(2):458-463.

127. Mahil SK, Capon F, Barker JN. Genetics of psoriasis. Dermatol Clin. 2015;33(1):1-11.

128. Naik PP. Stem cell therapy as a potential treatment option for psoriasis. An Bras Dermatol. 2022;97(4):471-477.

129. Nardis C. Latent virus reactivation risk and biological drugs: Chronic inflammatory and immune-mediated disorders. Int J Immunopathol Pharmacol. 2013;26(4):983-989.

130. Singh A, Easwari TS. Recent advances in psoriasis therapy: Trends and future prospects. Current Drug Targets. 2021;22(15):1760-1771.

131. Armstrong AW, Harskamp CT, Dhillon JS, Armstrong EJ. Psoriasis and smoking: A systematic review and meta-analysis. Br J Dermatol. 2014;170(2):304-314.

132. Xu Z, Xu P, Fan W, Yang G, Wang J, Cheng Q, et al. Risk of infection in patients with spondyloarthritis and ankylosing spondylitis receiving antitumor necrosis factor therapy: A meta-analysis of randomized controlled trials. Exp Ther Med. 2017;14(4):3491-3500.

133. Menter A, Strober BE, Kaplan DH, Kivelevitch D, Prater EF, Stoff B, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. J Am Acad Dermatol. 2019;80(4):1029-1072.

134. Diotallevi F, Paolinelli M, Radi G, Offidani A. Latest combination therapies in psoriasis: Narrative review of the literature. Dermatol Ther. 2022;35(10):e15759.

135. Hodak E, Gottlieb AB, Segal T, Politi Y, Maron L, Sulkes J, et al. Climatotherapy at the Dead Sea is a remittive therapy for psoriasis: Combined effects on epidermal and immunologic activation. J Am Acad Dermatol. 2003;49(3):451-457.

136. Perrotta FM, Scriffignano S, Benfaremo D, Ronga M, Luchetti MM, Lubrano E. New insights in physical therapy and rehabilitation in psoriatic arthritis: A review. Rheumatol Ther. 2021;8(2):639-649.

137. Yang XY, Cai WL, Guo CL, Chen QH. Chinese medicine as supporting therapy for psoriasis: Past, present, and future. Chin J Integr Med. 2023;29(3):280-288.

138. Ma X, Li D, Zhao M, He J, Yang F, Kong J. Bloodletting cupping combined with conventional measures therapy for psoriasis: A systematic review and meta-analysis of randomized controlled trials. Front Med. 2023;10:1132928.

139. Jensen P, Zachariae C, Christensen R, Geiker NR, Schaadt BK, Stender S, et al. Effect of weight loss on the severity of psoriasis: A randomized clinical study. JAMA Dermatol. 2013;149(7):795-801.

140. Kunchok A, Aksamit AJ, Davis JM, Kantarci OH, Keegan BM, Pittock SJ, et al. Association between tumor necrosis factor inhibitor exposure and inflammatory central nervous system events. JAMA Neurol. 2020;77(8):937-946.

141. Singla S, Putman M, Liew J, Gordon K. Association between biological immunotherapy for psoriasis and time to incident inflammatory arthritis: A retrospective cohort study. Lancet Rheumatol. 2023;5(4):e200-e207.

142. Singla S, Putman M, Liew J, Gordon K. Differentiating biologics to prevent psoriatic arthritis in patients with psoriasis-Authors' reply. Lancet Rheumatol. 2023;5(6):e313.

143. Thorley J. Biological therapy for psoriasis and development of psoriatic arthritis. Lancet. 2021; 3(11): E755-E.

144. Gordon KB, Foley P, Krueger JG, Pinter A, Reich K, Vender R, et al. Bimekizumab efficacy and safety in moderate to severe plaque psoriasis (Be ready): A multicentre, double-blind, placebo-controlled, randomised withdrawal phase 3 trial. Lancet. 2021;397(10273): 475-486.

145. Papp K, Warren RB, Green L, Reich K, Langley RG, Paul C, et al. Safety and efficacy of mirikizumab *versus* secukinumab and placebo in the treatment of moderate-to-severe plaque psoriasis (OASIS-2): A phase 3, multicentre, randomised, double-blind study. Lancet Rheumatol. 2023;5(9):e542-E552.

146. Reich K, Papp KA, Blauvelt A, Langley RG, Armstrong A, Warren RB, et al. Bimekizumab *versus* ustekinumab for the treatment of moderate to severe plaque psoriasis (BE VIVID): Efficacy and safety from a 52-week, multicentre, double-blind, active comparator and placebo controlled phase 3 trial. Lancet. 2021;397(10273):487-498.

147. Tehlirian C, Peeva E, Kieras E, Scaramozza M, Roberts ES, Singh RS, et al. Safety, tolerability, efficacy, pharmacokinetics, and pharmacodynamics of the oral TYK2 inhibitor PF-06826647 in participants with plaque psoriasis: A phase 1, randomised, double-blind, placebo-controlled, parallel-group study. Lancet Rheumatol. 2021;3(3):e204-e213.