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Research article

Research trends and hotspots in biologics for plaque psoriasis: A bibliometric study from 2004 to 2023

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ABSTRACTS

Background and objective: Biologics have revolutionized the management of plaque psoriasis and are flourishing. We aimed to construct a knowledge structure in this field through bibliometrics, analyze research trends and cutting-edge hotspots to inspire future research directions, and provide valuable references for clinical decisions.

Methods: Publications on biologics for plaque psoriasis in the Web of Science database core collection from 2004 to 2023 were searched. Bibliometric analysis and scientific knowledge mapping were performed with R, CiteSpace, and VOSviewer software.

Results: 2,672 articles written by 9,474 authors from 67 countries were included in the study. The number of annual publications has steadily increased over the last 20 years. The most prolific countries, institutions, and authors were the United States, Novartis, and Prof. Reick K., respectively. Reference analysis categorized the research base of the field into 10 main clusters. "Efficacy" and "safety" were the most frequent keywords, and cluster analysis categorized the research in this area into four groups. Burst detection captured current hot keywords including interleukin (IL)-17 inhibitors, IL-23 inhibitors, "drug survival," "discontinuation," "Covid-19," "real-world," and "clinical features."

Conclusion: Global publications on biologics research in plaque psoriasis have grown steadily and rapidly over the past two decades. Efficacy and safety are the highest topics of concern for researchers, and IL-17 inhibitors, IL-23 inhibitors, real-world studies, efficacy prediction, and retreatment after biologics failure or discontinuation are current research hotspots.

1. Introduction

Psoriasis is a chronic, inflammatory, systemic disease characterized by erythematous scales that affects 0.51%–11.43 % of adults and 0%–1.37 % of children worldwide, with the prevalence increasing year by year [1–3]. The disfiguring outward appearance of psoriasis places a heavy psychological burden on patients, with 21%–34 % suffering from anxiety, 28 % from alexithymia, and 12.7 % reporting suicidal ideation [4–7]. In addition, systemic inflammation and immune disorders often lead to multisystem co-morbidities such as psoriatic arthritis, cardiovascular disease, and metabolic syndrome, which seriously jeopardize patients' health and shorten

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their life expectancy [8,9].

Chronic activation of the innate and adaptive immune systems is involved in psoriasis, leading to increased release of pro-inflammatory factors such as tumor necrosis factor-alpha (TNF-α), interleukin (IL)-17, IL-12, and IL-23 [10]. These pro-inflammatory factors stimulate aberrant proliferation of keratinocytes, promote increased release of vascular endothelial growth factor, and attract circulating inflammatory cells, forming the basis of the pathology of plaque psoriasis [10]. In recent years, growing knowledge of pathogenesis and refinements in biologics technology have catalyzed therapeutic innovations. More than a dozen biologics such as targeted TNF-alpha inhibitors (Etanercept, Infliximab, and Adalimumab, Certolizumab), IL-12/IL-23p40 inhibitors (Ustekinumab), IL-17 inhibitors (Secukinumab, Ixekizumab, and Brodalumab), and IL-23p12 inhibitors (Guselkizumab, Tildrakizumab, and Risankizumab) have been successively applied in plaque psoriasis [11,12].

Although biologics have only been approved for plaque psoriasis for two decades, remarkable advancements have been made in the field. Scholars have conducted numerous studies, and extensive articles have been published. However, the proliferation of literature poses a challenge for researchers seeking to quickly and accurately grasp the latest developments in the field.

Bibliometrics is a discipline that describes, analyzes, and predicts the general situation, hotspots, and trends in a field based on publication information using mathematics, applied statistics, and visualization techniques [13,14]. In contrast to expert reviews, systematic reviews, and meta-analyses that focus on a particular aspect, bibliometrics tends to provide a comprehensive and visual presentation of the knowledge structure of the field, such as global trends in research, contribution levels of countries, institutions, and authors, the development of the discipline, and current hot frontiers. However, to the best of our knowledge, there are no bibliometric studies on biologics for plaque psoriasis to date. To fill this gap, we conducted a bibliometric study in this field using Bibliometrix R-package, VOSviewer, and CiteSpace, which described the global trends, core journals, contributions of countries, institutions, and authors, and explored cutting-edge hotspots. This study aimed to provide clinicians and researchers with accurate and comprehensive information in this field, inspire future research directions, and provide a valuable reference for clinical decisions.

2. Methods

2.1. Data sources and search strategies

We searched the Web of Science Core Collection (WOSCC) database on January 14, 2024, for relevant literature in the field of biologics research in plaque psoriasis. Search strategy: TS = ("biological agents" OR "biologics" OR "Infliximab" OR "Etanercept" OR "Adalimumab" OR "Certolizumab" OR "Ustekinumab" OR "Secukinumab" OR "Brodalumab" OR "Ixekizumab" OR "Tildrakizumab" OR "Guselkumab" OR "Brazikumab" OR "Mirikizumab" OR "Itolizumab" OR "Alefacept" OR "Risankizumab" OR "Certolizumab" OR "Efalizumab") AND TS=("psoriasis"). The language of publication is limited to English, the type is limited to article, and the publication period is set from January 1, 2004, to December 31, 2023. Initially, 5,304 documents were retrieved. To ensure the relevance of the publications to the research topic, two researchers independently evaluated the articles based on their titles and abstracts. Duplicate articles were eliminated using Citespace, resulting in a total of 2,672 documents.

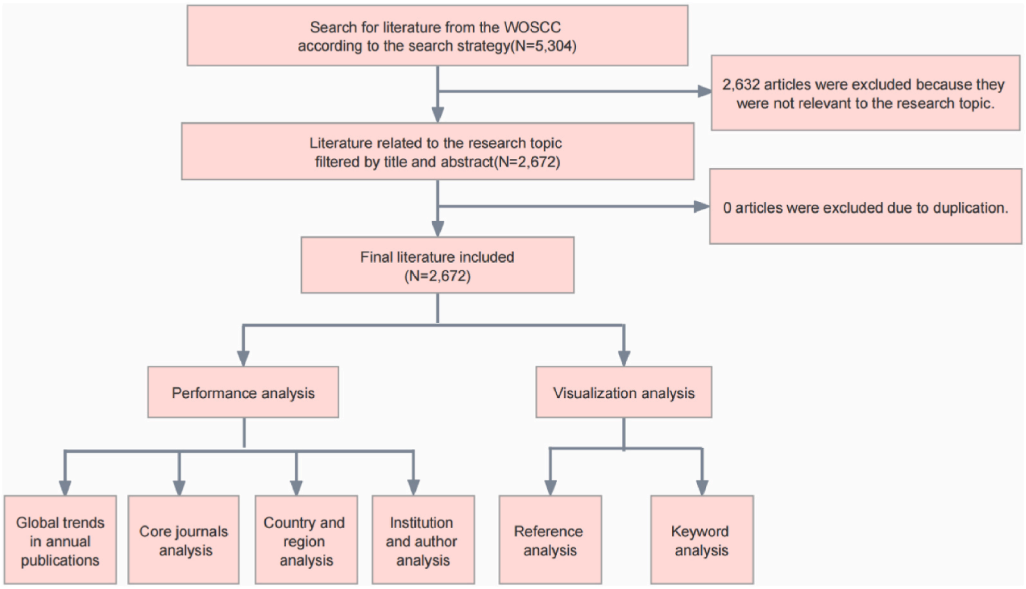


Fig. 1. Literature search, screening, and analysis process.

2.2. Data analysis and visualization

For data analysis and visualization, the Bibliometrix R-package, Citespace (5.7.R3), and VOSviewer (V.1.6.18) were utilized. The Bibliometrix R-package [15] is a bibliometric analysis tool that relies on the R language. In this study, it was used to summarize the number of annual publications and to conduct performance analysis of countries, institutions, and authors. VOSviewer [16], a software for visualizing knowledge graphs based on collaborative or co-occurrence data, was used to construct collaborative networks of countries, institutions, and authors, as well as keyword co-occurrence networks. Citesspace [17], a bibliometrics software, was used for reference co-citation analysis and keyword burst detection to identify trends in research areas and emerging hotspots. The parameterization of the software is described in the Supplementary Material. Fig. 1 Fig. 1 illustrates the process of literature search, screening, and analysis.

The visualization network in this study mainly consists of nodes and lines. The size of the nodes indicates the number of publications, while the connecting lines between nodes represent collaborations or co-occurrences in the same article. In burst detection, red line segments were used to indicate periods of high frequency. Betweenness centrality (BC) [18] is an index used to quantify a node's centrality in the relationship mapping, identifying nodes that serve as important bridges or mediators. Larger values indicate a stronger intermediary role, and a node with BC $>$ 0.1 is generally considered an important hub. Modularity Q and Mean Silhouette are employed for the quality evaluation of clustering results in Citespace [19]. Generally, S $>$ 0.5 means the clustering structure is reasonable, S $>$ 0.7 means the clustering result is convincing, Q $>$ 0.3 means the clustering structure is significant, and a Q value closer to 1 indicates a stronger clustering structure [19].

3. Results

3.1. Global trends in annual publications

A total of 2672 articles on biologics for plaque psoriasis were identified. Fig. 2 illustrates the trend of annual publications. The number of annual publications has been increasing steadily over the past 20 years, with an average annual growth rate of 14.07 %. Notably, there has been an explosive growth in publications since 2020. Plotting the trend line for annual publications yielded $R^2 = 0.9298$, indicating a strong upward trend in publications in the future. These findings collectively demonstrate the increasing interest in the field of psoriasis biologics research, which is expected to continue to grow in the future.

3.2. Core journals analysis

The included articles were published in 329 journals that cover a wide range of disciplines, such as dermatology, immunology, and integrative medicine. Fig. 3 displays the 10 most productive journals in the field and identifies five of them as core journals according to Bradford's Law. These core journals are the *British Journal of Dermatology* (246), *Journal of Dermatological Treatment* (227), *Journal of the European Academy of Dermatology and Venereology* (201), *Dermatologic Therapy* (153), and *Journal of the American Academy of Dermatology* (134). The H-index is a mixed quantitative metric based on the number of papers by a researcher/journal and the times their papers are cited, which is used to assess the quantity and level of scholarly output of a researcher [20]. As measured by the H-index, the most influential journal in the field is the *British Journal of Dermatology* (66), followed by the *Journal of the American Academy of Dermatology* (53) and the *Journal of the European Academy of Dermatology and Venereology* (42).

3.3. Cooperation network

3.3.1. Country/region cooperation network

Fig. 4a illustrates the scientific production of countries, with the shade of the color reflecting the amount of national scientific production. 67 countries contribute to the development of knowledge in this field, with the United States being the most productive

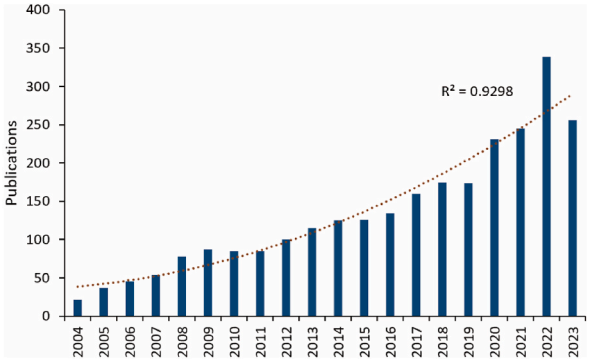


Fig. 2. Annual publications on biologics for plaque psoriasis from 2004 to 2023.

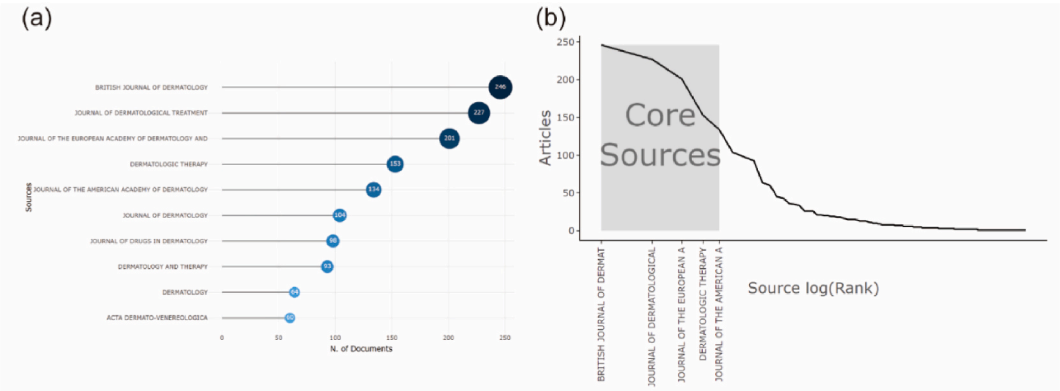


Fig. 3. Journal analysis on biologics for plaque psoriasis. (a) The top 10 journals with the most publications. (b) Core journals according to Bradford's Law.

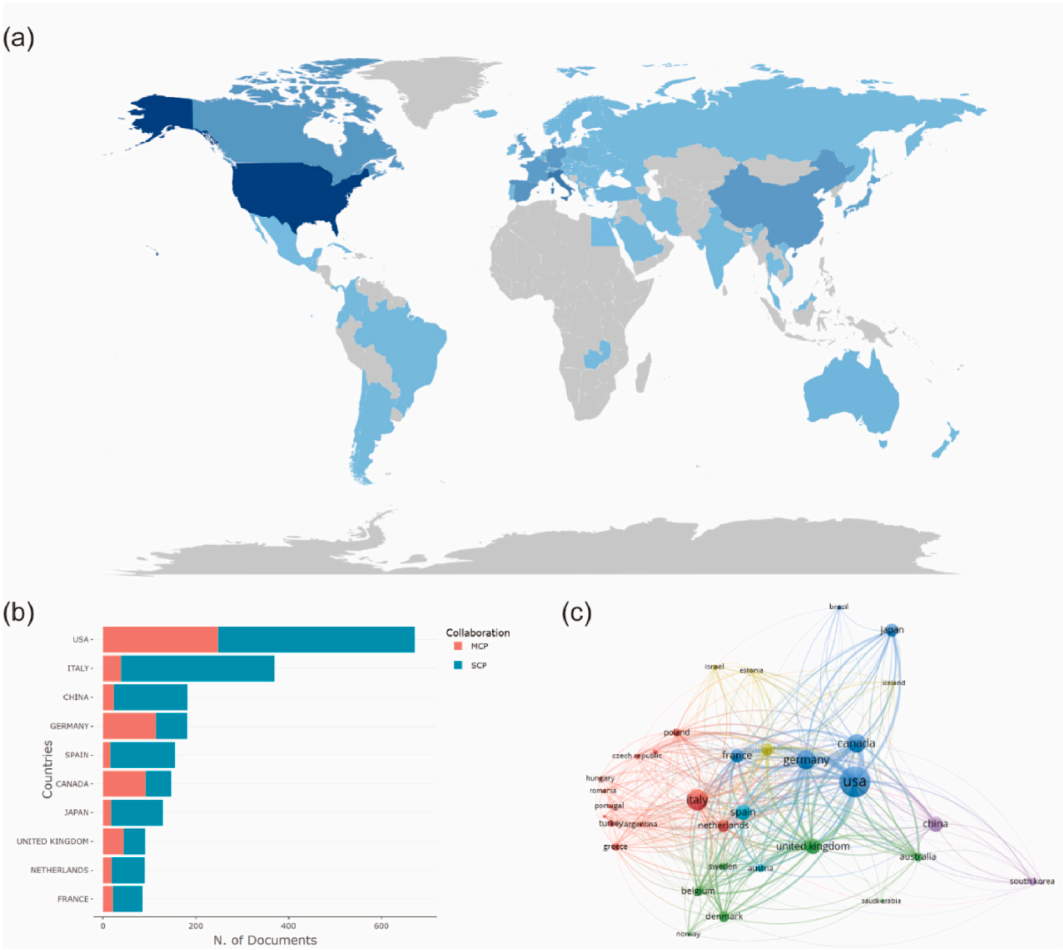


Fig. 4. Visualization of countries/regions analysis. (a) Country production map. (b) Corresponding author's country. (c) Country cooperation networks. SCP, single country publications. MCP, multiple country publications.

country (672), followed by Italy (370) and China (183). Publications from the United States also received the most frequent citations (33,114), followed by Canada (9,060) and Germany (7,941). It is obvious that the United States is the most influential country in the field, contributing a large number of high-quality articles to the discipline. Fig. 4b illustrates the productivity of the corresponding author's country, where Multi-Country Publication (MCP) represents the number of articles co-authored with other countries,

suggesting the intensity of international cooperation, while Single Country Publication (SCP) represents the number of articles whose co-authors are from the same country. The international co-authorship rate of publications is 28.59 %, with the United States exhibiting the most frequent international collaborations, while those of Italy and China need to be strengthened. Fig. 4c shows the international collaborations of 34 countries with ≥10 cumulative publications utilizing VOSviewer. Clustered by color distinction, the results show that six major research collaboration groups are currently formed centered in the United States, Italy, the United Kingdom, Spain, China, and Switzerland.

3.3.2. Institution and author collaboration network

Fig. 5 illustrates the research institutions and authors in the field, with a total of 9,474 authors from 2,079 institutions publishing articles in this field. Fig. 5a shows the top 10 institutions with the largest number of publications. Novartis is the most prolific institution, with 215 cumulative publications over 20 years, followed by Johnson & Johnson (205) and Manchester University (145). Fig. 5b displays a visualization of inter-institutional collaborations. Pharmaceutical companies such as Novartis and Johnson & Johnson have led numerous international multi-institutional collaborative studies. However, the regional barriers to institutional collaboration have not yet been fully dismantled, and the collaboration network is clearly geographically defined.

Fig. 5c displays the top 10 most productive authors. The most prolific author is Prof. Reick K. from Germany, who has published 134 relevant articles and is the most influential scholar in the field, with an h-index of 52. According to formula $N = 0.749 \times \sqrt{Nmax}$ for core authors' publications, we identified 426 core authors with more than 8 articles, and the visual mapping of author collaboration is shown in Fig. 5d. The results show that the core authors worked closely, and 11 major collaborative groups were initially formed.

3.4. Reference analysis

References play a crucial role in research as they form the knowledge base of a discipline. Analyzing cited references can reveal the knowledge structure, trace the evolutionary process, and highlight research hotspots. A total of 29,310 references were cited in 2,672 publications, and CiteSpace was used to analyze the co-citation of references and calculate BC. Fig. 6a illustrates the co-citation of references. The color of the nodes in the graph represents the year in which they were cited. Purple nodes indicate early references, while yellow nodes represent more recent references. Nodes with BC > 0.1 are marked with pink circles.

The most-cited reference in the field was published by Prof. Langley RG in 2014 in The New England Journal of Medicine, with a cumulative total of 304 citations in the field [21]. This paper synthesizes the results of two large phase 3 clinical trials reporting the efficacy of Secukinumab for moderate-to-severe plaque psoriasis [21]. The trials demonstrated that the psoriasis area and severity index (PASI) remission rate in the Secukinumab 300 mg group was superior to that of the 150 mg group and significantly better than

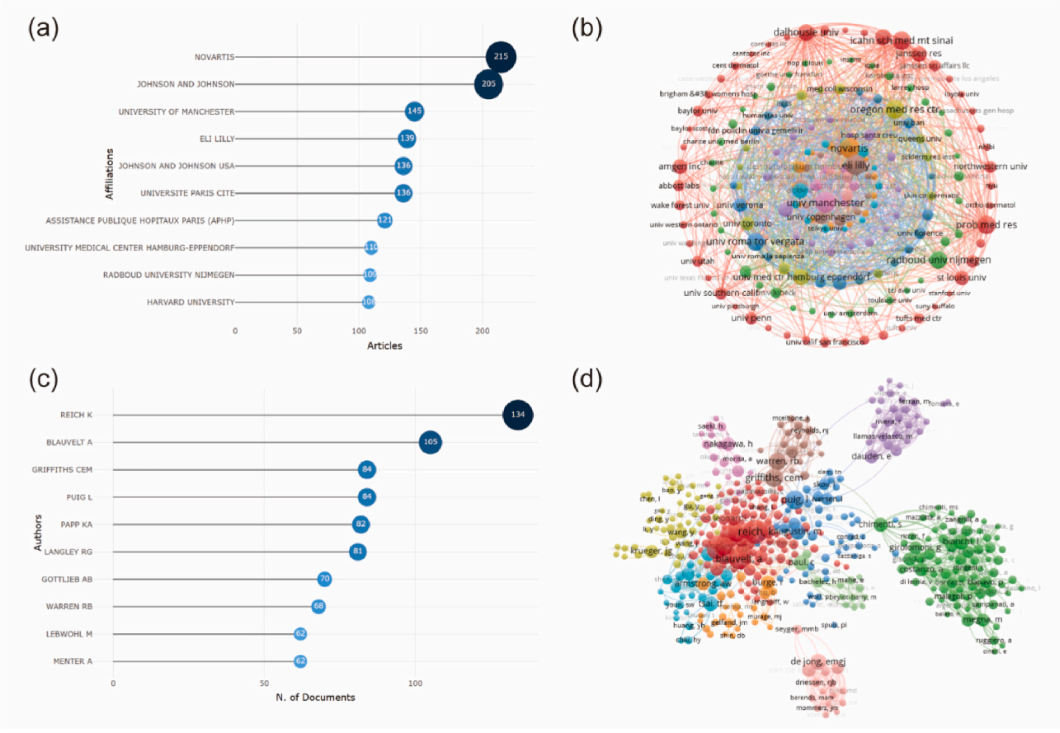


Fig. 5. Visualization of institutional and author analysis. (a) Top 10 institution with the most publications. (b) Institutional cooperation networks. (c) Top 10 author with the most publications. (d) Author cooperation networks.

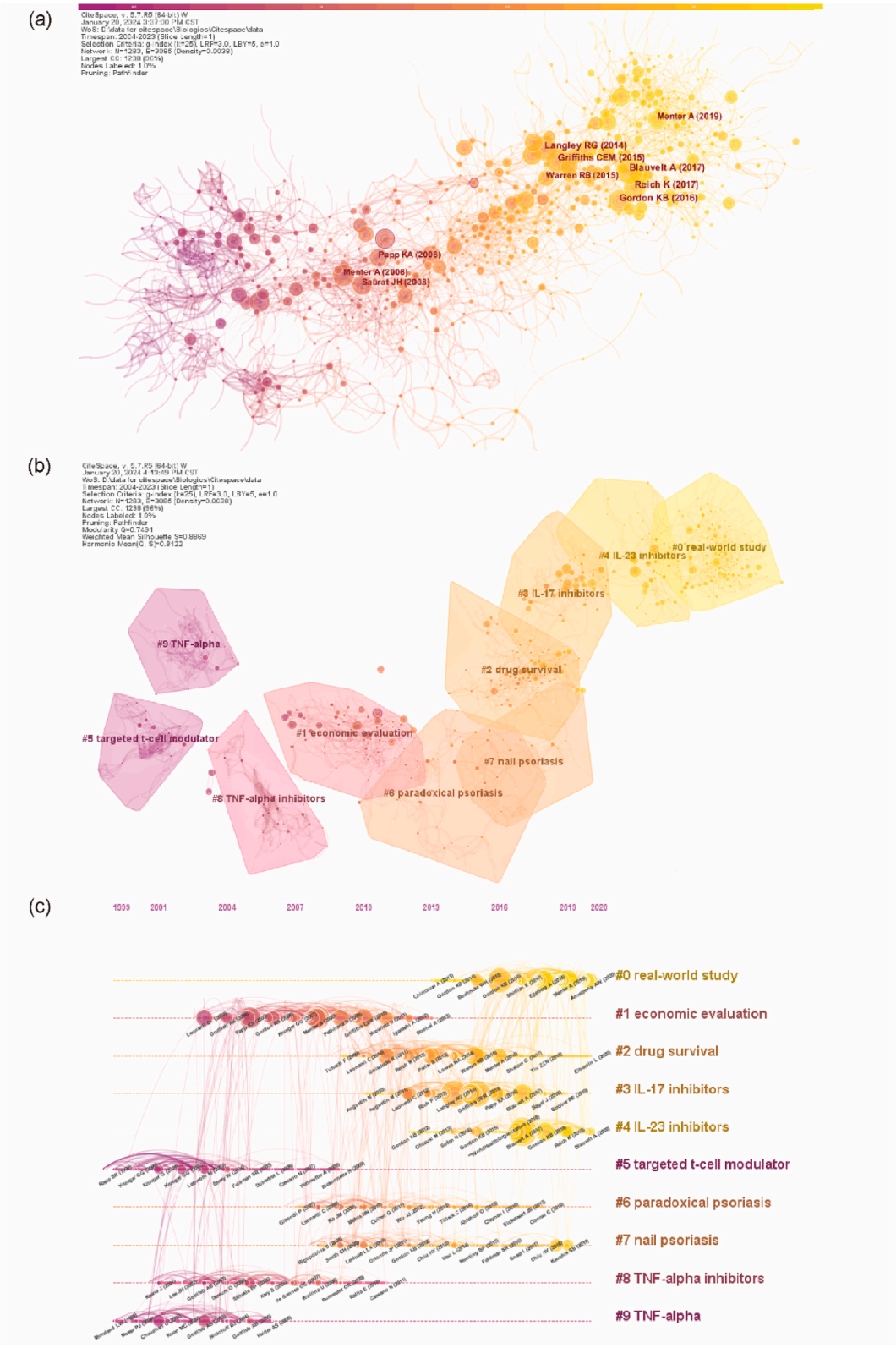
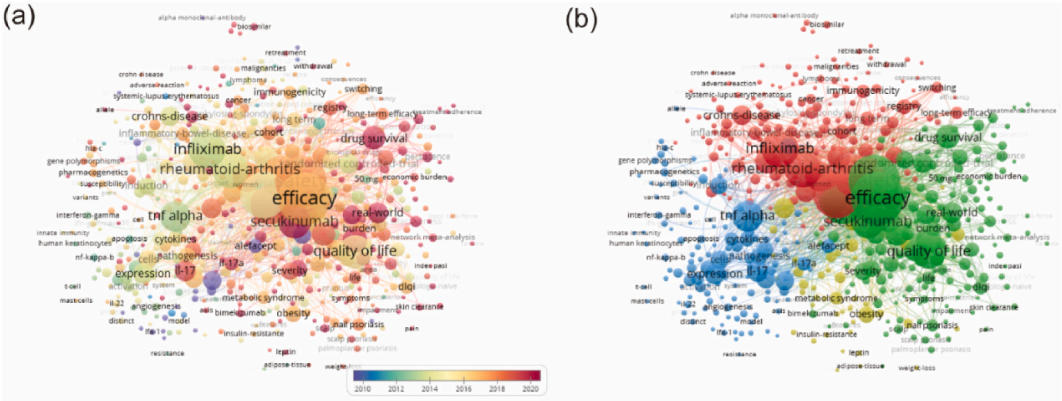


Fig. 6. Visualization of reference analysis. (a) Reference co-cited map. (b) Reference cluster analysis. (c) Reference clustering timeline map.

that of the Etanercept and placebo groups. This study provides high-quality evidence supporting the targeted blockade of IL-17A in the treatment of psoriasis and significantly contributes to the advancement of biological treatments for psoriasis. Notably, a total of 2 references with high BC were identified, which may inspire new research directions. The article published by Prof. Leonardi CL in the Lancet in 2008 (BC = 0.18) has been cited 244 times in the field. The study included three phases: placebo-controlled (weeks 0–12), placebo crossover and active treatment (weeks 12–40), and randomized discontinuation (weeks 40–76) [22]. It provided detailed evidence for the treatment of psoriasis with Ustekinumab across various dimensions, including short-term efficacy, long-term efficacy, safety, quality of life, relapse after discontinuation, and retreatment after discontinuation [22]. The article by Prof. Hueber W published in Science Translational Medicine in 2010 (BC = 0.17) has accumulated 51 citations in the field. The study comprehensively reported the efficacy and safety of the IL-17 inhibitor Secukinumab (AIN457) in the treatment of psoriasis, rheumatoid arthritis, and non-infectious uveitis [23]. It corroborated the role of IL-17A in the pathophysiology of a variety of inflammatory disorders and laid the groundwork for treating autoimmune disorders by targeting IL-17A [23].

Furthermore, we conducted a cluster analysis and created a timeline graph to illustrate the research progress in this discipline, as shown in Fig. 6b and c. The references were mainly clustered into 10 groups with a clear clustering structure and reasonably reliable clustering results (Modularity Q = 0.7491, Mean Silhouette = 0.8869). The distribution of nodes in the timeline graph represents the



Keywords	Year	Strength	Begin	End	2004 - 2023
efalizumab	2004	38.97	2004	2012	
infliximab	2004	28.91	2004	2013	
tnf alpha	2004	27.73	2004	2013	
alefacept	2004	22.22	2004	2011	
combination therapy	2004	4.26	2004	2011	
exacerbation	2005	3.45	2005	2017	
etanercept	2004	9.3	2007	2011	
anti-il12/23	2009	20.25	2010	2015	
anti tnf alpha	2005	7.26	2013	2015	
immunogenicity	2010	4.44	2013	2017	
myocardial infarction	2008	4.18	2013	2020	
il 22	2011	3.78	2013	2015	
metabolic syndrome	2008	3.25	2013	2014	
long term	2014	3.9	2014	2018	
pharmacogenomics	2014	5.34	2015	2018	
anti-drug antibody	2010	4.2	2015	2017	
drug survival	2013	10.93	2017	2023	
secukinumab	2015	23.31	2018	2023	
ustekinumab	2009	9.37	2018	2019	
discontinuation	2016	4.4	2018	2023	
ixekizumab	2017	20.17	2019	2023	
anti-il-17	2013	10.84	2019	2023	
guselkumab	2017	19.07	2020	2023	
brodalumab	2015	10.67	2020	2023	
covid-19	2020	10.36	2020	2023	
real-world	2016	18.97	2021	2023	
risankizumab	2019	11.36	2021	2023	
tildrakizumab	2020	9.27	2021	2023	
bimekizumab	2021	5.54	2021	2023	
clinical feature	2008	3.77	2021	2023	

Fig. 7. Visualization of keyword analysis. (a) Keyword co-cited map. (b) Keyword cluster analysis. (c) Top 30 keywords with the strongest citation bursts.

publication time of the references, reflecting the changes in the knowledge structure of the field and the evolutionary trend of the research topic. Early research themes focused on targeted T-cell modulators (#5), TNF-alpha (#9), and TNF-alpha inhibitors (#8). Later, studies in economic evaluation (#1) and paradoxical psoriasis (#6) gradually increased. Recently, studies on nail psoriasis (#7), drug survival (#2), IL-17 inhibitors (#3), IL-23 inhibitors (#4), and real-world (#0) have gained more attention, indicating current research hotspots.

3.5. Keyword analysis

Keywords are a highly condensed representation of the literature, and keyword analysis can indicate the research focus and cutting-edge trends within a discipline. After removing keywords such as "psoriasis," "plaque psoriasis," and "biologics" from each study and merging synonyms, we analyzed the remaining keywords using VOSviewer. The top 10 keywords were efficacy (674), safety (642), Etanercept (528), Adalimumab (438), Ustekinumab (373), Infliximab (332), rheumatoid arthritis (317), quality of life (272), Secukinumab (257), and TNF-alpha (242), indicating a research focus in this area. In Fig. 7a, the color of the nodes represents the time of the keywords, while in Fig. 7b, the color of the nodes is used to distinguish different clusters. Cluster analysis categorized the studies in this field into four major groups. These include green clusters for clinical studies represented by "efficacy" and "safety", blue clusters for mechanistic studies represented by "TNF-alpha" and "IL-17″, red clusters for co-morbidities represented by "rheumatoid arthritis" and "inflammatory bowel disease", and yellow clusters for efficacy association factors represented by "obesity" and "BMI".

Keyword burst detection can identify keywords that experience rapid growth within a short period, enabling researchers to promptly recognize emerging research trends. Fig. 7c shows the top 30 keywords with the strongest citation bursts in the field over the past 20 years. Among them, "Efalizumab" is the keyword with the strongest citation bursts and was the research hotspot between 2004 and 2012, with a burst intensity of 38.97. The keyword "exacerbation" experienced the longest citation burst, receiving sustained attention from 2005 to 2017. This led to further research on "immunogenicity," "anti-drug antibody," and "pharmacogenomics." There are a total of 11 keywords with high citation bursts in 2023, suggesting current research hotspots. These keywords can be categorized into two groups. One group consists of emerging biologics represented by IL-17 inhibitors and IL-23 inhibitors, including "Secukinumab," "Ixekizumab," "Guselkumab," "Brodalumab," "Risankizumab," "Tildrakizumab," and "Bimekizumab." The other group represents the emerging research hotspots in this field, including "drug survival," "discontinuation," "Covid-19," "real-world," and "clinical feature."

4. Discussion

Although biologics have only been approved for plaque psoriasis for a little over two decades, the development of the field has been rapid and significant. In this study, we summarized and analyzed trends and research hotspots and identified the main keywords, authors, institutions, countries, and journals in the field for the first time using bibliometrics.

Global publications in this field have increased rapidly over the past two decades. Due to the delay in including articles in the database, the publication volume of 2023 cannot cover all articles, which explains the decline in the publication volume of 2023. Despite slight fluctuations, there is a clear upward trend in annual publications, and the forecast curve suggests that the field will continue to grow in the future. The *British Journal of Dermatology* is the most popular and influential journal in the field, based on the number of publications, H-index, and G-index evaluations. The *Journal of Dermatological Treatment* has experienced rapid growth in the last three years and has become the second most popular journal since 2022. Researchers should pay attention to the core journals in the field, which provide valuable insights for staying updated on the latest knowledge and for submitting manuscripts.

The United States is the most productive country, maintaining rapid growth momentum and contributing more than a quarter of the publications in the field. The U.S. engages in frequent transnational collaborations, with an international co-authorship rate of 36.9 %, and has established close partnerships with Canada and Germany. At the institutional level, pharmaceutical companies such as Novartis, Johnson & Johnson, and Eli Lilly are committed to the field and have led numerous international and inter-institutional studies. The University of Manchester, the University of Paris, and the European Hospital Federation have also made significant contributions to the development of the field through their research. However, overall, inter-institutional collaborations have yet to overcome geographical barriers.

The most influential author is Prof. Reick K from Germany, with 134 publications over the past two decades. He has led phase 2 or 3 clinical trials of Infliximab [24], Certolizumab [25], Ixekizumab [26], Ustekinumab [27], and Brodalumab [28] for the treatment of moderate-to-severe psoriasis. Additionally, he has compared the short-term efficacy of five biologics based on randomized, controlled trials through a network meta-analysis. The results showed that the highest mean response rates of PASI 50 (93 %), 75 (80 %), and 90 (54 %) were achieved with Infliximab at 10–16 weeks from baseline, followed by Ustekinumab 90 mg, Ustekinumab 45 mg, Adalimumab, Etanercept, and Efalizumab [29]. This result has been updated with the introduction of new biologics and clinical trials. IL-17 inhibitors and IL-23 inhibitors have shown higher rates of skin lesion clearance, making them current research hotspots. Among them, Risankizumab showed the highest PASI 90 response rate (71.6 %), followed by Ixekizumab (70.8 %), Brodalumab (70.6 %), and Guselkumab (67.3 %) [30].

Efficacy and safety were the most frequent keywords, suggesting a research focus in this area. Randomized controlled trials remain the gold standard for evaluating efficacy and safety, with the top 10 most cited articles in the field being such studies. However, due to the extended duration of treatment with biologics and the complexity of real-world patients, randomized controlled trials are subject to numerous limitations. Keyword burst analysis has revealed that the term "real world" has been frequently used in recent years and has become a current research hotspot. Real-world studies have demonstrated the efficacy and safety of biologics in the treatment of

psoriasis, both in the short and long term. These studies have also provided valuable experience in treating special populations, including children [31], pregnant women [32], elderly patients [33], and oncology patients [34].

In addition, keyword bursts indicate that drug survival, discontinuation, drug switching, and factors associated with efficacy are currently hot research topics drawing significant attention. Drug survival, defined as the duration of continuous therapy from the first dose to discontinuation, is strongly influenced by various factors such as efficacy, safety, adherence, convenience, and economics [35]. It is a crucial evaluation parameter for real-world studies of biologics. Previous studies have shown that the median drug survival of biologics for psoriasis ranges from 24.7 to 38.0 months [36]. The most important factors affecting drug survival are efficacy, financial pressure, and adverse effects. Specifically, 43.5 % of patients discontinue the drug due to loss of efficacy, 23.9 % are unable to afford the financial burden of biologics, and 7.6 % attribute discontinuation to adverse effects [37]. Recent studies have shown that IL-23 inhibitors have higher drug survival rates, possibly because of their favorable efficacy, safety, and ease of administration [38].

Discontinuation of medication is common in patients with psoriasis, which often leads to relapse. More than half of patients experience a psoriasis relapse within 6 months of discontinuation [39]. Moreover, the time to relapse after discontinuation tends to shorten as the number of prior biological treatments experienced by the patient increases [40]. Therefore, retreatment after discontinuation has become a hot topic of current interest. Thankfully, with the exception of infliximab, interrupting biological therapy seems to be safe [41]. Etanercept, Adalimumab, Ustekinumab, Brodalumab, Ixekizumab, Guselkumab, Risankizumab, and Tildrakizumab demonstrated comparable efficacy to the initial therapy in patients who were retreated after discontinuation [41–43]. Emerging IL-23 inhibitors have demonstrated sustained responses even after discontinuation. This prolonged effect may be due to their ability to inhibit tissue-resident memory T cells while leaving Treg cells unaffected [44].

Despite the significant efficacy of biologics, secondary failure is common in patients with psoriasis as the treatment cycle prolongs, which may be associated with the immune-mediated production of anti-drug antibodies [45]. These anti-drug antibodies may prevent drug-target interactions or increase drug clearance, thereby altering the efficacy and bioavailability of biologics [45]. When faced with this situation, clinicians often provide guidance on switching medications. According to the survey, the overall switching rates for biologics at 12 and 24 months of treatment for psoriasis patients in the United States were 14.4 % and 26.0 %, respectively. Biologics were more commonly switched among patients with prior targeted immune modulators, those aged 51–64 years, and female patients [46]. However, the effectiveness of some biologics after switching was not satisfactory. Patients who experienced primary nonresponse to adalimumab, as opposed to secondary failure, showed poor response rates after switching to etanercept [47]. In patients who switched to Secukinumab and Ustekinumab after experiencing failure of TNF-alpha inhibitor therapy, most responded well, but the overall response rate may be decreased [47]. Combination therapy is another common approach in response to treatment failure. Studies now show that combining biological agents with NB-UVB results in higher lesion clearance in a shorter period of time [48]. Combining methotrexate reduces the production of anti-drug antibodies for better long-term efficacy [49,50], and combining small molecules is more effective in treating recalcitrant psoriasis [51,52].

Clinical practice has found that some patients with psoriasis may experience worsening of symptoms after treatment with biologics. Additionally, individuals with autoimmune disorders but no history of psoriasis may develop psoriasis after biologic therapy, a phenomenon referred to as paradoxical psoriasis. This phenomenon is most common in patients treated with TNF-α inhibitors [53] and has also been reported in patients using IL-12/23 inhibitors [54], IL-17 inhibitors [55], and IL-23 inhibitors [56]. Paradoxical psoriasis is associated with genetic susceptibility and immune dysregulation following treatment with biologics [57]. While some patients may achieve remission with continued use of biologics [58], it is generally safer and more effective to discontinue biologics and switch to alternative treatments [59]. In addition, biologic-associated autoimmune diseases are a challenge that cannot be ignored. Studies have shown that biologics may induce autoimmune diseases such as inflammatory bowel disease [60], herpetic pemphigoid [61], and lupus erythematosus [62]. Immune disorders caused by specific cytokine blockades may be responsible for this phenomenon, but the exact pathogenesis remains to be further investigated. Atopic dermatitis was previously considered to involve a mechanism of inflammatory response centered on Th2/Th22 cells, distinct from psoriasis, which is characterized by a Th1/Th17-type inflammatory response [63]. Subsequent studies have found that psoriasis and atopic dermatitis can be classified as two ends of the same spectrum, referred to as "psoriatic dermatitis" [64]. The two are interchangeable, especially in patients with biologics, which is attributed to immune drift [65,66]. It has been investigated that paradoxical eczema is most frequent in patients receiving IL-17 inhibitors, followed by patients receiving TNF inhibitors, patients receiving IL-12/23 inhibitors, and patients receiving IL-23 inhibitors [67].

Over the past 20 years, an increasing number of biologics have been approved for plaque psoriasis. The wide variety of biologics has made treatment selection challenging. Individualized precision therapy and factors influencing its efficacy have become a hot topic for researchers. In order to select the most appropriate biologics, researchers have explored various predictors of efficacy to establish a predictive model for the effectiveness of biologics from dimensions such as genomics, inflammatory markers, and clinical features [68–70]. Previous studies have shown that a variety of genes, such as HLA-C*06 and IL-12B, are associated with the effectiveness of biologics [68]. Patients with positive HLA-C*06 genes have shown better clinical efficacy with Ustekinumab [68]. However, specific HLA alleles may be involved in the production of anti-drug antibodies. For example, HLA-DRB1*01 positivity is more prevalent in patients with anti-drug antibodies to adalimumab, while HLA-DRB1*03 is considered a protective factor [71]. Furthermore, it has been suggested that microRNA in the skin at baseline can serve as a potential marker of biological efficacy [71]. It has also been found that obesity can reduce the efficacy of TNF-α inhibitors and Ustekinumab [70], while not affecting the efficacy of emerging IL-23 inhibitors [72]. These findings provide support for the personalized and precise selection of biologics in clinical settings. However, further studies are necessary for validation.

Despite tremendous progress achieved in the field of biologics for plaque psoriasis over the past 20 years, shortcomings and challenges remain, such as primary and secondary treatment failure, long-term management of psoriasis, relapse after discontinuation of therapy, re-treatment after biologics treatment failure or discontinuation, biologics-related adverse events, and selection of biologics

for precision. We hope to inspire future research directions for investigators through a review of the current status and challenges of treatment in this field.

4.1. Limitations

Firstly, there is a delay in the inclusion of literature in the WOSCC database, which means that it may not include all literature in 2023, resulting in a lack of comprehensive coverage. Second, due to the citation delay, recently published articles may be underestimated because they have not yet accumulated extensive citations. Additionally, we only selected literature published in English in WOSCC for our study data due to the limitations of the bibliometric software, and relevant papers published in other languages or included in other databases may be missed, which may affect the generalizability of the findings. Moreover, we only included literature from the last 20 years, which may not capture long-term trends, thus limiting the robustness of the findings.

5. Conclusions

This is the first bibliometric study in the field of biological therapy for plaque psoriasis that summarizes the research trends and hotspots, providing insights into key journals, countries, institutions, and authors in the field. Currently, IL-17 inhibitors, IL-23 inhibitors, real-world studies, drug survival, retreatment after biological treatment failure or discontinuation, and efficacy prediction are the hot spots and frontiers of research.

Data availability statement

Data sharing does not apply to this paper; the data currently used in this study is from Web of Science, so access to the data requires permission through Web of Science.

Ethics declarations

Not applicable.

CRediT authorship contribution statement

Shan Huang: Writing – original draft, Visualization, Software, Methodology, Conceptualization. **Xing-wu Duan:** Writing – review & editing, Supervision. **Yan-ping Bai:** Writing – review & editing, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e35446.

References

[1] National Psoriasis Foundation. Available from: https://www.psoriasis.org/content/statistics.
[2] C.E.M. Griffiths, et al., Psoriasis, Lancet 397 (10281) (2021) 1301–1315.
[3] World Health Organization, Global report on psoriasis, Available from: https://www.who.int/publications/i/item/9789241565189, 2016.
[4] I. Jalenques, et al., Prevalence and odds of anxiety disorders and anxiety symptoms in children and adults with psoriasis: systematic review and meta-analysis, Acta Derm. Venereol. 102 (2022) adv00769.
[5] L. Liu, et al., Epidemiology of mental health comorbidity in patients with psoriasis: an analysis of trends from 1986 to 2019, Psychiatr. Res. 321 (2023) 115078.
[6] F.Y. Tang, et al., The prevalence of alexithymia in psoriasis: a systematic review and meta-analysis, J. Psychosom. Res. 161 (2022) 111017.
[7] T.L. Hedemann, et al., Associations between psoriasis and mental illness: an update for clinicians, Gen. Hosp. Psychiatr. 75 (2022) 30–37.
[8] S. Huang, Y. Bai, Knowledge mapping and research hotspots of comorbidities in psoriasis: a bibliometric analysis from 2004 to 2022, Medicina (Kaunas) 59 (2) (2023) 393.
[9] S.C.S. Hu, C.C.E. Lan, Psoriasis and cardiovascular comorbidities: focusing on severe vascular events, cardiovascular risk factors and implications for treatment, Int. J. Mol. Sci. 18 (10) (2017) 34.
[10] M. Vicic, et al., Current concepts of psoriasis immunopathogenesis, Int. J. Mol. Sci. 22 (21) (2021) 14.
[11] W.H. Boehncke, N.C. Brembilla, Pathogenesis-oriented therapy of psoriasis using biologics, Expet Opin. Biol. Ther. (2022) 11.
[12] C. Reid, C.E.M. Griffiths, Psoriasis and treatment: past, present and future aspects, Acta Derm. Venereol. 100 (2020) 69–79.
[13] C. Chen, M. Song, Visualizing a field of research: a methodology of systematic scientometric reviews, PLoS One 14 (10) (2019) e0223994.
[14] S. Nakagawa, et al., Research weaving: visualizing the future of research synthesis, Trends Ecol. Evol. 34 (3) (2019) 224–238.
[15] M. Aria, C. Cuccurullo, bibliometrix: an R-tool for comprehensive science mapping analysis, Journal of Informetrics 11 (4) (2017) 959–975.
[16] N.J. van Eck, L. Waltman, Software survey: VOSviewer, a computer program for bibliometric mapping, Scientometrics 84 (2) (2010) 523–538.

[17] X. Pan, et al., Examining the usage, citation, and diffusion patterns of bibliometric mapping software: a comparative study of three tools, Journal of Informetrics 12 (2) (2018) 481–493.
[18] O. Artiles, F. Saeed, TurboBC: a memory efficient and scalable GPU based betweenness centrality algorithm in the language of linear algebra, Proc Int Workshops Parallel Proc (2021) 2021.
[19] A. Amrapala, et al., Neuropsychiatric disturbances in mild cognitive impairment: a scientometric analysis, Ageing Res. Rev. 92 (2023) 102129.
[20] J.E. Hirsch, An index to quantify an individual's scientific research output, Proc Natl Acad Sci U S A 102 (46) (2005) 16569–16572.
[21] R.G. Langley, et al., Secukinumab in plaque psoriasis–results of two phase 3 trials, N. Engl. J. Med. 371 (4) (2014) 326–338.
[22] C.L. Leonardi, et al., Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 1), Lancet 371 (9625) (2008) 1665–1674.
[23] W. Hueber, et al., Effects of AIN457, a fully human antibody to interleukin-17A, on psoriasis, rheumatoid arthritis, and uveitis, Sci. Transl. Med. 2 (52) (2010) 52ra72.
[24] J. Barker, et al., Efficacy and safety of infliximab vs. methotrexate in patients with moderate-to-severe plaque psoriasis: results of an open-label, active-controlled, randomized trial (RESTORE1), Br. J. Dermatol. 165 (5) (2011) 1109–1117.
[25] K. Reich, et al., Successful treatment of moderate to severe plaque psoriasis with the PEGylated Fab' certolizumab pegol: results of a phase II randomized, placebo-controlled trial with a re-treatment extension, Br. J. Dermatol. 167 (1) (2012) 180–190.
[26] K.B. Gordon, J.F. Colombel, D.S. Hardin, Phase 3 trials of ixekizumab in moderate-to-severe plaque psoriasis, N. Engl. J. Med. 375 (21) (2016) 2102.
[27] K. Reich, et al., Comparison of ixekizumab with ustekinumab in moderate-to-severe psoriasis: 24-week results from IXORA-S, a phase III study, Br. J. Dermatol. 177 (4) (2017) 1014–1023.
[28] K.A. Papp, et al., A prospective phase III, randomized, double-blind, placebo-controlled study of brodalumab in patients with moderate-to-severe plaque psoriasis, Br. J. Dermatol. 175 (2) (2016) 273–286.
[29] K. Reich, et al., Efficacy of biologics in the treatment of moderate to severe psoriasis: a network meta-analysis of randomized controlled trials, Br. J. Dermatol. 166 (1) (2012) 179–188.
[30] A.W. Armstrong, et al., Comparison of biologics and oral treatments for plaque psoriasis: a meta-analysis, JAMA Dermatol 156 (3) (2020) 258–269.
[31] V. Di Lernia, et al., Effectiveness of etanercept in children with plaque psoriasis in real practice: a one-year multicenter retrospective study, J Dermatolog Treat 29 (3) (2018) 217–219.
[32] A.B. Kimball, et al., Pregnancy outcomes in women with moderate-to-severe psoriasis from the psoriasis longitudinal assessment and registry (PSOLAR), JAMA Dermatol 157 (3) (2021) 301–306.
[33] M. Megna, et al., Treating psoriasis in the elderly: biologics and small molecules, Expet Opin. Biol. Ther. (2022) 18.
[34] L. Rusiñol, G. Camiña-Conforto, L. Puig, Biologic treatment of psoriasis in oncologic patients, Expet Opin. Biol. Ther. 22 (12) (2022) 1567–1578.
[35] D. Thein, et al., Drug survival of adalimumab, Secukinumab, and ustekinumab in psoriasis as determined by either dose escalation or drug discontinuation during the first 3 Years of treatment - a nationwide cohort study, J. Invest. Dermatol. 143 (11) (2023) 2211–2218.e4.
[36] D.J. No, et al., Drug survival of biologic treatments in psoriasis: a systematic review, J Dermatolog Treat 29 (5) (2018) 460–466.
[37] M. Mashor, et al., A retrospective study on drug survival of biologic among patients with psoriasis seen in tertiary hospital in Johor Malaysia, Med. J. Malaysia 77 (6) (2022) 689–695.
[38] L. Rusiñol, E. Carmona-Rocha, L. Puig, Durability and long-term outcomes of biologic therapies in psoriasis, Expet Rev. Clin. Immunol. 20 (1) (2024) 71–82.
[39] X.-Y. Wang, C.-L. Zhang, W.-H. Wang, Time to relapse after treatment withdrawal for different biologics used to treat plaque psoriasis, Chin. Med. J. 133 (24) (2020) 2998–3000.
[40] W. Owczarek, et al., Real-world evidence on time to relapse of plaque psoriasis after discontinuation of biologic treatment in Poland, Dermatol. Ther. 34 (5) (2021) e15052.
[41] C.Y. Wang, et al., Biological therapy interruption and Re-treatment in chronic plaque psoriasis, J Drugs Dermatol 20 (10) (2021) 1063–1071.
[42] K.B. Gordon, et al., Adalimumab retreatment successfully restores clinical response and health-related quality of life in patients with moderate to severe psoriasis who undergo therapy interruption, J. Eur. Acad. Dermatol. Venereol. 29 (4) (2015) 767–776.
[43] K. Papp, et al., Long-term efficacy and safety of brodalumab in psoriasis through 120 weeks and after withdrawal and retreatment: subgroup analysis of a randomized phase III trial (AMAGINE-1), Br. J. Dermatol. 183 (6) (2020) 1037–1048.
[44] H. Mehta, et al., Differential changes in inflammatory mononuclear phagocyte and T-cell profiles within psoriatic skin during treatment with Guselkumab vs. Secukinumab, J. Invest. Dermatol. 141 (7) (2021) 1707–1718.e9.
[45] V. Patel, et al., Immunogenicity of biologics used in the treatment of moderate to severe psoriasis, Hum. Antibodies 29 (3) (2021) 171–178.
[46] A.W. Armstrong, et al., Real-world switching patterns and associated characteristics in patients with psoriasis treated with biologics in the United States, J Dermatolog Treat 34 (1) (2023) 2200870.
[47] T.S. Wang, T.F. Tsai, Biologics switch in psoriasis, Immunotherapy 11 (6) (2019) 531–541.
[48] C. De Simone, et al., Combined treatment with etanercept 50 mg once weekly and narrow-band ultraviolet B phototherapy in chronic plaque psoriasis, Eur. J. Dermatol. 21 (4) (2011) 568–572.
[49] W. Wang, et al., Investigation of the mechanism of therapeutic protein-drug interaction between methotrexate and golimumab, an anti-TNFα monoclonal antibody, AAPS J. 20 (3) (2018) 63.
[50] A.M. van Huizen, et al., Adalimumab combined with methotrexate versus adalimumab monotherapy in psoriasis: three-year follow-up data of a single-blind randomized controlled trial, J. Eur. Acad. Dermatol. Venereol. : JEADV 37 (9) (2023) 1815–1824.
[51] S. Takamura, et al., Combination therapy of apremilast and biologics in patients with psoriasis showing biologic fatigue, J. Dermatol. 47 (3) (2020) 290–294.
[52] M. Gyldenløve, et al., Combination therapy with apremilast and biologics for psoriasis: a systematic review, Am. J. Clin. Dermatol. 23 (5) (2022) 605–613.
[53] C.M. Townsend, et al., Review article: paradoxical psoriasis as a consequence of tumour necrosis factor antagonists in patients with inflammatory bowel disease, Aliment. Pharmacol. Ther. 55 (11) (2022) 1379–1388.
[54] H.Y. Lee, C.H. Woo, S. Haw, Paradoxical flare of psoriasis after ustekinumab therapy, Ann. Dermatol. 29 (6) (2017) 794–795.
[55] M. El-Komy, et al., Secukinumab retreatment associated psoriasis flare with pustules, J Dermatolog Treat 33 (2) (2022) 1107–1110.
[56] O. McFeely, et al., Risankizumab-induced paradoxical pustular psoriasis, Clin. Exp. Dermatol. 47 (3) (2022) 616–617.
[57] A. Mylonas, C. Conrad, Psoriasis: classical vs. Paradoxical. The Yin-Yang of TNF and type I interferon, Front. Immunol. 9 (2018) 2746.
[58] N. Lian, L. Zhang, M. Chen, Tumor necrosis factors-α inhibition-induced paradoxical psoriasis: a case series and literature review, Dermatol. Ther. 33 (6) (2020) e14225.
[59] A. Chokshi, et al., Paradoxical tumor necrosis factor-alpha (TNF-α) inhibitor-induced psoriasis: a systematic review of pathogenesis, clinical presentation, and treatment, Cureus 15 (8) (2023) e42791.
[60] P. Nehring, A. Przybyłkowski, Is psoriasis treatment a risk factor for inflammatory bowel disease? Pharmaceut. Med. 34 (4) (2020) 257–262.
[61] H. Husein-ElAhmed, M. Steinhoff, Bullous pemphigoid induced by biologic drugs in psoriasis: a systematic review, J Dermatolog Treat 33 (7) (2022) 2886–2893.
[62] S. Mirali, et al., Development of chronic cutaneous lupus erythematosus during biologic therapy: a systematic review, J. Am. Acad. Dermatol. 84 (3) (2021) 835–838.
[63] D. Malajian, E. Guttman-Yassky, New pathogenic and therapeutic paradigms in atopic dermatitis, Cytokine 73 (2) (2015) 311–318.
[64] S. Kapila, E. Hong, G. Fischer, A comparative study of childhood psoriasis and atopic dermatitis and greater understanding of the overlapping condition, psoriasis-dermatitis, Australas. J. Dermatol. 53 (2) (2012) 98–105.
[65] M. Napolitano, et al., Increased expression of interleukin-23A in lesional skin of patients with atopic dermatitis with psoriasiform reaction during dupilumab treatment, Br. J. Dermatol. 184 (2) (2021) 341–343.
[66] M. Napolitano, et al., Eczematous reaction to ixekizumab successfully treated with dupilumab, Dermatol. Ther. 33 (2) (2020) e13218.

[67] A. Al-Janabi, et al., Risk of paradoxical eczema in patients receiving biologics for psoriasis, JAMA Dermatol 160 (1) (2024) 71–79.
[68] M. Corbett, et al., Biomarkers of systemic treatment response in people with psoriasis: a scoping review, Br. J. Dermatol. 187 (4) (2022) 494–506.
[69] A.C. Foulkes, et al., A framework for multi-omic prediction of treatment response to biologic therapy for psoriasis, J. Invest. Dermatol. 139 (1) (2019) 100–107.
[70] J. Zweegers, et al., Frequency and predictors of a high clinical response in patients with psoriasis on biological therapy in daily practice: results from the prospective, multicenter BioCAPTURE cohort, Br. J. Dermatol. 176 (3) (2017) 786–793.
[71] M. Liu, et al., Identification of HLA-DRB1 association to adalimumab immunogenicity, PLoS One 13 (4) (2018) e0195325.
[72] F. Ricceri, et al., Successful use of anti-IL-23 molecules in overweight-to-obese psoriatic patients: a multicentric retrospective study, Dermatol. Ther. 35 (11) (2022) e15793.