Bibliometric Study on Belimumab for Systemic Lupus Erythematosus: Advances and Trends from 2015 to 2025

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Abstract: This study conducted a bibliometric analysis of research on belimumab in the treatment of systemic lupus erythematosus (SLE) between 2015 and 2025. A total of 709 relevant publications were identified during this decade, with an annual publication output showing steady growth and a notable increase observed in 2022, which correlates with updates in treatment guidelines and a rising interest in biologic agents. The United States contributed the highest number of publications (244), while China demonstrated a concentrated research effort in recent years. Among institutions, GlaxoSmithKline (GSK) produced the most publications (83), whereas institutions such as Karolinska Institute achieved higher average citation counts. Two core research teams were identified, and the phase III clinical trials led by Furie R formed the knowledge foundation of the field. Research hotspots included the BAFF mechanism, clinical trials, and end-stage renal disease. Recent studies have further revealed that beyond neutralizing BAFF, belimumab modulates multiple pathways, including interferon signaling, demonstrating multidimensional immunoregulatory effects and potential value in managing secondary antiphospholipid syndrome. Future research should focus on biomarker development, combination therapy strategies, and overcoming drug resistance mechanisms to enhance treatment precision and improve long-term patient outcomes.

Keywords: Belimumab; Systemic Lupus Erythematosus; Bibliometric; CiteSpace; VOSviewe

1. Introduction

Systemic Lupus Erythematosus (SLE) is a complex chronic autoimmune disease whose core pathological mechanism involves abnormal activation of B lymphocytes and massive production of autoantibodies, leading to inflammatory damage across multiple organs throughout the body[1]. Despite the widespread clinical use of traditional treatments such as glucocorticoids and immunosuppressants, many patients still face challenges including inadequate efficacy, frequent relapses, and drug-related toxicity[2]. This has created an urgent need for targeted therapies that address specific pathogenic pathways. Against this backdrop, belimumab—a fully humanized monoclonal antibody—emerged as a specific inhibitor of B lymphocyte activating factor (BLyS/BAFF). By precisely binding serum BLyS and blocking its interaction with B-cell receptors, it effectively induces apoptosis in autoreactive B cells and suppresses their differentiation into antibody-producing cells. Since receiving Food and Drug Administration (FDA) approval in 2011 for treating active, autoantibody-positive SLE, Belimumab has become a landmark in the era of targeted SLE therapy. Its efficacy and safety have been thoroughly validated through pivotal Phase III trials like BLISS-52 and BLISS-76, along with their long-term extension studies[3-5]. These demonstrate that adding Belimumab to standard therapy significantly reduces disease activity, decreases steroid dosage, and delays disease recurrence. As evidence accumulates, its clinical application has expanded from moderate-to-severe SLE unresponsive to conventional therapy to more challenging areas like lupus nephritis. Over the past decade, studies have progressed from initial efficacy validation to exploring biomarkers and mechanisms of action, forming a vast and complex knowledge system [6]. Therefore, systematically organizing this rapidly evolving field to clarify its knowledge structure and

research frontiers is crucial for guiding future scientific directions and clinical practice.

In the face of a rapidly evolving research field, traditional literature review methods, while capable of providing in-depth qualitative analysis, struggle to objectively and comprehensively depict the entire discipline's landscape, evolutionary trajectory, and cutting-edge trends. Bibliometrics—a field employing mathematical and statistical methods to quantitatively analyze academic literature—precisely addresses this shortcoming. By analyzing intrinsic quantitative characteristics within vast literature datasets—such as publication volume, country, institution, author, journal, citations, and keywords—it objectively reveals a discipline's developmental patterns, research hotspots, collaboration models, and knowledge foundations. Therefore, applying bibliometric methods to the dynamic and productive field of Belimumab treatment for SLE is particularly necessary and timely. This study aims to conduct a comprehensive retrieval and quantitative analysis of literature published between 2015 and 2025 concerning Belimumab and SLE. It seeks to systematically reveal the evolutionary trajectory of research paradigms in Belimumab treatment for SLE and provide data-driven insights and prospects for future research directions in this field.

2. Materials and Methods

2.1 Search Strategy

This study searched the Web of Science Core Collection (WoSCC) SCI-EXPANDED sources using the following search strategy: TS = ("systemic lupus erythematosus" and "belimumab").

2.2 Inclusion Criteria

Inclusion criteria: 1) Research topic focused on Belimumab treatment for SLE; 2) Language: English; 3) Document type: articles and review articles; 4) Publication date: January 1, 2015, to October 30, 2025.

2.3 Exclusion Criteria

Exclusion criteria: 1) Non-research literature such as conference papers, newspapers, patents, or research reports; 2) Duplicate publications (only the most comprehensive version retained); 3) Literature unrelated to belimumab treatment for SLE (title, abstract, or content mismatch); 4) Literature with incomplete bibliographic information (e.g., lacking abstract keywords or other essential details).

2.4 Data Processing

Following screening, 709 eligible documents were obtained. Visual analysis of annual publication volume, country, institution, author, journal, references, and keywords was conducted using Excel 2016, VOSviewer 1.6.20, and CiteSpace 6.4.R.

3. Results

3.1 Annual Production

From January 1, 2015, to October 30, 2025, a total of 709 research papers were published on belimumab treatment for SLE. Figure 1 illustrates the annual publication volume trends in this field from 2015 to 2024. As 2025 data is not yet fully compiled, it is excluded from this analysis. The annual publication volume in this field exhibits a relatively stable upward trend, indicating increasing attention. Notably, research interest in belimumab for SLE surged rapidly in 2022, likely influenced by the 2019 EULAR guidelines update, which included belimumab in clinical recommendations. Additionally, this trend may be linked to the FDA approval of Anifrolumab in July 2021. As another biologic agent for SLE treatment, both drugs collectively spurred researchers to explore the role of biologics in SLE therapy.

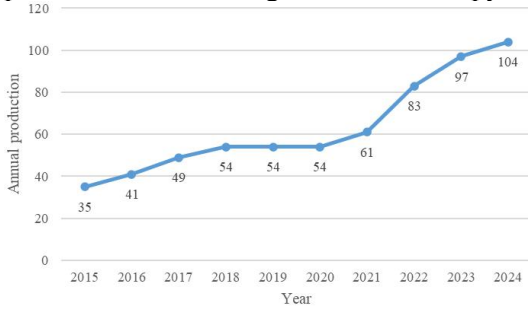


Figure 1. Annual Number of Publications of Belimumab Treatment for SLE

3.2 Countries

A total of 67 countries have researched "belimumab treatment for SLE". Figure 2 displays the publication output across all countries, where circle size represents publication volume, and circles appear more yellow as the average citation per paper increases. Connecting lines indicate collaborative relationships between institutions.

Although several countries have a low publication output, their high average citation count, as exemplified by Greece, indicates substantial research influence. The top ten countries by publication volume are detailed in Table 1. The United States leads with the highest publication volume, contributing 244 articles and significantly advancing the field. China also demonstrates a high publication output, coupled with a recent average publication date, indicating a recent surge in research in this area over the past two years. This trend may correlate with belimumab receiving marketing approval from China's National Medical Products Administration in 2019 and its expanded usage scope in 2022.

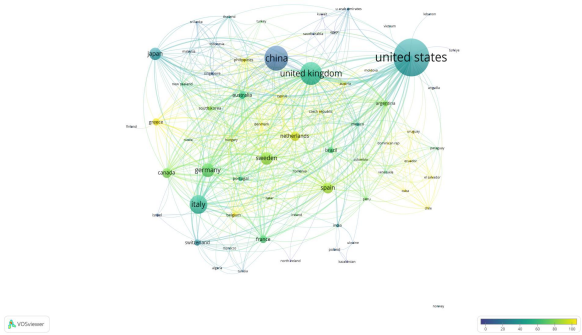


Figure 2. Countries' Analysis of Belimumab Treatment for SLE

Table 1. Top 10 Productive Countries

Rank	Counties	Documents	Avg. pub. year	Citations	Avg. citations
1	United states	244	2020.4959	8843	36.2418
2	China	137	2022.7007	2143	15.6423
3	United kingdom	122	2020.1311	6446	52.8361
4	Italy	92	2020.663	4533	49.2717
5	Germany	61	2020.377	4264	69.9016
6	Sweden	54	2021.1296	4324	80.0741
7	Japan	52	2022.2692	1705	32.7885
8	Spain	44	2021.3864	3663	83.25
9	Canada	37	2020.4865	2789	75.3784
10	Netherlands	36	2021.3056	3351	93.0833

3.3 Institutions

A total of 1,282 institutions have published research papers on “belimumab treatment for SLE.” Figure 3 illustrates the publication activity of selected representative institutions. In this visualization, color progression toward yellow indicates more recent publication or collaboration dates, while the radius of each circle corresponds to the volume of publications. Publication volumes vary significantly among institutions in this field, with frequent inter-institutional collaboration. Table 2 lists the top 10 institutions publishing papers on “belimumab treatment for SLE.” Among the listed institutions, GlaxoSmithKline (83 publications) contributed the most substantial research output in this field, which aligns with its role as the developer of belimumab. Meanwhile, Karolinska Institute not only demonstrated high publication volume but also achieved a notably high citation count per publication. Consequently, other institutions may consider pursuing collaborations or seeking research support from GlaxoSmithKline and Karolinska Institute to advance their work in this domain.

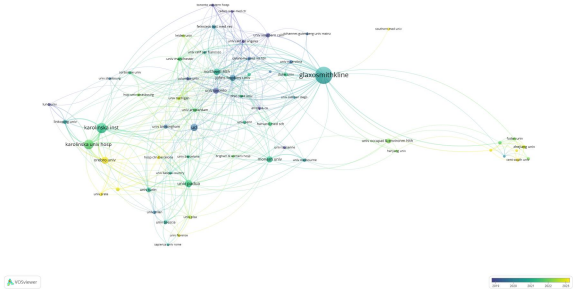


Figure 3. Institutions' analysis of belimumab treatment for SLE

Table 2. Top 10 Productive Institutions

Rank	Institutions	Documents	Avg. pub. year	Citations	Avg. citations
1	GlaxoSmithKline	83	2020.5542	2539	30.5904
2	Karolinska Inst	40	2021.225	1962	49.05
3	Karolinska Univ Hosp	37	2021.7297	811	21.9189
4	UCL	24	2019.6667	969	40.375
5	Univ Padua	24	2021.4167	778	32.4167
6	Orebro Univ	23	2023.5652	225	9.7826

7	Northwell Hlth	21	2020.8571	858	40.8571
8	Monash Univ	20	2021.15	733	36.65
9	Johns Hopkins Univ	19	2019.9474	662	34.8421
10	Univ Toronto	18	2019.1667	1700	94.4444

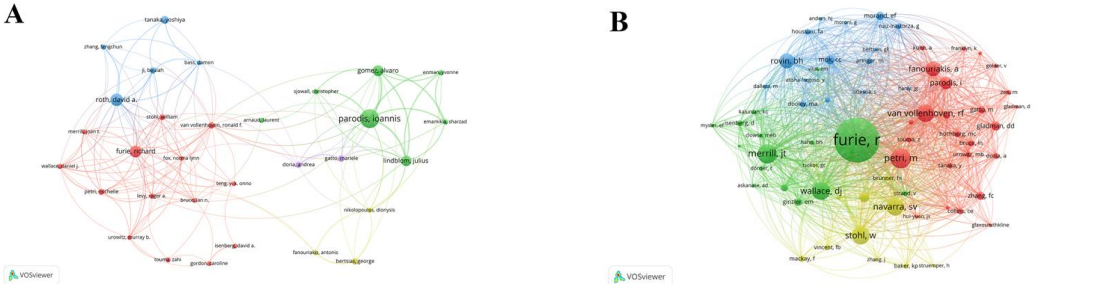
3.4 Authors and Cited Authors

A total of 3,490 authors have published papers on "belimumab treatment for SLE," with the top 10 most prolific authors listed in Table 3. Figure 4A displays a co-occurrence network of scholars with 9 or more publications. Different circle colors represent distinct clusters, while connecting lines indicate collaboration strength—authors with frequent collaborations share the same circle color. The figures reveal significant disparities in publication volume among authors, with frequent collaborations forming an interwoven network. Parodis, Ioannis and Roth, David A., as the two most prolific authors, respectively spearheaded collaborations between two research groups.

A total of 11,016 authors were cited in research papers on "belimumab treatment for SLE." Table 3 lists the top ten highly cited authors in this field, while Figure 4B displays the co-citation network of these high-impact authors. Connections between circles indicate that two references were cited together in the same article. Furie, R. received the highest number of citations. His publication, "A phase III, randomized, placebo-controlled study of belimumab, a monoclonal antibody that inhibits B lymphocyte stimulator, in patients with systemic lupus erythematosus," is the most frequently cited reference in this field.

Table 3. Top 10 Productive Authors and Most Cited Authors

Rank	Authors	Documents	Cited authors	Citation
1	Parodis, Ioannis	37	Furie, R	1169
2	Roth, David A.	24	Petri, M	455
3	Furie, Richard	23	Merrill, Jt	436
4	Gomez, Alvaro	21	Stohl, W	407
5	Lindblom, Julius	20	Wallace, Dj	404
6	Tanaka, Yoshiya	15	Navarra, Sv	394
7	Bertsias, George	12	Van Vollenhoven, Rf	393
8	Gatto, Mariele	12	Rovin, Bh	325
9	Ji, Beulah	12	Fanouriakis, A	320
10	Van Vollenhoven, Ronald F.	12	Parodis, I	265



(A) Clustering Map of the Authors of Belimumab Treatment for SLE. **(B) Clustering Map of the Cited Authors of Belimumab Treatment for SLE**

Figure 4. Analysis of Authors and Cited Authors of Belimumab Treatment for SLE

3.5 Journals and Cited Journals

Table 4 shows the top ten journals publishing research on belimumab treatment for SLE and the most frequently cited journal in this field. *Ann Rheum Dis* (IF: 20.6) has the highest citation count, indicating its published papers exert significant influence on this field. *Lupus* (IF: 1.9) not only ranks highest in publication volume but also boasts a very high citation count. The dual-layer network diagram illustrates relationships between journal topics: the left side shows citing disciplines, the right side shows cited disciplines, and the central paths represent citation relationships. In Figure 5, the "MOLECULAR, BIOLOGY, GENETICS" discipline cluster on the right extends a thick yellow strand to form the "MOLECULAR, BIOLOGY, IMMUNOLOGY" cluster on the left. This

cluster then connects with the "HEALTH, NURSING, MEDICINE" and "SPORTS, REHABILITATION, SPORT" clusters on the right, each extending a green strand to form the "MEDICINE, MEDICAL, CLINICAL" cluster. Researchers new to this field can explore foundational knowledge on "belimumab treatment for SLE" through the right-side discipline cluster, while leveraging the left-side clusters to uncover cutting-edge developments in "belimumab treatment for SLE".

Table 4. Top 10 Productive Journals and most Cited Journals

Rank	Journals	Documents	Cited journals	Citation
1	lupus	77	ann rheum dis	3387
2	rheumatology	38	arthritis rheum-us	2318
3	lupus science & medicine	32	lupus	2146
4	frontiers in immunology	30	arthritis rheumatol	1552
5	annals of the rheumatic diseases	22	rheumatology	1354
6	arthritis & rheumatology	19	j rheumatol	924
7	clinical rheumatology	18	new engl j med	895
8	autoimmunity reviews	17	j immunol	761
9	frontiers in medicine	14	lancet	722
10	expert opinion on biological therapy	13	lupus sci med	692

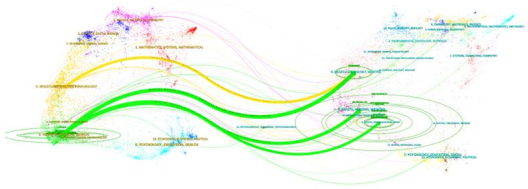


Figure 5. The Dual-map Overlay of Journals of Belimumab Treatment for SLE

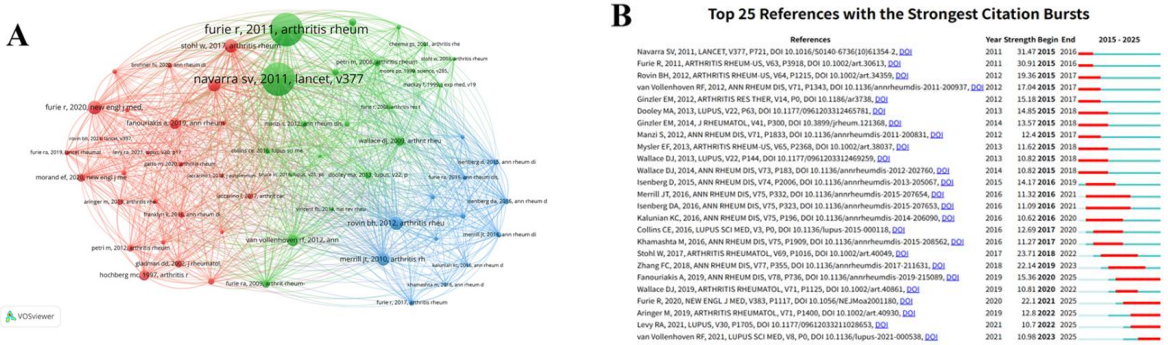
3.6 Cited References

The top ten most cited references are shown in Table 5. Among them, the most frequently cited reference, "A phase III, randomized, placebo-controlled study of belimumab, a monoclonal antibody that inhibits B lymphocyte stimulator, in patients with systemic lupus erythematosus," serves as an early observational clinical trial paper on belimumab, laying the foundation for research on "belimumab treatment for SLE." Figure 6A illustrates that the cited references form three distinct clusters. Figure 6B highlights the top 25 references with the highest citation bursts, enabling identification of references experiencing high citation activity within a short timeframe. The reference with the strongest burst intensity is "Efficacy and safety of belimumab in patients with active systemic lupus erythematosus: a randomized, placebo-controlled, phase 3 trial," published by Navarra, S.V. in 2011.

Table 5. Top 10 Most Cited References

Rank	References	DOI	Citation
1	A phase III, randomized, placebo-controlled study of belimumab, a monoclonal antibody that inhibits B lymphocyte stimulator, in patients with systemic lupus erythematosus	10.1002/art.30613	395
2	Efficacy and safety of belimumab in patients with active systemic lupus erythematosus: a randomised, placebo-controlled, phase 3 trial	10.1016/s0140-6736(10)61354-2	394
3	Two-Year, Randomized, Controlled Trial of Belimumab in Lupus Nephritis	10.1056/nejmoa2001180	160
4	Efficacy and safety of rituximab in patients with active proliferative lupus nephritis: the Lupus Nephritis Assessment with Rituximab study	10.1002/art.34359	156
5	Efficacy and Safety of Subcutaneous Belimumab in Systemic Lupus Erythematosus: A Fifty-Two-Week Randomized, Double-Blind, Placebo-Controlled Study	10.1002/art.40049	156
6	Efficacy and safety of rituximab in moderately-to-severely active systemic lupus erythematosus: the randomized, double-blind, phase II/III systemic lupus erythematosus evaluation of rituximab trial	10.1002/art.27233	146

7	A pivotal phase III, randomised, placebo-controlled study of belimumab in patients with systemic lupus erythematosus located in China, Japan and South Korea	10.1136/annrheumdis-2017-211631	145
8	Belimumab in the treatment of systemic lupus erythematosus: high disease activity predictors of response	10.1136/annrheumdis-2011-200937	133
9	2019 update of the EULAR recommendations for the management of systemic lupus erythematosus	10.1136/annrheumdis-2019-215089	130
10	Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus	10.1002/art.1784000928	121



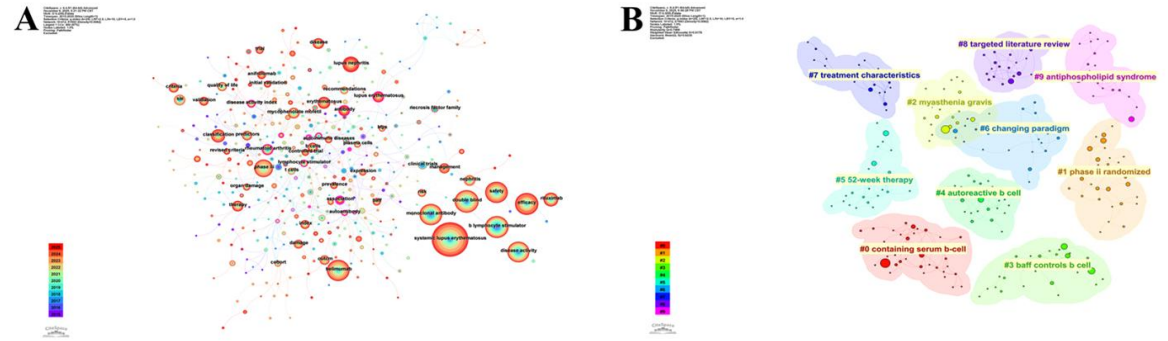
(A) Clustering map of references of belimumab treatment for SLE

(B) Top 25 references with the strongest citation bursts of belimumab treatment for SLE

Figure 6. References analysis of belimumab treatment for SLE.

3.7 Keywords

Figure 7A illustrates keyword activity levels, with redder hues indicating higher recent activity. Typically, clustering is considered highly reliable when Q exceeds 0.3 and S surpasses 0.7. In the clustering diagram shown in Figure 7B, Q=0.7468 and S=0.9178. The keyword clustering map displays the top 10 clusters, each represented by a distinct color. As noted in cluster #9, antiphospholipid syndrome (APS) is an autoimmune disorder defined by thrombosis and obstetric morbidity, and is frequently secondary to SLE. The high positivity rate of antiphospholipid antibodies in SLE patients means their co-occurrence markedly elevates thrombotic risk.



(A) Co-occurrence map of the Keywords of Belimumab Treatment for SLE

(B) Clustering Map of the Keywords of Belimumab Treatment for SLE

Figure 7. Keywords Analysis of Belimumab Treatment for SLE

The primary function of keyword timeline charts is to help newcomers to a field quickly grasp its developmental trajectory and predict future directions. Figure 8A shows that BAFF was the earliest keyword to emerge in research over the past decade and has remained consistently active. This is because studies on belimumab treatment for SLE suggest that belimumab blocks BAFF binding to its receptor, thereby inhibiting B-cell survival and activation to ultimately treat SLE. Citespace can generate keyword burst maps to uncover research hotspots and trends. Figure 8B indicates that “clinical trials” exhibits the highest burst intensity, signifying its status as a prominent research topic, while “stage renal disease” has garnered significant attention in recent years.

(A) Timeline Map of Belimumab Treatment for SLE **(B) Top 18 Keywords with the Strongest Citation Bursts of Belimumab Treatment for SLE**

Figure 8. Research Trends of Belimumab Treatment for SLE

4. Discussion

This study conducted a bibliometric analysis of research on belimumab treatment for SLE from 2015 to 2025, revealing the development trends and research landscape in this field. Over the decade, 709 papers were published, with a steady upward trend in related literature, particularly showing significant growth in 2022. This surge is closely linked to the inclusion of belimumab in the 2019 EULAR guidelines as a recommended treatment[7], while also benefiting from the wave of biologic research sparked by the FDA approval of anifrolumab in 2021[8]. By country, the United States led global research with 244 publications, while China demonstrated concentrated recent activity, reflecting scientific follow-up after the drug's 2019 market approval in China. Institutional collaboration networks show GlaxoSmithKline, as the originator company, produced the highest number of publications (83). However, academic institutions like Karolinska Institutet outperformed in average citations per paper, indicating superior research quality. Author collaboration networks reveal two primary research teams centered around Parodis, Ioannis and Roth, David A., demonstrating strong academic synergy. Regarding knowledge foundations, the Phase III clinical trial study by Furie R et al., as the most cited literature, established the evidence base for this field. The *Annals of the Rheumatic Diseases* and *Lupus* serve as the most significant knowledge dissemination platforms. Interdisciplinary analysis indicates the field is evolving from foundational molecular biology and genetics research toward molecular immunology and clinical medicine, providing a clear knowledge progression pathway for subsequent researchers. These findings systematically map the overall landscape of belimumab treatment research for SLE, offering a reference framework for future research direction selection and collaboration establishment.

Based on the knowledge graph analysis from this study and combined with the latest research advances, a deeper understanding of the development trajectory and future directions in this field can be formed. The results of this study indicate that BAFF, as an early-appearing and persistently active core keyword, confirms the fundamental role of targeting the BAFF pathway in autoimmune disease research. In recent years, with the widespread clinical application of BAFF inhibitors such as belimumab, their mechanisms of action have been further elucidated. Recent transcriptomic studies reveal that this drug not only inhibits B-cell activation by neutralizing BAFF but also downregulates type I/II interferon signaling, IL-6/STAT3 pathways, and genes associated with neutrophil activation, demonstrating multidimensional immunomodulatory effects[9]. This partially explains its clinical benefits in inducing disease-modifying effects. Benlimab, as a BAFF inhibitor, demonstrates potential regulatory effects on secondary APS while reducing SLE damage[10-11]. Current research indicates that it can partially lower antiphospholipid antibody titers and may reduce the incidence of thrombotic events, suggesting its potential to intervene in the immune pathogenesis of APS via the B-cell pathway[12-13]. However, this effect cannot replace standard anticoagulant therapy. Its precise role in APS prevention and management, particularly as a primary prevention or combination therapy strategy, has become a current research focus and requires urgent validation through prospective clinical trials. Concurrently, keyword emergence analysis indicates that “stage renal disease” has emerged as a prominent term in recent years, highlighting the prevention and treatment of end-stage renal disease as a critical research frontier[14-15]. The high emergence intensity of “clinical trials” reflects a comprehensive

shift in research focus toward clinical translation and protocol optimization. Looking ahead, this field faces several key challenges and development directions: First, establishing reliable biomarker systems for precision medicine is essential, such as predictive models based on genes like S100A12 and IFIT3 currently under exploration. Second, optimizing combination therapy strategies is crucial, particularly for severe complications like lupus nephritis, by considering co-administration with drugs targeting plasma cells or T cells. Third, overcoming potential resistance mechanisms, such as compensatory activation of the APRIL pathway. Fourth, expanding therapeutic applications represents a key direction, with belimumab currently under clinical investigation in novel fields such as cancer immunotherapy (e.g., combination with venetoclax for chronic lymphocytic leukemia). In summary, this field is evolving from fundamental mechanism research toward precision medicine and cross-disease applications. Future progress in precise patient stratification and innovative combination strategies holds promise for ultimately improving long-term organ outcomes for patients.

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