International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	CURRENT APPROACHES TO THE TREATMENT OF SJÖGREN'S DISEASE – A REVIEW OF IMMUNOMODULATORY AND BIOLOGICAL THERAPIES
DOI	https://doi.org/10.31435/ijitss.2(50).2026.5477
RECEIVED	25 February 2026
ACCEPTED	21 April 2026
PUBLISHED	30 April 2026
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

CURRENT APPROACHES TO THE TREATMENT OF SJÖGREN'S DISEASE – A REVIEW OF IMMUNOMODULATORY AND BIOLOGICAL THERAPIES

Aleksandra Płecka *(Corresponding Author, Email: olaplecka13@interia.pl)*
Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland
ORCID ID: 0009-0007-0075-5234

Maksymilian Szklarski
Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland
ORCID ID: 0009-0001-6977-0666

Karol Józef Szkarłat
Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland
ORCID ID: 0009-0004-2889-8382

Szymon Targosz
Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland
ORCID ID: 0009-0005-2251-5229

Jędrzej Sztajura
Students' Scientific Club, Department of Neurosurgery, Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland
ORCID ID: 0009-0009-8975-731X

Ewa Maraszewska
Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland
ORCID ID: 0009-0003-0992-7144

Michał Stachel
Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland
ORCID ID: 0009-0008-3264-4747

Weronika Szymacha
Faculty of Medical Sciences in Katowice, Medical University of Silesia in Katowice, Poland
ORCID ID: 0009-0000-1592-5602

Karol Zimnicki
Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland
ORCID ID: 0009-0001-9687-2641

Alicja Stępień
Voivodship Dental Clinic, Consulting Dental Prosthetics Department, Cracow, Poland
ORCID ID: 0009-0003-2717-6030

ABSTRACT

Introduction and purpose: Sjögren's disease (SjD) is a systemic autoimmune process in which traditional symptomatic treatment often fails to prevent organ complications. Thanks to intensive research into its pathogenesis, new therapeutic targets are being discovered, which may enable the causal treatment of the disease. This paper provides a review of modern therapeutic strategies, with a particular focus on JAK/BTK/SYK inhibitors, the CD40-CD40L pathway, and anti-CD20 therapy. Based on the latest clinical trial results, the article analyzes the potential of immunomodulation in modifying the course of SjD and preventing its systemic manifestations.
Description of the state of knowledge: Current scientific consensus defines Sjögren's disease as a complex, multifactorial autoimmune condition. The progression of the disease is primarily driven by the overexpression of factors such as BAFF and APRIL, excessive interferon production, and specific lymphocyte populations, including follicular helper T-cells (Tfh) and CD8+ GZMK+ T-cells. Despite a detailed understanding of these molecular mechanisms, effective disease-modifying treatment remains elusive. Currently, researchers' attention is focused on therapies targeting novel signaling pathways.
Conclusions: Modern treatment of Sjögren's disease is evolving toward disease-modifying therapies that target the molecular mechanisms of epithelial inflammation and the type I interferon signature. Key strategies include targeted B- and T-cell immunomodulation and the inhibition of intracellular signaling pathways, which effectively reduce systemic activity and offer a significant steroid-sparing effect. The future of therapy relies on personalized medicine and the use of regenerative medicine, including exosomes, to restore the function of damaged glands.

KEYWORDS

Sjögren's Disease, Interferon Signature, Immunomodulation, Targeted Therapies, Monoclonal Antibodies, JAK Inhibitors

CITATION

Aleksandra Płecka, Maksymilian Szklarski, Karol Józef Szkarłat, Szymon Targosz, Jędrzej Sztajura, Ewa Maraszewska, Michał Stachel, Weronika Szymacha, Karol Zimnicki, Alicja Stępień. (2026) Current Approaches to the Treatment of Sjögren's Disease – A Review of Immunomodulatory and Biological Therapies. *International Journal of Innovative Technologies in Social Science*. 2(50). doi: 10.31435/ijitss.2(50).2026.5477

Introduction and purpose

Sjögren's disease is a chronic, systemic autoimmune process in which the dominant histopathological feature is lymphocytic infiltration within the exocrine glands [1]. Although xerostomia and xerophthalmia represent the core symptoms of this entity, many patients develop systemic manifestations that extend beyond the epithelial barrier. Organ involvement in the course of SjD exhibits significant clinical variability, manifesting as dysfunction of the respiratory, renal, circulatory, articular, or neurological systems, as well as hematological disorders and skin lesions of diverse etiology [1,2,3,4,5,6,7]. Despite numerous studies, the factors determining the etiopathogenesis and clinical dynamics of SjD have not yet been fully elucidated. Traditional therapeutic strategies in Sjögren's disease focused almost exclusively on symptom relief through the use of tear and saliva substitutes, muscarinic receptor agonists, or nonspecific anti-inflammatory drugs. However, given the moderate effectiveness of these interventions in inhibiting the progression of systemic changes and the increasing knowledge of molecular pathogenesis, including the roles of B-cells, T-cells, dendritic cells, and specific cytokine pathways, researchers' attention has shifted toward targeted therapies.

This study aims to analyze current and emerging therapeutic strategies in Sjögren's disease, with a particular focus on immunomodulation and biological therapies. The article reviews the latest clinical trial reports regarding molecular targets such as the CD40-CD40L and JAK/BTK/SYK pathways, as well as the CD20 molecule.

Materials and methods

This literature review of Sjögren's disease utilized articles published between 2015 and 2026 from the PubMed database. The review focused on studies addressing the treatment of Sjögren's disease. A total of 51 articles were analyzed to provide a comprehensive synthesis of current knowledge.

Epidemiology

A synthetic compilation of global epidemiological data from the PubMed and Embase databases positions Sjögren's syndrome as an entity with significant population prevalence. The prevalence is estimated at 60.82 cases per 100,000 inhabitants, which corresponds to a diagnosis in one out of every 1,644 individuals. With a global incidence rate of 6.92 per 100,000 person-years, an analysis of trends from the last fifteen years confirms a dominant female participation in the disease structure. Furthermore, the data identifies 56 years of age as the statistical peak for the clinical manifestation of this condition [8].

Pathophysiology

Sjögren's disease, being a primary autoimmune disorder, exhibits a unique histopathological heterogeneity that can also manifest in patients with other diagnosed rheumatic conditions, such as rheumatoid arthritis, systemic lupus erythematosus, or systemic sclerosis. Currently, there is a shift away from the historical term "secondary Sjögren's syndrome" in favor of a precise description of the glandular features accompanying these established disease entities [9].

Clinical manifestations of SjD are currently classified in a manner that extends beyond simple epithelial damage. These include nonspecific symptoms such as chronic fatigue, depression, and anxiety, affecting nearly half of the patient population [51], as well as periepithelial and extraepithelial changes, and potential transformation into lymphomas, most commonly MALT [10]. Organ involvement can affect the respiratory, cardiovascular, and renal systems, as well as the central and peripheral nervous systems, which drastically reduces patients' quality of life and increases morbidity rates [30,21].

The pathogenesis of Sjögren's disease is defined as a multi-stage process resulting from the complex interaction of genetic, epigenetic, hormonal, and environmental factors. The contemporary model posits that the initiation of inflammation depends on the innate immune system, whereas the perpetuation of the autoimmune process requires continuous interaction with the adaptive immune system [11].

Triggering Factors and Genetic Predispositions

The development of the disease is driven by a loss of self-tolerance, which is closely linked to specific genetic variants of the major histocompatibility complex class II, including HLA-DRB1, HLA-DQA1, and HLA-DQB1 [12]. It is suspected that the primary trigger for the pathological inflammatory cascade may be a viral infection, induced by pathogens such as the Epstein-Barr virus, cytomegalovirus, or Coxsackie viruses [13].

The Role of the Epithelium and the Interferon Signature

A key element of the pathophysiology is salivary gland epithelial cells (SGECs), which are not merely targets of attack but active mediators of inflammation. SGECs express MHC class II molecules and co-stimulatory molecules CD80, CD40, enabling them to perform direct antigen presentation [14]. The inflammatory process, initiated even before the onset of overt xerostomia, is driven by the ability of SGECs to synthesize pro-inflammatory cytokines and present antigens to T-cells [15]. An essential mechanism is the ectopic overexpression of the LAMP3 protein, which induces signaling through the TLR7 receptor, leading to increased production of type I interferon [16]. It has been shown that the degree of activation of type I interferon-dependent signaling pathways correlates closely with the presence of anti-Ro/SSA antibodies Ro52+/Ro60+, as well as the severity of systemic extra-glandular manifestations [17,14].

Mitochondria

Recent studies highlight the significant role of mitochondrial dysfunction in SGECs. Morphological abnormalities (such as swelling and elongation) and proteomic shifts in lipid metabolism and amino acid degradation pathways are observed, which induce cellular stress and promote a proinflammatory phenotype. Additionally, the loss of specific PRR4+CST3+ acinar cells results from a direct attack by cytotoxic CD8+ GZMK+ T-cells [11]. These CD8+ GZMK+ T-cells affect the glandular epithelium through a sub-cytolytic mechanism, in which granzyme K induces mitochondrial dysfunction [18].

B-Cell Proliferation

Ectopic germinal center formation occurs within the glandular tissue, a process regulated by follicular helper T-cells (Tfh) and Th17 cells [19]. Chronic antigenic stimulation, the overexpression of cytokines such as APRIL, and BTK gene overexpression lead to uncontrolled B-cell proliferation. Autoreactive B-cells expressing rheumatoid factor exhibit a distinct preneoplastic potential, representing a critical step in the transformation toward B-cell lymphomas in SjD patients [11].

T-Cell-Dependent Pathogenesis

In the course of Sjögren's disease, a profound disruption of immune homeostasis occurs, resulting from a deficiency and impaired function of regulatory T-cells (Tregs) [35]. The weakening of this protective barrier paves the way for the uncontrolled activity of pro-inflammatory subpopulations, including Th17 and follicular helper T (Tfh) cells [20]. The latter, through the secretion of IL-21 and the CD40-CD40L interaction, provide signals essential for pathological B-cell activation [12]. Concurrently, CD8+ T-cells, specifically the GZMK+ population exhibit sub-cytolytic activity against the epithelium [18], while tissue-resident memory T-cells (Trm) are responsible for maintaining the local inflammatory state and its recurrent nature [12].

Advanced Therapeutic Strategies and Treatment Personalization in Sjögren's Disease

The current therapeutic paradigm in Sjögren's disease is undergoing a fundamental transformation. For over a century, since its initial clinical description, treatment was limited almost exclusively to symptomatic relief of xerostomia and xerophthalmia, alongside nonspecific, off-label immunosuppression that failed to alter the biological progression of the disorder. However, advances in understanding its pathogenesis, specifically the role of the epithelium as an active participant in the inflammatory process have enabled the development of targeted interventions. Modern clinical evidence suggests we are entering the era of disease-modifying therapies. By precisely targeting signaling pathways such as CD40, BAFF/APRIL, or interferon signaling, these therapies offer the potential to effectively inhibit immunological activity and preserve glandular function [21,13].

B-cell Targeted Therapies

The most significant success in recent years has been recorded in the field of therapies targeting B-cell survival and activation factors. One of the key mechanisms of action involves B-cell depletion. This group includes Ianalumab, a fully human monoclonal antibody that acts by blocking the BAFF-R receptor and inducing rapid B-cell depletion through enhanced antibody-dependent cellular cytotoxicity (ADCC) [13,22,23]. Unlike older therapies, Ianalumab depletes B-cells not only from the peripheral blood but also directly from the salivary gland tissues, as confirmed by advanced analyses using STAR and CRESS indices in Phase 2b trials. Currently, the drug is being evaluated in an extensive Phase 3 clinical program called NEPTUNUS [13]. Observations to date indicate a favorable safety profile, showing a sustained clinical response and efficacy in reducing systemic disease activity [24]. Another drug in this category is Rituximab, a chimeric monoclonal antibody targeting the CD20 antigen on the surface of B-cells [25]. Its action leads to the elimination of these cells by triggering antibody-dependent and complement-dependent cytotoxicity (ADCC/CDC) and inducing apoptosis. Historically, this agent held great promise for patients with Sjögren's patients; however, results from large, controlled clinical trials such as TEARS and TRACTISS proved unsatisfactory in alleviating core symptoms like mucosal dryness or chronic fatigue [13]. According to recent analyses, including data from the Portuguese PORTRESS registry published in 2026, the drug shows high effectiveness in patients with active systemic forms of the disease. A significant reduction in systemic activity (measured by the ESSDAI score) was noted, along with a crucial steroid-sparing effect, allowing for a substantial reduction or total discontinuation of glucocorticosteroids in a large proportion of treated patients [25]. Currently, per international EULAR recommendations, Rituximab is primarily used for severe organ complications when standard treatments fail [26]. Its safety profile is well-documented and predictable [31], though the potential for new-onset or prolonged hypogammaglobulinemia remains a key concern, necessitating regular monitoring of serum IgG levels [32,25]. Another mechanism involves blocking the BAFF and APRIL factors, which inhibits the development of pathological B-cells, thereby lowering autoantibody levels while maintaining the stability of other parts of the immune system [33,34]. Telitacicept, a fusion protein, represents this group. Patients treated with Telitacicept reported marked improvements in symptoms of dryness, pain, and fatigue [36]. Telitacicept may be an effective solution for treating severe extraglandular complications, such as optic neuritis, and allows for safe tapering of steroid doses [37,38]. Acting through a similar mechanism is Iguratimod, which blocks the BAFF factor but also exhibits immunomodulatory effects by inhibiting the

production of pro-inflammatory cytokines. Clinical studies confirm its effectiveness in reducing disease activity (ESSDAI) and symptom burden (ESSPRI), including a significant improvement in eye hydration. The therapy is well-tolerated, potential adverse effects are usually mild gastrointestinal complaints or a transient increase in liver enzymes [39,40].

T-cell Directed Therapies and Costimulatory Pathway Inhibition

The CD40-CD40L pathway is strictly regulated in a healthy organism; however, in patients with Sjögren's disease, this communication is overactive and chronic. Drugs targeting this pathway include Dazodalibep and Iscalimab. Dazodalibep is a CD40L antagonist that blocks costimulatory signals between T- and B-cells, thereby inhibiting inflammatory processes. In a Phase 2 trial, the drug significantly reduced systemic activity in patients with severe disease and improved ESSPRI scores in patients with high subjective symptoms, reducing fatigue and dryness. The therapy is characterized by a favorable safety profile, with respiratory tract infections being the most commonly reported side effects [41]. In contrast, Iscalimab is a fully human monoclonal antibody that blocks the pathway without inducing B-cell depletion. This mechanism prevents the interaction of the CD40 receptor on B-cells with the CD154 ligand on T-cells, inhibiting immune costimulatory signals while maintaining B-cell counts [27,28]. The drug's efficacy was evaluated in a Phase 2b trial across two patient populations: those with high systemic activity and those with predominant symptoms of dryness and pain. In both groups, Iscalimab failed to demonstrate a statistically significant advantage over placebo regarding the primary endpoints, such as changes in ESSDAI or ESSPRI scores at week 24. Despite this, the drug was generally well-tolerated, with the most frequent adverse events being upper respiratory tract infections and headaches. Due to its non-lytic design, Iscalimab avoided the thrombotic complications observed in earlier therapies targeting this pathway [27]. Restoring immune balance represents another mechanism to combat disease symptoms. Low-dose interleukin-2 therapy is an immunomodulatory approach that restores immune equilibrium by selectively stimulating protective regulatory T-cells (Tregs). By suppressing inflammation, this treatment significantly lowers systemic disease activity (ESSDAI) and alleviates subjective symptoms such as dryness, pain, and fatigue. This method is safe, well-tolerated, and, unlike traditional immunosuppression, it is not associated with an increased risk of infection [29].

Signal Modulation: Intracellular Pathway Inhibitors

The modulation of intracellular signals allows for the simultaneous inhibition of multiple cytokines that depend on shared transduction pathways. One class of such modulators is Janus kinase inhibitors, which include Baricitinib and Filgotinib. These agents demonstrate the ability to dampen the so-called "interferon signature" that predominates in most patients with SjD. By blocking type I IFN signaling, these drugs reduce epithelial inflammation and secondary BAFF production [21, 42]. Filgotinib is a selective JAK1 inhibitor. It was evaluated in a Phase 2 clinical trial comparing its efficacy to placebo in patients with active SjD. Although a higher response rate was recorded at week 12 (16.6%) compared to the placebo group, this difference did not reach statistical significance. However, studies suggest its potential role in improving parameters within the glandular domain of the ESSDAI score [43]. Baricitinib is a selective JAK1 and JAK2 inhibitor, the efficacy of which was assessed in a pilot study of 11 female patients with active Sjögren's syndrome (ESSDAI $\geq$ 5). The drug's mechanism involves blocking cytokine pathways crucial to disease progression, including type I interferon and interleukins 6 and 17. Over six months of treatment at a dose of 2 mg daily, a statistically significant reduction in disease activity was observed on the ESSDAI and ESSPRI scales, alongside clinical improvement in arthritis, skin lesions, and interstitial lung disease. A transient decrease in serum IgG levels was also noted. The authors emphasize that due to the pilot nature of the study and the lack of a control group, these results are preliminary and require verification in randomized controlled trials [44]. Bruton's tyrosine kinase (BTK) inhibitors, including Tirabrutinib and Remibrutinib, target B-cell hyperactivity. Tirabrutinib is a selective, oral BTK inhibitor. In a Phase 2 study, the drug was well-tolerated and demonstrated biological activity by reducing serum immunoglobulin levels. However, it did not reach the predefined endpoint, no statistically significant improvement in ESSDAI or ESSPRI clinical indices was found compared to placebo at week 12. These results suggest that while blocking the BTK pathway modifies the patient's immunological profile, translating this effect into clear symptomatic improvement in SjD requires further research into patient selection or treatment duration [45]. In contrast, Remibrutinib in a Phase 2 study (LOUiSSe) significantly lowered systemic disease activity (ESSDAI) and levels of inflammatory biomarkers such as CXCL13, while showing a trend toward improving salivary gland secretory function. Although no significant change in subjective perceptions of dryness has been reported yet, the therapy proved safe and well-tolerated, with mild

respiratory infections being the most common side effect [46]. Another modulator is Lanraplenib, acting as a selective spleen tyrosine kinase (SYK) inhibitor. SYK kinase plays a pivotal role in signaling through B-cell receptors and Fc receptors. In a Phase 2 study of patients with active Sjögren's syndrome (ESSDAI ≥ 5), the drug was administered orally at a dose of 30 mg once daily. Although Lanraplenib did not achieve a statistically significant advantage over placebo in the primary composite endpoint ($p = 0.16$), secondary endpoint analysis showed significant improvement in the objective measurement of tear secretion via Schirmer's test ($p = 0.046$). The mean decrease in systemic activity on the ESSDAI scale was 2.48 points at week 12. The therapy was well-tolerated, with nasopharyngitis being the most common mild to moderate adverse event [43].

Neonatal Fc Receptor (FcRn) Inhibitors as a Strategy for Autoantibody Elimination

The mechanism of action for neonatal fragment crystallizable receptor (FcRn) inhibitors, such as Nipocalimab and Efgartigimod, is based on the competitive blocking of the receptor's binding domain. This disrupts the physiological recycling pathway of immunoglobulin G (IgG), leading to its rapid degradation. In Sjögren's disease, this approach allows for a significant reduction in the levels of pathogenic autoantibodies, such as anti-Ro and anti-La. Nipocalimab is a fully human monoclonal antibody. The Phase 2 DAHLIAS study demonstrated that a dose of 15 mg/kg administered intravenously every two weeks leads to a clinically significant improvement in disease activity, as measured by the ClinESSDAI score, alongside a reduction in symptoms of dryness, pain, and fatigue. The drug is characterized by a safety profile similar to placebo, with upper respiratory tract infections being the most frequently reported adverse events [47]. Efgartigimod, in a Phase 2 study of patients with Sjögren's syndrome, reduced IgG levels by an average of 60%, yielding clear clinical improvement. Currently, the OASIS trial is evaluating its efficacy in alleviating persistent dryness in individuals with low systemic activity [48].

Inhibition of the Interferon Axis via Nuclease-Mediated Elimination of Circulating RNA

RSLV-132 is a fusion protein that functions as an enzyme digesting circulating free RNA molecules, thereby preventing the activation of immune receptors and dampening interferon-driven inflammation. In clinical trials, this agent demonstrated particular efficacy in alleviating severe fatigue, providing patients with distinct and statistically significant relief as measured by specialized quality-of-life scales, such as FACIT-Fatigue. The therapy is characterized by a very favorable safety profile and represents a promising option, especially for individuals for whom exhaustion is the most burdensome symptom of Sjögren's disease[49].

The Future: Regenerative Medicine

Exosome therapy utilizes small vesicles, ranging from 30 to 150 nm, to transport molecules such as miRNA and proteins that regulate the immune response. In Sjögren's disease, stem cell-derived exosomes inhibit inflammation and restore lymphocyte balance, while those derived from dental pulp regenerate salivary glands, improving their secretory function. As a stable and safe cell-free approach, exosomes represent a promising alternative to conventional therapies; however, their widespread clinical application requires the standardization of isolation methods and confirmation of efficacy in human clinical trials [50].

Conclusions

Due to the complex, multifactorial pathogenesis of Sjögren's disease, treatment has historically been limited to symptomatic relief. However, recent discoveries have provided a deeper understanding of the molecular pathogenesis, enabling the development of novel targeted therapies aimed at modifying the disease course. Recent scientific research highlights the pivotal role of salivary gland epithelial cells, which are no longer viewed merely as targets of attack but as active mediators of inflammation capable of antigen presentation and driving the interferon signature. Consequently, research into inflammation-quenching agents, such as JAK and BTK inhibitors, is crucial; these represent promising tools for inhibiting the interferon signature, leading to the stabilization of organ function and a steroid-sparing effect. Furthermore, the significant role of CD8+ GZMK+ T-cells, which produce granzyme K and induce mitochondrial dysfunction, has been demonstrated, paving the way for interventions that directly protect the secretory apparatus. Excessive and uncontrolled B-cell proliferation is another key component of the pathogenesis. Autoreactive B-cells represent a critical stage in the transformation toward B-cell lymphomas; therefore, immunomodulating drugs such as Ianalumab, which can achieve rapid B-cell depletion not only in peripheral blood but directly within glandular tissues, could represent a breakthrough in SjD treatment. Factors such as BAFF and APRIL drive excessive B-cell production, thus, therapies targeting these factors, as well as the CD40-CD40L pathway, allow

for a significant reduction in systemic activity (measured by the ESSDAI index) and subjective improvements in pain and fatigue. The use of exosomes derived from stem cells and dental pulp represents the horizon of regenerative medicine, offering hope not only for inhibiting the autoimmune process but also for restoring the function of damaged glands. Although some targeted therapies still require verification in Phase III trials to confirm statistical significance, the accumulated evidence suggests that personalized treatment based on the patient's molecular profiling will become the clinical standard in the coming years. The future of SjD therapy lies in combining early immunomodulatory intervention with modern tissue regeneration methods, effectively preventing severe organ complications and significantly improving patients' quality of life.

Author's contribution:
All authors contributed to the article.
All authors have read and agreed with the published version of the manuscript.
Conflict of interest: The authors declare no conflict of interest.
Funding statement: No external funding was received to perform this review
Declaration of the use of generative AI and AI-assisted technologies in the writing process: In preparing this review, the authors used Google Gemini for the purpose of grammar checking and improving the readability of the text. After using this tool, the authors have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

REFERENCES

1. Manfrè, V., Chatzis, L. G., Cafaro, G., Fonzetti, S., Calvacchi, S., Fulvio, G., Navarro Garcia, I. C., La Rocca, G., Ferro, F., Perricone, C., Bartoloni, E., & Baldini, C. (2022). Sjögren's syndrome: One year in review 2022. *Clinical and Experimental Rheumatology, 40*(12), 2211–2224. https://doi.org/10.55563/clinexprheumatol/43z8gu
2. Björk, A., Mofors, J., & Wahren-Herlenius, M. (2020). Environmental factors in the pathogenesis of primary Sjögren's syndrome. *Journal of Internal Medicine, 287*(5), 475–492. https://doi.org/10.1111/joim.13032
3. Yao, Y., Ma, J. F., Chang, C., Xu, T., Gao, C. Y., Gershwin, M. E., & Lian, Z. X. (2021). Immunobiology of T cells in Sjögren's syndrome. *Clinical Reviews in Allergy & Immunology, 60*(1), 111–131. https://doi.org/10.1007/s12016-020-08793-7
4. Brito-Zerón, P., Retamozo, S., & Ramos-Casals, M. (2023). Sjögren syndrome. Síndrome de Sjögren. *Medicina Clínica, 160*(4), 163–171. https://doi.org/10.1016/j.medcli.2022.10.007
5. Demarchi, J., Papasidero, S., Medina, M. A., Klajn, D., Chaparro Del Moral, R., Rillo, O., Martiré, V., Crespo, G., Secco, A., Catalan Pellet, A., Amitrano, C., Crow, C., Asnal, C., Pucci, P., Caeiro, F., Benzanquen, N., Pirola, J. P., Mayer, M., Zazzetti, F., Velez, S., … Raiti, L. (2017). Primary Sjögren's syndrome: Extraglandular manifestations and hydroxychloroquine therapy. *Clinical Rheumatology, 36*(11), 2455–2460. https://doi.org/10.1007/s10067-017-3822-3
6. Brito-Zerón, P., Flores-Chávez, A., Horváth, I. F., Rasmussen, A., Li, X., Olsson, P., Vissink, A., Priori, R., Armagan, B., Hernandez-Molina, G., Praprotnik, S., Quartuccio, L., Inanç, N., Özkızıltaş, B., Bartoloni, E., Sebastian, A., Romão, V. C., Solans, R., Pasoto, S. G., Rischmueller, M., … Sjögren Big Data Consortium. (2023). Mortality risk factors in primary Sjögren syndrome: A real-world, retrospective, cohort study. *EClinicalMedicine, 61*, 102062. https://doi.org/10.1016/j.eclinm.2023.102062
7. Behbodikhah, J., Ding, B., Jacob, B., Batool, N., Belilos, E., De Leon, J., Carsons, S. E., & Reiss, A. B. (2025). Sjogren's disease and elevated cardiovascular risk: Mechanisms and treatment. *Journal of Cardiovascular Development and Disease, 12*(9), 367. https://doi.org/10.3390/jcdd12090367
8. Qin, B., Wang, J., Yang, Z., Yang, M., Ma, N., Huang, F., & Zhong, R. (2015). Epidemiology of primary Sjögren's syndrome: A systematic review and meta-analysis. *Annals of the Rheumatic Diseases, 74*(11), 1983–1989. https://doi.org/10.1136/annrheumdis-2014-205375
9. Ramos-Casals, M., Baer, A. N., Brito-Zerón, M. D. P., Hammitt, K. M., Bouillot, C., Retamozo, S., Mackey, A., Yarowsky, D., Turner, B., Blanck, J., Fisher, B. A., Akpek, E. K., Baldini, C., Bootsma, H., Bowman, S. J., Dörner, T., Laing, L., Lieberman, S. M., Mariette, X., Pflugfelder, S. C., … International Task Force on Nomenclature of Sjögren Disease. (2025). 2023 International Rome consensus for the nomenclature of Sjögren disease. *Nature Reviews Rheumatology, 21*(7), 426–437. https://doi.org/10.1038/s41584-025-01268-z
10. Goules, A. V., Chatzis, L., Pezoulas, V. C., Patsouras, M., Mavragani, C., Quartuccio, L., Baldini, C., De Vita, S., Fotiadis, D. I., & Tzioufas, A. G. (2024). Identification and evolution of predictors of Sjögren's disease-associated mucosa-associated lymphoid tissue lymphoma development over time: A case-control study. *The Lancet Rheumatology, 6*(10), e693–e702. https://doi.org/10.1016/S2665-9913(24)00183-8

11. Baldini, C., Chatzis, L. G., Fulvio, G., La Rocca, G., Pontarini, E., & Bombardieri, M. (2024). Pathogenesis of Sjögren's disease: One year in review 2024. *Clinical and Experimental Rheumatology, 42*(12), 2336–2343. https://doi.org/10.55563/clinexprheumatol/i8iszc
12. Verstappen, G. M., Pringle, S., van der Geest, K. S., Kroese, F. G., & Bootsma, H. (2026). T cells in Sjögren's disease: Update on their role in salivary gland pathogenesis and treatment. *Current Opinion in Immunology, 99*, 102739. https://doi.org/10.1016/j.coi.2026.102739
13. Pelkas, C., Franke, K. B., Vincent, F. B., & Rischmueller, M. (2025). Novel therapies in Sjögren's disease: A systematic review of the literature. *Best Practice & Research Clinical Rheumatology, 39*(4), 102084. https://doi.org/10.1016/j.berh.2025.102084
14. Baldini, C., Fulvio, G., La Rocca, G., & Ferro, F. (2024). Update on the pathophysiology and treatment of primary Sjögren syndrome. *Nature Reviews Rheumatology, 20*(8), 473–491. https://doi.org/10.1038/s41584-024-01135-3
15. Dela Cruz, A., Kartha, V., Tilston-Lunel, A., Mi, R., Reynolds, T. L., Mingueneau, M., Monti, S., Jensen, J. L., Skarstein, K., Varelas, X., & Kukuruzinska, M. A. (2021). Gene expression alterations in salivary gland epithelia of Sjögren's syndrome patients are associated with clinical and histopathological manifestations. *Scientific Reports, 11*(1), 11154. https://doi.org/10.1038/s41598-021-90569-w
16. Nakamura, H., Tanaka, T., Noguchi, M., Atsumi, T., Warner, B. M., & Chiorini, J. A. (2025). Investigation of lysosome-associated membrane protein 3 highlighting the role of lysosome in pathophysiology and treatment of Sjögren disease. *Arthritis & Rheumatology*. Advance online publication. https://doi.org/10.1002/art.43347
17. Bettacchioli, E., Saraux, A., Tison, A., Cornec, D., Dueymes, M., Foulquier, N., Hillion, S., Roguedas-Contios, A. M., Benyoussef, A. A., Alarcon-Riquelme, M. E., Pers, J. O., Devauchelle-Pensec, V., PRECISESADS Clinical Consortium, & PRECISESADS Sjögren Consortium. (2024). Association of combined anti-Ro52/TRIM21 and anti-Ro60/SSA antibodies with increased Sjögren disease severity through interferon pathway activation. *Arthritis & Rheumatology, 76*(5), 751–762. https://doi.org/10.1002/art.42789
18. Pranzatelli, T. J. F., Perez, P., Ku, A., Matuck, B., Huynh, K., Sakai, S., Abed, M., Jang, S. I., Yamada, E., Dominick, K., Ahmed, Z., Oliver, A., Wasikowski, R., Easter, Q. T., Baer, A. N., Pelayo, E., Khavandgar, Z., Kleiner, D. E., Magone, M. T., Gupta, S., … Warner, B. M. (2024). GZMK+CD8+ T cells target a specific acinar cell type in Sjögren's disease. *Research Square*. https://doi.org/10.21203/rs.3.rs-3601404/v2
19. Matsui, K., & Sano, H. (2017). T helper 17 cells in primary Sjögren's syndrome. *Journal of Clinical Medicine, 6*(7), 65. https://doi.org/10.3390/jcm6070065
20. Blinova, V. G., Vasilyev, V. I., Rodionova, E. B., & Zhdanov, D. D. (2023). The role of regulatory T cells in the onset and progression of primary Sjögren's syndrome. *Cells, 12*(10), 1359. https://doi.org/10.3390/cells12101359
21. Vivino, F. B., Bunya, V. Y., Massaro-Giordano, G., Johr, C. R., Giattino, S. L., Schorpion, A., Shafer, B., Peck, A., Sivils, K., Rasmussen, A., Chiorini, J. A., He, J., & Ambrus, J. L., Jr. (2019). Sjogren's syndrome: An update on disease pathogenesis, clinical manifestations and treatment. *Clinical Immunology, 203*, 81–121. https://doi.org/10.1016/j.clim.2019.04.009
22. Dörner, T., Posch, M. G., Li, Y., Petricoul, O., Cabanski, M., Milojevic, J. M., Kamphausen, E., Valentin, M. A., Simonett, C., Mooney, L., Hüser, A., Gram, H., Wagner, F. D., & Oliver, S. J. (2019). Treatment of primary Sjögren's syndrome with ianalumab (VAY736) targeting B cells by BAFF receptor blockade coupled with enhanced, antibody-dependent cellular cytotoxicity. *Annals of the Rheumatic Diseases, 78*(5), 641–647. https://doi.org/10.1136/annrheumdis-2018-214720
23. Bowman, S. J., Fox, R., Dörner, T., Mariette, X., Papas, A., Grader-Beck, T., Fisher, B. A., Barcelos, F., De Vita, S., Schulze-Koops, H., Moots, R. J., Junge, G., Woznicki, J. N., Sopala, M. A., Luo, W. L., & Hueber, W. (2022). Safety and efficacy of subcutaneous ianalumab (VAY736) in patients with primary Sjögren's syndrome: A randomised, double-blind, placebo-controlled, phase 2b dose-finding trial. *Lancet, 399*(10320), 161–171. https://doi.org/10.1016/S0140-6736(21)02251-0
24. Dörner, T., Bowman, S. J., Fox, R., Mariette, X., Papas, A., Grader-Beck, T., Fisher, B. A., Barcelos, F., De Vita, S., Schulze-Koops, H., Moots, R. J., Junge, G., Woznicki, J., Sopala, M., Avrameas, A., Luo, W. L., & Hueber, W. (2025). Safety and efficacy of ianalumab in patients with Sjögren's disease: 52-week results from a randomized, placebo-controlled, phase 2b dose-ranging study. *Arthritis & Rheumatology, 77*(5), 560–570. https://doi.org/10.1002/art.43059
25. Campinho Ferreira, C., Bandeira, M., Pereira da Costa, R., Matias, S., Duarte, A. C., Marques-Gomes, C., Fernandes Esteves, B., Cunha, A., Santos, M., Silva, L., Oliveira, C., Almeida, I., Augusto, D., Rua, C., Melo, A. T., Romão, V. C., & Leite Silva, J. (2026). Safety and effectiveness of rituximab therapy in Sjögren's disease: A PORTRESS—the Portuguese registry of Sjögren's disease-based study. *Clinical Rheumatology, 45*(2), 1091–1098. https://doi.org/10.1007/s10067-026-07930-5
26. Ramos-Casals, M., Brito-Zerón, P., Bombardieri, S., Bootsma, H., De Vita, S., Dörner, T., Fisher, B. A., Gottenberg, J. E., Hernandez-Molina, G., Kocher, A., Kostov, B., Kruize, A. A., Mandl, T., Ng, W. F., Retamozo, S., Seror, R., Shoenfeld, Y., Sisó-Almirall, A., Tzioufas, A. G., Vitali, C., … EULAR-Sjögren Syndrome Task Force Group. (2020). EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies. *Annals of the Rheumatic Diseases, 79*(1), 3–18. https://doi.org/10.1136/annrheumdis-2019-216114

27. Fisher, B. A., Mariette, X., Papas, A., Grader-Beck, T., Bootsma, H., Ng, W. F., van Daele, P. L. A., Finzel, S., Noaiseh, G., Elgueta, S., Hermann, J., McCoy, S. S., Akpek, E., Bookman, A., Sopala, M., Montecchi-Palmer, M., Luo, W. L., Scheurer, C., Hueber, W., & TWINSS Study Group. (2024). Safety and efficacy of subcutaneous iscalimab (CFZ533) in two distinct populations of patients with Sjögren's disease (TWINSS): Week 24 results of a randomised, double-blind, placebo-controlled, phase 2b dose-ranging study. *Lancet, 404*(10452), 540–553. https://doi.org/10.1016/S0140-6736(24)01211-X
28. Espié, P., He, Y., Koo, P., Sickert, D., Dupuy, C., Chokoté, E., Schuler, R., Mergentaler, H., Ristov, J., Milojevic, J., Verles, A., Groenewegen, A., Auger, A., Avrameas, A., Rotte, M., Colin, L., Tomek, C. S., Hernandez-Illas, M., Rush, J. S., & Gergely, P. (2020). First-in-human clinical trial to assess pharmacokinetics, pharmacodynamics, safety, and tolerability of iscalimab, an anti-CD40 monoclonal antibody. *American Journal of Transplantation, 20*(2), 463–473. https://doi.org/10.1111/ajt.15661
29. He, J., Chen, J., Miao, M., Zhang, R., Cheng, G., Wang, Y., Feng, R., Huang, B., Luan, H., Jia, Y., Jin, Y., Zhang, X., Shao, M., Wang, Y., Zhang, X., Li, J., Zhao, X., Wang, H., Liu, T., Xiao, X., … Li, Z. (2022). Efficacy and safety of low-dose interleukin 2 for primary Sjögren syndrome: A randomized clinical trial. *JAMA Network Open, 5*(11), e2241451. https://doi.org/10.1001/jamanetworkopen.2022.41451
30. Retamozo, S., Acar-Denizli, N., Rasmussen, A., Horváth, I. F., Baldini, C., Priori, R., Sandhya, P., Hernandez-Molina, G., Armagan, B., Praprotnik, S., Kvarnstrom, M., Gerli, R., Sebastian, A., Solans, R., Rischmueller, M., Pasoto, S. G., Valim, V., Nordmark, G., Kruize, A., Nakamura, H., … Sjögren Big Data Consortium. (2019). Systemic manifestations of primary Sjögren's syndrome out of the ESSDAI classification: Prevalence and clinical relevance in a large international, multi-ethnic cohort of patients. *Clinical and Experimental Rheumatology, 37*(Suppl. 118, 3), 97–106.
31. Kaegi, C., Wuest, B., Schreiner, J., Steiner, U. C., Vultaggio, A., Matucci, A., Crowley, C., & Boyman, O. (2019). Systematic review of safety and efficacy of rituximab in treating immune-mediated disorders. *Frontiers in Immunology, 10*, 1990. https://doi.org/10.3389/fimmu.2019.01990
32. Tieu, J., Smith, R. M., Gopaluni, S., Kumararatne, D. S., McClure, M., Manson, A., Houghton, S., & Jayne, D. R. W. (2021). Rituximab associated hypogammaglobulinemia in autoimmune disease. *Frontiers in Immunology, 12*, 671503. https://doi.org/10.3389/fimmu.2021.671503
33. Zeng, L., Yang, K., Wu, Y., Yu, G., Yan, Y., Hao, M., Song, T., Li, Y., Chen, J., & Sun, L. (2024). Telitacicept: A novel horizon in targeting autoimmunity and rheumatic diseases. *Journal of Autoimmunity, 148*, 103291. https://doi.org/10.1016/j.jaut.2024.103291
34. Shi, F., Xue, R., Zhou, X., Shen, P., Wang, S., & Yang, Y. (2021). Telitacicept as a BLyS/APRIL dual inhibitor for autoimmune disease. *Immunopharmacology and Immunotoxicology, 43*(6), 666–673. https://doi.org/10.1080/08923973.2021.1973493
35. Lim, Z. F. S., Hoi, A. Y., Vincent, F. B., Ooi, J. D., Morand, E. F., Rischmueller, M., & Ting, Y. T. (2025). Regulatory T cell therapy for Sjögren's disease: From pathogenesis to targeted treatment. *Journal of Translational Autoimmunity, 11*, 100311. https://doi.org/10.1016/j.jtauto.2025.100311
36. Xu, D., Fang, J., Zhang, S., Huang, C., Huang, C., Qin, L., Li, X., Chen, M., Liu, X., Liu, Y., Li, Z., Hu, J., Bao, C., Wei, W., Tian, J., Duan, X., & Zeng, X. (2024). Efficacy and safety of telitacicept in primary Sjögren's syndrome: A randomized, double-blind, placebo-controlled, phase 2 trial. *Rheumatology, 63*(3), 698–705. https://doi.org/10.1093/rheumatology/kead265
37. Chen, X., Sun, M., Wang, L., Yang, Y., & Dai, H. (2025). Response to telitacicept in optic neuritis associated with Sjogren's syndrome: A case report and literature review. *Journal of Neurology, 272*(7), 462. https://doi.org/10.1007/s00415-025-13099-9
38. Wu, J., Song, Y., Wang, W., Yuan, X., & Du, R. (2025). Case series: Effectiveness and safety of telitacicept in Chinese patients with primary Sjögren's disease. *International Journal of Rheumatic Diseases, 28*, Article e70174. https://doi.org/10.1111/1756-185X.70174
39. Jiang, W., Zhang, L., Zhao, Y., He, X., Hu, C., & Liu, Y. (2020). The efficacy and mechanism for action of iguratimod in primary Sjögren's syndrome patients. *International Ophthalmology, 40*(11), 3059–3065. https://doi.org/10.1007/s10792-020-01490-6
40. Shao, Q., Wang, S., Jiang, H., & Liu, L. (2021). Efficacy and safety of iguratimod on patients with primary Sjögren's syndrome: A randomized, placebo-controlled clinical trial. *Scandinavian Journal of Rheumatology, 50*(2), 143–152. https://doi.org/10.1080/03009742.2020.1809701
41. St Clair, E. W., Baer, A. N., Ng, W. F., Noaiseh, G., Baldini, C., Tarrant, T. K., Papas, A., Devauchelle-Pensec, V., Wang, L., Xu, W., Pham, T. H., Sikora, K., Rees, W. A., & Alevizos, I. (2024). CD40 ligand antagonist dazodalibep in Sjögren's disease: A randomized, double-blinded, placebo-controlled, phase 2 trial. *Nature Medicine, 30*(6), 1583–1592. https://doi.org/10.1038/s41591-024-03009-3
42. Blagov, A. V., Kashtalap, V. V., Lapshina, K. O., Karimova, A. E., Asoyan, A. Z., & Orekhov, A. (2025). New strategies for treating Sjogren's syndrome. *Cellular and Molecular Biology, 71*(4), 111–119. https://doi.org/10.14715/cmb/2025.71.4.14

43. Price, E., Bombardieri, M., Kivitz, A., Matzkies, F., Gurtovaya, O., Pechonkina, A., Jiang, W., Downie, B., Mathur, A., Mozaffarian, A., Mozaffarian, N., & Gottenberg, J. E. (2022). Safety and efficacy of filgotinib, lanraplenib and tirabrutinib in Sjögren's syndrome: A randomized, phase 2, double-blind, placebo-controlled study. *Rheumatology, 61*(12), 4797–4808. https://doi.org/10.1093/rheumatology/keac167
44. Bai, W., Liu, H., Dou, L., Yang, Y., Leng, X., Li, M., Zhang, W., Zhao, Y., & Zeng, X. (2022). Pilot study of baricitinib for active Sjogren's syndrome. *Annals of the Rheumatic Diseases, 81*(7), 1050–1052. https://doi.org/10.1136/annrheumdis-2021-222053
45. Dhillon, S. (2020). Tirabrutinib: First approval. *Drugs, 80*(8), 835–840. https://doi.org/10.1007/s40265-020-01318-8
46. Dörner, T., Kaul, M., Szántó, A., Tseng, J. C., Papas, A. S., Pylvaenaeinen, I., Hanser, M., Abdallah, N., Grioni, A., Santos Da Costa, A., Ferrero, E., Gergely, P., Hillenbrand, R., Avrameas, A., Cenni, B., & Siegel, R. M. (2024). Efficacy and safety of remibrutinib, a selective potent oral BTK inhibitor, in Sjögren's syndrome: Results from a randomised, double-blind, placebo-controlled phase 2 trial. *Annals of the Rheumatic Diseases, 83*(3), 360–371. https://doi.org/10.1136/ard-2023-224691
47. Noaiseh, G., Sivils, K. L., Campbell, K., Idokogi, J., Lo, K. H., Liva, S. G., Leu, J. H., Dhatt, H., Ma, K., Leonardo, S., Li, H., Hubbard, J. J., Gottenberg, J. E., & DAHLIAS Study Investigators. (2026). Nipocalimab for the treatment of moderate-to-severe Sjögren's disease: A plain language summary of the DAHLIAS study. *Expert Review of Clinical Immunology, 22*(1), 5–18. https://doi.org/10.1080/1744666X.2026.2623948
48. Endo, Y., Hosogaya, N., Fukushige, Y., Narita, S., Jacobs, J., Reiss, W., Imai, Y., Shimizu, T., Koga, T., Yamamoto, H., Sakai, T., Takagi, Y., Sumi, M., & Kawakami, A. (2026). Efficacy and safety of efgartigimod PH20 SC for Sjögren's disease-associated dryness: Study protocol for an investigator-initiated, multicenter, phase 2, randomized, double-blind, placebo-controlled trial (OASIS study). *Frontiers in Medicine, 12*, 1719757. https://doi.org/10.3389/fmed.2025.1719757
49. Posada, J., Valadkhan, S., Burge, D., Davies, K., Tarn, J., Casement, J., Jobling, K., Gallagher, P., Wilson, D., Barone, F., Fisher, B. A., & Ng, W. F. (2021). Improvement of severe fatigue following nuclease therapy in patients with primary Sjögren's syndrome: A randomized clinical trial. *Arthritis & Rheumatology, 73*(1), 143–150. https://doi.org/10.1002/art.41489
50. Hong, Y., Chen, S., Jiang, X., Zhang, J., Liang, X., Yao, J., Gao, S., & Hua, C. (2025). Exosomes as immunomodulators in autoimmune inflammation: Implications for primary Sjögren's disease. *Inflammation Research, 74*(1), 91. https://doi.org/10.1007/s00011-025-02053-0
51. Miglianico, L., Cornec, D., Devauchelle-Pensec, V., Berrouiguet, S., Walter, M., Nabbé, P., Bettacchioli, E., & Stéphan, F. (2022). Identifying clinical, biological, and quality of life variables associated with depression, anxiety, and fatigue in pSS and sicca syndrome patients: A prospective single-centre cohort study. *Joint Bone Spine, 89*(6), 105413. https://doi.org/10.1016/j.jbspin.2022.105413