



## The Role Of Biologic Therapies In Improving Joint Health In Autoimmune Arthritis

**Shayim Saud Alanazi<sup>1\*</sup>, Ibrahim Hassan Almalki<sup>2</sup>, Abdulaziz Amin Alandijani<sup>3</sup>, Hassan Mohammed Thubab<sup>4</sup>, Haifa Saud Alkheledan<sup>5</sup>, Shahad Ali Alsufyani<sup>6</sup>, Salma Awadh Alharthi<sup>7</sup>, Abdullah Mansoor Al nass<sup>8</sup>, Ibrahim Ali AlSultan<sup>8</sup>, Ali Mohammed Alshahrani<sup>9</sup>, Abdullah Fuad Aborukbah<sup>10</sup>**

<sup>1\*</sup>Department of Orthopaedic, King Khalid Hospital, Tabuk, Saudi Arabia

<sup>2</sup> Ain Shams Primary Healthcare Center, Mecca Health Cluster, Mecca, Saudi Arabia

<sup>3</sup> Department of Pediatric Emergency, Al Aziziya Children Hospital, Jeddah, Saudi Arabia

<sup>4</sup> Occupational Health Department, King Fahad Central Hospital, Jazan, Saudi Arabia

<sup>5</sup> Public Health, Riyadh First Health Cluster, Riyadh, Saudi Arabia

<sup>6</sup> Wast Almadinah Primary Healthcare Center, Ministry of Health, Taif, Saudi Arabia

<sup>7</sup> Department of Internal Medicine, King Abdulaziz Specialist Hospital, Taif, Saudi Arabia

<sup>8</sup> Department of Family Medicine, Qatif Health Network, Qatif, Saudi Arabia

<sup>9</sup> Department of Nephrology, King Abdulaziz Hospital, Jeddah, Saudi Arabia

<sup>10</sup> Department of Orthopedics, Al Thager Hospital, Jeddah, Saudi Arabia

**\*Corresponding Author:** Shayim Saud Alanazi

<sup>\*</sup>Department of Orthopaedic, King Khalid Hospital, Tabuk, Saudi Arabia. Email: Shayim@msn.com

### Abstract

The field of autoimmune arthritis treatment has seen changes due to the introduction of therapies transforming how conditions like rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) are managed. For RA, starting treatments like tumor necrosis factor alpha (TNF  $\alpha$ ) inhibitors, interleukin 6 (IL 6) receptor antagonists, and Janus kinase (JAK) inhibitors are crucial for achieving remission and preventing joint damage. JAK inhibitors like tofacitinib offer options with administration. Managing Psoriatic arthritis involves using TNF  $\alpha$  inhibitors as therapies, while IL-17A inhibitors address joint and skin issues comprehensively. Tailoring treatment plans based on characteristics leads to better results in this complex condition. Ankylosing spondylitis poses challenges where TNF  $\alpha$  inhibitors and IL 17A inhibitors vital in reducing disease activity and enhancing spinal mobility. Incorporating physical therapy highlights the approach needed for outcomes in ankylosing spondylitis. The conversation explores the intricacies of using therapies, highlighting how clinical management continues to evolve. Regular monitoring, involving patients in decision-making, and having an understanding of backgrounds are key elements for navigating the ups and downs linked with biological treatments. To sum up, the analysis highlights how biological treatments have significantly changed the way autoimmune arthritis is handled. Tailored approaches that take into account the nature of the disease and individual patient choices play a role in enhancing joint health and overall quality of life.

**Keyword:** *Ankylosing Spondylitis, Biologic Therapies, Rheumatoid Arthritis, Psoriatic Arthritis, Joint Health*

### Introduction

Biological treatments have become a game changer in managing autoimmune arthritis, bringing about an era that significantly influences health. Autoimmune conditions such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis are categorized as types of autoimmune arthritis (1, 2). In these conditions, the immune system incorrectly attacks joints, causing inflammation, pain, and lasting harm. Throughout history, disease-modifying antirheumatic drugs (DMARDs) have often been utilized as a treatment approach. The introduction of biologics has offered a more focused and efficient alternative. The key feature of therapies is their ability to target elements of the immune system involved in causing autoimmune arthritis (3, 4). Tumor necrosis factor alpha (TNF  $\alpha$ ) inhibitors, like infliximab etanercept and adalimumab, have shown success in managing arthritis (RA) and psoriatic arthritis (PSA), setting them apart in this area of treatment (5, 6). These medications work by blocking TNF  $\alpha$ , a cytokine in the inflammatory process, which helps reduce joint inflammation and stop disease advancement (7). Studies up the effectiveness of etanercept by demonstrating reduced progression and improved physical function and quality of life for RA patients. Similarly, adalimumab has proven beneficial for both RA and PsA by alleviating symptoms, limiting progression, and enhancing patient-reported outcomes (8). Moving beyond TNF  $\alpha$  blockers, drugs like tocilizumab that target the interleukin 6 (IL-6) receptor have become players in treating autoimmune arthritis. IL-6, a cytokine linked to RA development, is responsible for promoting inflammation and damage in the joints (9, 10). By inhibiting the IL 6 receptor, tocilizumab interrupts this process. Leads to better outcomes for joint health. Research has indicated that tocilizumab has proven to be effective in managing arthritis (RA) either on its own or when combined with treatments. It

has been successful in lowering disease activity and delaying the advancement of RA (11, 12). This success extends to arthritis (PsA), showing how blocking IL 6 can have an impact on various autoimmune arthritis conditions. The use of Janus kinase (JAK) inhibitors introduces a promising approach by targeting signaling pathways. Tofacitinib, a JAK inhibitor, has shown effectiveness in managing arthritis by inhibiting the signaling of cytokines associated with inflammation. Studies have shown that tofacitinib as a standalone treatment outperforms DMARDs in achieving remission and stopping disease progression, as seen in research findings (13, 14). Additionally, upadacitinib, another JAK inhibitor, has also shown effectiveness in treating RA, adding evidence to support the benefits of targeted signaling inhibition for joint health. In the field of arthritis, different biologics that target pathways have displayed potential efficacy. Medications such as secukinumab and ixekizumab, which work to block interleukin 17A, have demonstrated their effectiveness in reducing the impact of IL-17A (15) (16). Studies confirm that secukinumab is effective in improving joint and skin symptoms in PsA patients, highlighting the importance of IL 17A blockade. Similarly, ixekizumab has demonstrated efficacy in treating PsA, with research indicating improvements in issues and skin problems. Ankylosing spondylitis, a condition marked by inflammation in the spine and joints, has seen progress thanks to the development of biologics targeting tumor necrosis factor and interleukin 17A. Certolizumab pegol, a TNF inhibitor, has proven effective in treating AS by decreasing disease activity and enhancing flexibility. Furthermore, secukinumab has displayed potential in managing AS symptoms and preventing advancement. Biologic treatments have greatly improved health for those with autoimmune arthritis. There are ongoing worries about their safety and long-term effects. These treatments, which impact the system, can raise the risk of infections, some of which can be severe. Therefore, finding the balance between the benefits and risks involves evaluating individual patient characteristics and other health conditions. In essence, biological therapies have transformed how autoimmune arthritis is treated by offering solutions that tackle the root cause of immune-related issues. With options like TNF inhibitors, IL 6 receptor antagonists, and JAK inhibitors, these treatments have notably boosted health for conditions such as arthritis, psoriatic arthritis, and ankylosing spondylitis. The wealth of research supporting their effectiveness highlights the validity of incorporating therapies into the arsenal against autoimmune arthritis. It's crucial to consider safety issues and long-term effects to strike a balance between benefits and risks in enhancing health for patients with autoimmune arthritis. This review aims to provide an overview of The role of biologic therapies in improving joint health in autoimmune arthritis.

### Method

The role of biological therapies in improving joint health in autoimmune arthritis was investigated. English studies from PubMed and Scopus since 2008 were reviewed, along with references from these papers, to ensure comprehensive coverage. Keywords including biologic therapies, autoimmune arthritis, joint health, inflammation, treatment outcomes, and disease-modifying antirheumatic drugs directed the search process.

### Discussion

There are types of autoimmune arthritis, such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS), each having its own set of challenges that require personalized approaches. Biologic treatments like tumor necrosis factor alpha (TNF  $\alpha$ ) inhibitors, interleukin-6 (IL-6) receptor antagonists, and Janus kinase (JAK) inhibitors have shown effectiveness in managing symptoms, reducing inflammation, and protecting joints from damage. In the treatment of arthritis, starting medications early, typically TNF  $\alpha$  inhibitors or IL 6 receptor blockers, is essential for reaching a state of clinical remission and stopping the progression of the disease (17). The use of JAK inhibitors like tofacitinib adds another option, offering alternatives that cater to patients with preferences or those who cannot take other biologics. The management of arthritis revolves around using treatments strategically to address both joint and skin symptoms (18). While TNF  $\alpha$  inhibitors are fundamental, the introduction of interleukin 17A inhibitors presents an approach to managing this complex condition. Tailoring treatment plans based on characteristics and responses to therapy is crucial for achieving optimal outcomes. For spondylitis, TNF  $\alpha$  inhibitors and IL-17A inhibitors play roles in reducing disease activity and enhancing spinal flexibility. The challenge lies in customizing treatments according to each patient's characteristics, taking into account factors such as health conditions and concurrent medications. The changing landscape of management highlights the importance of regular monitoring involving patients in decision-making processes and understanding each individual's specific health profile thoroughly. While biological therapies offer benefits in treatment efficacy, challenges, such as infection risks and financial considerations, need to be managed for a comprehensive patient-centered approach.

### Clinical Manifestation

Biological treatments play a role in enhancing health for individuals with autoimmune arthritis by targeting specific pathways involved in the development of these conditions. Diseases like rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis, and other autoimmune joint conditions are recognized for triggering inflammation that leads to damage and limitations in movement (19, 20). Symptoms of autoimmune arthritis encompass pain, stiffness, swelling, and decreased mobility, all impacting the lives of patients. Biological medications, like tumor necrosis factor-alpha (TNF  $\alpha$ ) inhibitors, interleukin (IL) 6 inhibitors, and B cell-depleting agents, have transformed the management of autoimmune arthritis by managing disease activity and preventing harm. In cases of RA, biologic therapies have demonstrated results in achieving either remission or low disease activity levels, thereby helping to prevent structural damage to joints and disability. Adalimumab, etanercept, and infliximab, known as TNF  $\alpha$  inhibitors, have shown improvements in symptoms

and physical function for arthritis patients who do not benefit from disease-modifying drugs (DMARDs). IL 6 inhibitors like tocilizumab and sarilumab have also proven to be highly effective in RA treatment by suppressing cytokines and halting deterioration. In the way within spondylitis (AS), biological treatments have become crucial for managing the condition, especially for individuals not responding well to traditional treatments. Medications like etanercept, adalimumab, and infliximab have proven to be successful in decreasing disease activity, enhancing flexibility, and boosting the quality of life for AS patients. In addition, medications like secukinumab and ixekizumab, known as inhibitors, have proven effective in managing the progression of diseases and symptoms related to ankylosing spondylitis (AS) by targeting the IL 17 pathway, which is crucial for inflammation and bone erosion. In arthritis (PsA), biological treatments have transformed the way the disease is managed by addressing both inflammation and skin issues. Treatments like TNF  $\alpha$  inhibitors, IL 17 inhibitors, and IL 23 inhibitors have all demonstrated effectiveness in alleviating symptoms, reducing skin problems, and slowing down radiographic progression in patients with PsA. Furthermore, treatments targeting pathways, like Janus kinase (JAK) inhibitors, are proving to be options for PsA patients who do not have responses to traditional therapies. There is also increasing evidence suggesting that biological treatments may alter the course of autoimmune arthritis by leading to drug remission and preserving joint health. Recent research has shown responses and structural benefits with long-term use of biologic therapy in rheumatoid arthritis (RA) AS and PsA patients, underscoring the importance of timely and continuous treatment adjustments for optimal results. Furthermore, combining agents or pairing them with traditional disease-modifying antirheumatic drugs (DMARDs) has demonstrated synergistic effects in controlling disease activity and reducing treatment failure rates in autoimmune arthritis cases. Biological treatments play a role in treating arthritis as they focus on reducing inflammation and enhancing joint wellness. Biological drugs have revolutionized the treatment of conditions such as arthritis, ankylosing spondylitis, psoriatic arthritis, and other autoimmune joint diseases. They work by reducing inflammation, protecting joints from damage, and enhancing outcomes. Ongoing studies and progress in practices play a role in refining the application of biological treatments and enhancing the overall well-being of individuals with autoimmune forms of arthritis.

### Management

The treatment of autoimmune arthritis focusing on the impact of therapies on improving health is an ever-changing field within rheumatology. Autoimmune arthritis encompasses diseases such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) that result in problems causing inflammation, pain, and harm to structures. While traditional disease-modifying antirheumatic drugs (DMARDs) have been used to address these disorders, the introduction of therapies has brought about an era of personalized medicine that targets the underlying reasons for immune system irregularities. In arthritis specifically, the use of therapies has significantly altered how the disease is approached. Infliximab, etanercept, and adalimumab, which are known as TNF  $\alpha$  inhibitors, have shown success in decreasing disease activity and halting its advancement. Typically, treatment involves starting biologics in the disease progression, especially if conventional DMARDs are not effective enough. These medications do not help with symptoms. It also aims to achieve clinical remission and prevent permanent joint damage. Aside from TNF  $\alpha$  inhibitors, another treatment option involves using interleukin 6 (IL 6) receptor antagonists, such as tocilizumab. The use of the IL 6 pathway has shown success in treating arthritis in individuals with severe disease symptoms or those who cannot tolerate other biological treatments. Deciding between TNF inhibitors and IL 6 receptor blockers is typically influenced by factors like existing health conditions, patient preferences, and how well the treatment is working (21, 22). Tofacitinib and upadacitinib, which are part of the Janus kinase (JAK) inhibitors category, are considered biologics designed to impact signaling pathways. These medications are taken orally, offering an option for patients who prefer not to receive injections. Tofacitinib especially has shown effectiveness both when used alone and in combination with treatments highlighting its versatility in managing arthritis. In the treatment of arthritis, the approach often involves using therapies strategically. TNF  $\alpha$  inhibitors such as adalimumab and etanercept are frequently used as treatments due to their proven ability to control joint symptoms, reduce inflammation, and enhance overall function. If these medications do not produce results. Are not well tolerated other biologics that target different pathways may be considered. Interleukin 17A inhibitors like secukinumab and ixekizumab have shown promise in managing arthritis by not only relieving joint symptoms but also addressing related skin issues, offering a comprehensive approach to this complex condition. Biologic therapy selection is usually customized for patients depending on factors like the seriousness of skin issues or the level of impairment. Managing spondylitis can be tricky due to its inflammation in the spine and sacroiliac joints. In studies, TNF  $\alpha$  inhibitors, like adalimumab and certolizumab pegol, have shown effectiveness in decreasing disease activity. Enhancing flexibility. The treatment plan also emphasizes the importance of therapy and regular exercise to preserve mobility and avoid structural abnormalities. Secukinumab, a blocker of interleukin 17A, has displayed promising outcomes in treating spondylitis, providing an alternative for individuals who do not respond well to or cannot tolerate TNF  $\alpha$  inhibitors. When deciding between these biologics, factors like health conditions, response to treatment, and patient preferences often come into play. In the management of autoimmune arthritis, the careful usage of treatments entails continuously evaluating disease activity, treatment response, and potential side effects. Regular monitoring through assessments and imaging studies helps adjust treatments for optimal results. Collaborative decision-making involving rheumatologists and patients is crucial in customizing treatment plans based on requirements and taking lifestyle, preferences, and concurrent medical issues into consideration. Although biological therapies have transformed the way autoimmune arthritis is managed, it's essential to recognize obstacles. These challenges include the heightened risk of infections in patients with health conditions and the financial aspects linked to these treatments. Integrating biological therapies into management strategies requires an understanding of a patient's clinical background and staying informed about the changing landscape of therapeutic choices. To summarize, managing

autoimmune arthritis clinically with a focus on therapies signifies a shift toward medicine. From medications that target TNF  $\alpha$  to drugs that block the IL 6 receptor and JAK inhibitors, these specialized treatments provide methods for managing inflammation, easing symptoms, and maintaining functionality. The changing field of therapies plays a role in how healthcare professionals address autoimmune arthritis, highlighting the importance of tailored and thorough treatment plans to enhance patient results.

### Conclusion

The treatment of autoimmune arthritis has significantly changed due to the introduction of therapies. The strong evidence supporting the effectiveness of TNF  $\alpha$  inhibitors, IL 6 receptor antagonists, and JAK inhibitors in conditions underscores their role in improving joint health and overall patient well-being. As we navigate through this changing landscape, personalized and comprehensive treatment strategies are becoming increasingly important. Starting therapies early based on disease activity and response to treatment is vital in preventing joint damage, particularly in cases of rheumatoid arthritis. The range of treatment options, including JAK inhibitors and IL 17A inhibitors, provides tailored solutions for different types of patients. Managing arthritis poses challenges that require attention to both joint and skin symptoms. The effectiveness of interleukin 17A inhibitors in addressing these issues showcases the growing precision in treatment methods. In spondylitis, deciding between TNF  $\alpha$  inhibitors and IL-17A inhibitors necessitates consideration of individual patient characteristics. Incorporating therapy and exercise into the treatment plan emphasizes the approach needed for optimal results. While biological therapies have transformed the management of autoimmune arthritis, challenges like infection risks and financial concerns, require vigilance and collaboration in decision-making. In the coming years, we can expect advancements in treatment approaches that are personalized to meet needs, focusing on improving not only symptoms but also the overall well-being of patients.

### Reference

1. Raychaudhuri SP, Raychaudhuri SK. Biologics: target-specific treatment of systemic and cutaneous autoimmune diseases. *Indian J Dermatol.* 2009;54(2):100-9.
2. Takeuchi T. Treatment of rheumatoid arthritis with biological agents - as a typical and common immune-mediated inflammatory disease. *Proc Jpn Acad Ser B Phys Biol Sci.* 2017;93(8):600-8.
3. Jung SM, Kim WU. Targeted Immunotherapy for Autoimmune Disease. *Immune Netw.* 2022;22(1):e9.
4. Jang S, Kwon EJ, Lee JJ. Rheumatoid Arthritis: Pathogenic Roles of Diverse Immune Cells. *Int J Mol Sci.* 2022;23(2).
5. G C, M C, CA S, M B. - Tumor necrosis factor (TNF) inhibitors for the treatment of psoriatic arthritis. *Cochrane Database Syst Rev.* 2020;14(5).
6. Taylor PC, Matucci Cerinic M, Alten R, Avouac J, Westhovens R. Managing inadequate response to initial anti-TNF therapy in rheumatoid arthritis: optimising treatment outcomes. *Ther Adv Musculoskelet Dis.* 2022;14:1759720x221114101.
7. Jang D-i, Lee A-H, Shin H-Y, Song H-R, Park J-H, Kang T-B, et al. The Role of Tumor Necrosis Factor Alpha (TNF- $\alpha$ ) in Autoimmune Disease and Current TNF- $\alpha$  Inhibitors in Therapeutics. *International Journal of Molecular Sciences.* 2021;22(5):2719.
8. Wassenberg S, Rau R, Klopsch T, Plenske A, Jobst J, Klaus P, et al. Etanercept is Effective and Halts Radiographic Progression in Rheumatoid Arthritis and Psoriatic Arthritis: Final Results from a German Non-interventional Study (PRERA). *Rheumatol Ther.* 2023;10(1):117-33.
9. Hashizume M, Mihara M. The roles of interleukin-6 in the pathogenesis of rheumatoid arthritis. *Arthritis.* 2011;2011:765624.
10. Favalli EG. Understanding the Role of Interleukin-6 (IL-6) in the Joint and Beyond: A Comprehensive Review of IL-6 Inhibition for the Management of Rheumatoid Arthritis. *Rheumatol Ther.* 2020;7(3):473-516.
11. Ogata A, Tanaka T. Tocilizumab for the treatment of rheumatoid arthritis and other systemic autoimmune diseases: current perspectives and future directions. *Int J Rheumatol.* 2012;2012:946048.
12. Shetty A, Hanson R, Korsten P, Shawagfeh M, Arami S, Volkov S, et al. Tocilizumab in the treatment of rheumatoid arthritis and beyond. *Drug Des Devel Ther.* 2014;8:349-64.
13. Schwartz DM, Kanno Y, Villarino A, Ward M, Gadina M, O'Shea JJ. JAK inhibition as a therapeutic strategy for immune and inflammatory diseases. *Nat Rev Drug Discov.* 2017;17(1):78.
14. Mueller RB, Hasler C, Popp F, Mattow F, Durmisi M, Souza A, et al. Effectiveness, Tolerability, and Safety of Tofacitinib in Rheumatoid Arthritis: A Retrospective Analysis of Real-World Data from the St. Gallen and Aarau Cohorts. *J Clin Med.* 2019;8(10).
15. Lønnberg AS, Zachariae C, Skov L. Targeting of interleukin-17 in the treatment of psoriasis. *Clin Cosmet Investig Dermatol.* 2014;7:251-9.
16. Țiburcă L, Bembea M, Zaha DC, Jurca AD, Vesa CM, Rațiu IA, Jurca CM. The Treatment with Interleukin 17 Inhibitors and Immune-Mediated Inflammatory Diseases. *Curr Issues Mol Biol.* 2022;44(5):1851-66.
17. Wei ST, Sun YH, Zong SH, Xiang YB. Serum Levels of IL-6 and TNF- $\alpha$  May Correlate with Activity and Severity of Rheumatoid Arthritis. *Med Sci Monit.* 2015;21:4030-8.
18. Kamata M, Tada Y. Optimal Use of Jak Inhibitors and Biologics for Atopic Dermatitis on the Basis of the Current Evidence. *JID Innov.* 2023;3(3):100195.

19. Xiong Y, Cai M, Xu Y, Dong P, Chen H, He W, Zhang J. Joint together: The etiology and pathogenesis of ankylosing spondylitis. *Front Immunol.* 2022;13:996103.
20. Zhu W, He X, Cheng K, Zhang L, Chen D, Wang X, et al. Ankylosing spondylitis: etiology, pathogenesis, and treatments. *Bone Research.* 2019;7(1):22.
21. Pandolfi F, Franza L, Carusi V, Altamura S, Andriollo G, Nucera E. Interleukin-6 in Rheumatoid Arthritis. *Int J Mol Sci.* 2020;21(15).
22. Rose-John S, Jenkins BJ, Garbers C, Moll JM, Scheller J. Targeting IL-6 trans-signalling: past, present and future prospects. *Nature Reviews Immunology.* 2023;23(10):666-81.