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,
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ARTICLE TITLE	EFFECTS OF BIOLOGIC THERAPIES ON SYMPTOMS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NARRATIVE REVIEW
DOI	https://doi.org/10.31435/ijitss.3(51).2026.5898
RECEIVED	26 May 2026
ACCEPTED	11 August 2026
PUBLISHED	24 August 2026
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EFFECTS OF BIOLOGIC THERAPIES ON SYMPTOMS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NARRATIVE REVIEW

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ABSTRACT

Introduction: Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease causing progressive joint destruction, pain, disability, and reduced quality of life. Many patients respond inadequately to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), necessitating more effective treatment strategies.
Background: Biologic disease-modifying antirheumatic drugs (bDMARDs) and targeted synthetic therapies have transformed RA management by targeting inflammatory pathways such as tumor necrosis factor (TNF), interleukin-6 (IL-6), and Janus kinase (JAK) signaling.
Methods: A narrative-systematic review of randomized clinical trials and observational studies was conducted to evaluate the efficacy and safety of biologic therapies in RA patients with inadequate response to csDMARDs. Outcomes included ACR20/50/70 response rates, Disease Activity Score in 28 joints (DAS28), remission rates, functional outcomes, and adverse events.
Results: Biologic therapies significantly reduced disease activity and improved patient outcomes. TNF inhibitors combined with methotrexate achieved the most consistent efficacy, with ACR20, ACR50, and ACR70 responses reaching 78%, 57%, and 31%, respectively. Remission rates approached 40–50% in several studies. IL-6 inhibitors and JAK inhibitors provided rapid pain relief and functional improvement. Overall, remission or low disease activity was achieved in 30–60% of patients. Although biologic therapies increased the risk of adverse events, particularly infections, their safety profile remained acceptable with proper monitoring.
Discussion: The findings demonstrate that biologic and targeted therapies represent a major advancement in RA treatment, particularly in patients resistant to conventional therapies. Differences in efficacy and safety profiles support individualized treatment selection, while methotrexate combination therapy may further enhance clinical response.
Conclusion: Biologic therapies substantially improve disease control, physical function, and quality of life in RA patients. TNF inhibitors, IL-6 inhibitors, and JAK inhibitors remain central to modern RA management, although continued long-term safety monitoring and personalized therapeutic strategies are essential.

KEYWORDS

Rheumatoid Arthritis, Biologic Therapy, TNF Inhibitors, Interleukin-6 Inhibitors, Treatment Efficacy, Disease Activity (DAS28)

CITATION

Emilia Przybyszewska, Piotr Przybyszewski, Agnieszka Filarecka, Weronika Winiarska, Wiktoria Bełcikowska-Skowron, Aleksandra Siegmund, Marzena Chrapczyńska, Julia Gatniejewska, Martyna Sienicka, Paulina Prudzic. (2026) Effects of Biologic Therapies on Symptoms in Patients with Rheumatoid Arthritis: a Narrative Review. *International Journal of Innovative Technologies in Social Science*. 3(51). doi: 10.31435/ijitss.3(51).2026.5898

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1. Introduction

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune inflammatory disease that leads to progressive joint damage, pain, stiffness, and impairment of functional capacity. Untreated synovial inflammation results in cartilage and bone destruction, ultimately leading to permanent disability and increased mortality (Weinblatt et al., 2006). Despite significant therapeutic advances achieved with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), such as methotrexate or sulfasalazine, a substantial proportion of patients fail to achieve adequate disease control (Weinblatt et al., 2006).

In recent decades, advances in understanding RA pathogenesis—particularly the role of pro-inflammatory cytokines (e.g., TNF-α, IL-1, IL-6) and immune system cells—have enabled the development of biologic agents targeting specific molecular pathways (Weinblatt et al., 2006). Biologic disease-modifying antirheumatic drugs (bDMARDs), including TNF inhibitors (adalimumab, infliximab, etanercept), IL-6 inhibitors, and anti-CD20 monoclonal antibodies, have demonstrated high efficacy in reducing clinical symptoms, improving physical function, and inhibiting radiographic progression of joint damage (Strand et al., 2017).

Evidence from clinical trials and systematic reviews indicates that biologic therapies are significantly more effective than placebo, particularly when combined with methotrexate, leading to higher rates of clinical response (e.g., ACR20/50/70) (Strand et al., 2017). However, differences in efficacy between individual

biologic agents appear relatively small, highlighting the importance of individualized treatment strategies (Bitoun et al., 2023). Long-term studies have also demonstrated sustained therapeutic effects and the possibility of achieving disease remission in a substantial proportion of biologically treated patients (Aaltonen et al., 2012).

Despite their high efficacy, biologic therapies are associated with limitations, including the risk of adverse events (particularly infections) and variability in treatment response. The development of anti-drug antibodies has been identified as one factor potentially reducing therapeutic effectiveness (Schiff et al., 2006). Therefore, evaluating the real-world impact of these therapies on clinical outcomes and patient quality of life remains a key research priority.

2. Objective

The aim of this study is to analyze the impact of biologic therapies on the severity of clinical symptoms in patients with rheumatoid arthritis, with particular emphasis on their effectiveness in reducing disease activity, improving physical function, and enhancing quality of life. Additionally, the study seeks to assess factors influencing therapeutic response and to identify potential limitations of biologic treatment in clinical practice.

3. Background

Rheumatoid arthritis is a chronic, systemic autoimmune inflammatory disease leading to progressive joint destruction, disability, and reduced quality of life [Malinowska-Lipień et al., 2025]. It affects approximately 1% of the population, occurs more frequently in women, and is associated with significant socioeconomic burden, including loss of work capacity [Malinowska-Lipień et al., 2025 Clinically, RA is characterized by joint pain, stiffness, swelling, and systemic symptoms such as fatigue, which substantially impair daily functioning [Malinowska-Lipień et al., 2025].

Conventional synthetic DMARDs remain the cornerstone of treatment; however, a considerable proportion of patients fail to achieve adequate therapeutic response, necessitating more advanced treatment strategies [Toyoshima et al., 2021]. Biologic agents represent a major therapeutic breakthrough, as they selectively target key components of the immune response, including pro-inflammatory cytokines (e.g., TNF-α, IL-6) and immune cells [Malinowska-Lipień et al., 2025].

Clinical studies demonstrate that biologic therapy significantly reduces the number of tender and swollen joints, lowers inflammatory markers (CRP, ESR), and alleviates pain [Malinowska-Lipień et al., 2025]. Improvements in functional status and quality of life have also been consistently reported. Systematic reviews further indicate a beneficial effect on fatigue, one of the most prevalent and debilitating symptoms of RA [Almeida et al., 2016].

Despite their effectiveness, biologic therapies are not universally successful; approximately 30–40% of patients fail to achieve an adequate response [Toyoshima et al., 2021]. Consequently, further investigation into their clinical impact remains essential to optimize treatment strategies and improve patient outcomes.

4. Methods

This study is a narrative-systematic review of clinical trials evaluating the efficacy of biologic therapies in patients with rheumatoid arthritis. Only publications provided within this dataset were included, encompassing randomized controlled trials, cohort studies, and comparative analyses.

The analyzed studies involved adult patients meeting RA classification criteria, most commonly according to ACR/EULAR, with active disease despite prior csDMARD therapy [Bitoun et al., 2023, Leng et al., 2024]. Various biologic treatment regimens were evaluated, including TNF inhibitors, rituximab, and tocilizumab, administered either as monotherapy or in combination with methotrexate [Bitoun et al., 2023, Jones et al., 2010].

Primary endpoints included clinical efficacy assessed using standardized measures such as ACR response criteria (ACR20/50/70), Disease Activity Score (DAS28), and EULAR response criteria [Bitoun et al., 2023,Leng et al., 2024]. Safety parameters, immunogenicity, and serum drug concentrations were also considered [Leng et al., 2024].

Data were analyzed qualitatively by comparing outcomes across studies, with particular emphasis on the effects of biologic therapy on clinical symptoms, inflammatory activity, and therapeutic response in RA patients.

5. Results

Analysis of clinical trials, meta-analyses, and long-term studies demonstrated that biologic DMARDs (bDMARDs) and JAK inhibitors significantly reduce RA disease activity, improve physical function, and enhance quality of life. Therapeutic effects were observed as early as 12 weeks, including improvements in HAQ-DI, SF-36, and EQ-5D scores [Bergman et al., 2022].

The most robust evidence concerns TNF-α inhibitors. In combination therapy with methotrexate (e.g., adalimumab), ACR20/50/70 responses were achieved in 78%, 57%, and 31% of patients, respectively, with DAS28 remission in approximately 43%. In the PREMIER study, ACR50 response rates reached 62% versus 41–46% with monotherapy, and remission was achieved in up to 49% of patients after 2 years [26]. Comparable results were reported for certolizumab pegol (ACR20/50/70: 74.4%/57.3%/39.6% at 52 weeks; remission ~42%), with sustained responses up to 5 years (ACR20 63.1%) [Keystone et al., 2014].

IL-6 inhibitors also demonstrated high efficacy. Tocilizumab achieved ACR20 responses in 69.9% versus 52.5% with methotrexate, and DAS28 remission in 33.6% versus 12.1% (24 weeks, $p<0.001$), with rapid normalization of CRP levels. Sarilumab showed greater improvements in function and pain reduction compared to adalimumab [Weinblatt et al., 2006].

Costimulation inhibitors (abatacept) achieved ACR20 responses of 72.4% and ACR50 of 45.5%, with DAS28-CRP remission in 60.9% of patients after 12 months versus 45.2% with methotrexate ($p=0.010$) [30]. In the ATTEST trial, abatacept demonstrated superior efficacy compared to infliximab (ACR20: 72.4% vs 55.8%).

Targeted synthetic therapies also showed high efficacy. Baricitinib provided ≥50% pain reduction in 61 % of patients versus 52% with adalimumab (24 weeks), and ≥70% reduction in 41% versus 32%, respectively [Taylor et al., 2019]. Upadacitinib demonstrated significantly greater improvements in pain, HAQ-DI, and morning stiffness compared to abatacept ($p<0.05$).

Anti-CD20 therapy (rituximab) showed increasing efficacy with successive treatment cycles (ACR20: 62.0%→70.3%; ACR50: 30.8%→41.8%) and inhibition of radiographic progression [Smolen et al., 2015a].

A meta-analysis including 9,202 patients reported a rate of serious adverse events of 69.8 per 1,000 patient-years (RR=1.39 vs methotrexate), with no significant differences in serious infection rates [19]. In comparative studies, serious infections were less frequent with abatacept (1.9%) than with infliximab (8.5%).

Overall, biologic therapies—particularly when combined with methotrexate—enable remission or low disease activity in approximately 30–60% of patients, reduce DAS28 by approximately 3–3.4 points, and significantly improve clinical outcomes and quality of life.

6. Discussion

The findings confirm the high efficacy of biologic therapies and JAK inhibitors in RA treatment; however, their interpretation requires consideration of substantial heterogeneity across studies. Improvements in disease activity, physical function, and quality of life are well documented, but their magnitude varies depending on patient populations, follow-up duration, and outcome measures (ACR, DAS28, PROs) [Leng et al., 2024,Findeisen et al., 2021].

The most consistent evidence concerns TNF-α inhibitors, particularly in combination with methotrexate, where high response rates and inhibition of disease progression have been demonstrated [Strand et al., 2017, Emery et al., 2010]. Nevertheless, inter-study variability may reflect differences in inclusion criteria and prior treatment exposure. Long-term data suggest sustained efficacy, although durability is not uniform across studies [Keystone et al., 2014].

IL-6 inhibitors and JAK inhibitors appear to provide faster symptom relief, particularly regarding pain and functional outcomes; however, their superiority over TNF inhibitors is not consistently demonstrated [Weinblatt et al., 2006 Almeida et al., 2016, Taylor et al., 2019]. These differences may have limited clinical relevance and do not always translate into higher remission rates. Furthermore, long-term data for these therapies remain less extensive.

The efficacy of rituximab and abatacept has been confirmed, particularly in long-term disease control; however, the lack of direct comparative studies limits definitive conclusions regarding their relative effectiveness [Smolen et al., 2015a, Toyoshima et al., 2020]. Variability in treatment regimens further complicates cross-study comparisons.

Uncertainty also exists regarding safety profiles. Although meta-analyses suggest comparable risks of serious adverse events across therapies [Adas et al., 2021], individual studies indicate potential differences, likely due to variations in definitions and follow-up duration.

A key limitation is the heterogeneity of available data and incomplete evidence for all drug classes. Many conclusions rely on indirect comparisons, reducing their strength. Consequently, while biologic therapies are clearly effective, their relative superiority remains partially unresolved.

In summary, biologic and targeted therapies significantly improve RA outcomes; however, variability in study findings highlights the need for cautious interpretation and individualized treatment approaches.

7. Conclusions

Biologic DMARDs and JAK inhibitors demonstrate high efficacy in the treatment of rheumatoid arthritis, significantly reducing disease activity and improving patient function and quality of life [Leng et al., 2024, Jones et al., 2010, Best et al., 2015, Bergman et al., 2022, Li et al., 2011].

The strongest evidence supports TNF-α inhibitors combined with methotrexate, achieving ACR20/50/70 responses in approximately 70–80%, 50–60%, and 30–40% of patients, respectively, and DAS28 remission in 40–50% [Strand et al., 2017, Smolen et al., 2015b]. Long-term studies with certolizumab pegol confirm sustained clinical response for up to 5 years [Keystone et al., 2014, Keystone et al., 2009].

IL-6 inhibitors and JAK inhibitors may provide faster pain reduction and greater improvements in physical function and quality of life, with up to 61% of patients achieving ≥50% pain reduction and 41% achieving ≥70% reduction [Weinblatt et al., 2006 Almeida et al., 2016, Taylor et al., 2019].

Costimulation inhibitors (abatacept) and anti-CD20 therapies (rituximab) are effective in long-term disease control, with rituximab showing increasing efficacy over time and abatacept achieving remission in over 60% of selected populations [Smolen, Toyoshima et al., 2020].

Overall, biologic and targeted therapies enable remission or low disease activity in approximately 30–60% of patients, particularly with early initiation and combination therapy [Findeisen et al., 2021, Emery et al., 2010, Toyoshima et al., 2020]. Although associated with a risk of adverse events—primarily infections—the incidence of serious adverse events (~69.8/1000 patient-years) does not significantly differ between treatment strategies [Adas et al., 2021].

Despite limitations related to data heterogeneity and lack of direct comparisons, current evidence indicates that modern biologic therapies constitute the cornerstone of effective RA management, leading to substantial improvements in clinical, functional, and quality-of-life outcomes [Adas et al., 2021, Findeisen et al., 2021].

Conflicts of Interest: No conflicts of interest to declare.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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