ISSN: 2053-3578 I.F. 12.34

# DIFFERENCES BETWEEN JAK INHIBITORS AND TNF INHIBITORS IN TREATING RHEUMATOID ARTHRITIS

**Mohammed Faisal Hussain**

**Shalini Thakur**

Samarkand State Medical University

**Annotation:** Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammation and joint damage. Treatment options have evolved significantly with the development of targeted therapies such as Janus kinase (JAK) inhibitors and tumor necrosis factor (TNF) inhibitors. This article explores the differences between these two classes of drugs in terms of mechanism of action, efficacy, safety, and clinical application.

**Key words:**

## Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disorder characterized by chronic inflammation of the synovial joints, leading to progressive joint destruction, pain, swelling, and loss of function. Affecting approximately 0.5–1% of the global population, RA significantly impairs quality of life and increases the risk of comorbidities such as cardiovascular disease and osteoporosis. Early and effective treatment is critical to prevent irreversible joint damage and disability. Conventional disease-modifying antirheumatic drugs (DMARDs), such as methotrexate, have traditionally been the first line of treatment. However, not all patients respond adequately to these therapies. Advances in immunology and molecular biology have led to the development of targeted therapies that modulate specific components of the immune system. Among these, tumor necrosis factor (TNF) inhibitors and Janus kinase (JAK) inhibitors represent two important classes of drugs with distinct mechanisms of action. TNF inhibitors were among the first biologic agents approved for RA and have significantly improved disease management by specifically blocking TNF-α, a key pro-inflammatory cytokine involved in RA pathogenesis. JAK inhibitors, a newer class of targeted synthetic DMARDs, inhibit intracellular signaling pathways critical for the activity of multiple cytokines implicated in RA inflammation. Understanding the differences in mechanisms, efficacy, safety, and clinical application of JAK inhibitors and TNF inhibitors is essential for optimizing treatment strategies and improving patient outcomes.

## Literary analysis

ISSN: 2053-3578 I.F. 12.34

The scientific literature addressing the comparative effectiveness of JAK inhibitors and TNF inhibitors in rheumatoid arthritis (RA) employs a formal, precise, and evidence-based style typical of medical research. The language is characterized by specialized terminology and an emphasis on clarity and objectivity.

**1. Structure and Organization-** Research articles on this topic typically follow the conventional IMRAD format—Introduction, Methods, Results, and Discussion. This structure helps maintain logical flow and clarity, enabling readers to understand the rationale, methodology, findings, and implications clearly. The introduction often contextualizes RA as a chronic autoimmune disease and introduces both drug classes, highlighting their biological mechanisms and clinical relevance.

**2. Use of Technical Vocabulary-** The texts heavily use medical and biochemical terminology such as "cytokines," "immune modulation," "synovial inflammation," "biologic DMARDs," and "intracellular signaling pathways." This specialized vocabulary serves two purposes: it establishes authority and precision and communicates complex concepts efficiently to a knowledgeable audience, usually healthcare professionals and researchers.

**3. Tone and Objectivity-** The tone is formal and objective, avoiding personal opinions or emotive language. Authors rely on data and statistical analysis to support claims, emphasizing evidence over speculation. Words like "efficacy," "safety profile," "clinical trials," and "adverse events" are frequently used to describe outcomes in a neutral manner.

**4. Comparative and Analytical Language-** Because the topic involves comparing two treatment options, comparative structures are common. Phrases like "in contrast to," "compared with," "shows greater efficacy," and "has a different safety profile" are used to systematically contrast the benefits and limitations of each drug class. The writing often includes qualifiers such as "may," "suggests," and "potential" to indicate that conclusions are based on evolving evidence rather than absolute certainties.

**5. Emphasis on Evidence and Data-** The literature integrates data from randomized controlled trials, meta-analyses, and real-world studies, using numerical data and statistical significance to substantiate claims. This approach reinforces the credibility of findings and aligns with the scientific community's standards for reliability.

**6. Audience and Purpose-** The primary audience for this discourse includes rheumatologists, clinical researchers, pharmacologists, and healthcare policymakers. The purpose is to inform clinical decisions, guide research priorities, and enhance understanding of therapeutic mechanisms.

ISSN: 2053-3578 I.F. 12.34

**RESULT AND DISCUSSION**

Several clinical trials and meta-analyses have compared the effectiveness and safety of JAK inhibitors and TNF inhibitors in patients with rheumatoid arthritis (RA).

- **Efficacy:** Both JAK inhibitors (e.g., tofacitinib, baricitinib) and TNF inhibitors (e.g., etanercept, adalimumab) significantly reduced disease activity scores (DAS28) and improved physical function compared to placebo. Some studies reported that JAK inhibitors showed a faster onset of action, with noticeable improvement within the first few weeks of treatment.
- **Safety:** The safety profiles of both drug classes differ. TNF inhibitors are associated with a higher risk of infections such as tuberculosis and opportunistic infections, especially in endemic areas. JAK inhibitors carry risks related to blood clots, elevated cholesterol levels, and herpes zoster reactivation.
- **Patient Response:** Some patients who did not respond to TNF inhibitors showed clinical improvement when switched to JAK inhibitors, suggesting different mechanisms of action can benefit patients with refractory RA.
- **Comparative Studies:** Head-to-head trials such as the ORAL Strategy trial showed non-inferiority of JAK inhibitors compared to TNF inhibitors in achieving clinical remission at 6 months. Long-term data is still being collected to confirm sustained efficacy and safety.

The comparison between JAK inhibitors and TNF inhibitors reveals important differences that can guide personalized treatment choices for rheumatoid arthritis patients. JAK inhibitors offer the advantage of oral administration and a faster therapeutic response, which may improve patient adherence and quality of life. Their ability to target intracellular signaling pathways broadly impacts multiple cytokines involved in RA pathogenesis, which might explain their efficacy in patients unresponsive to TNF inhibitors. However, the safety concerns, particularly the increased risk of thromboembolic events and viral infections, require careful patient screening and monitoring. TNF inhibitors, with a longer history of use, have well-established efficacy and safety profiles. Their injectable administration route can be a limitation for some patients but is generally well tolerated. The higher risk of serious infections, particularly in patients with latent tuberculosis, necessitates pre-treatment screening protocols. Ultimately, treatment decisions should consider individual patient factors, including disease severity, comorbidities, lifestyle preferences, and prior treatment responses. The evolving evidence base supports the use of both drug classes as effective options, with ongoing research required to

optimize sequencing and combination therapies. Further studies focusing on long-term safety, real-world effectiveness, and cost-effectiveness will enhance clinical guidelines and improve outcomes for RA patients.

**CONCLUSION**

In summary it should be noted that both Janus kinase (JAK) inhibitors and tumor necrosis factor (TNF) inhibitors represent significant advancements in the treatment of rheumatoid arthritis (RA), offering patients effective options to control disease progression and improve quality of life. JAK inhibitors, with their oral administration and relatively rapid onset of action, have introduced a convenient alternative to traditional biologic therapies. They work by targeting intracellular signaling pathways involved in the inflammatory process, providing a broad immunomodulatory effect. On the other hand, TNF inhibitors, which have been a cornerstone of RA therapy for many years, specifically block the pro-inflammatory cytokine TNF-α, reducing inflammation and joint damage effectively. Each class of medication carries distinct advantages and limitations. JAK inhibitors may be preferred for patients who have inadequate responses or intolerance to TNF inhibitors or other biologics, whereas TNF inhibitors benefit from extensive long-term safety data and proven efficacy. However, both therapies pose risks such as infections and other adverse effects, necessitating careful patient selection and monitoring. Ultimately, the choice between JAK inhibitors and TNF inhibitors should be individualized, considering factors like disease severity, patient comorbidities, lifestyle preferences, and previous treatment history. Ongoing clinical trials and real-world studies will continue to clarify the optimal sequencing and combination of these agents to maximize patient outcomes. As research progresses, these therapeutic options hold promise not only to alleviate symptoms but also to alter the disease course, bringing hope for improved long-term management of rheumatoid arthritis.

**REFERENCES:**

1. Smolen, J. S., Aletaha, D., & McInnes, I. B. (2016). Rheumatoid arthritis. *The Lancet*, 388(10055), 2023–2038. https://doi.org/10.1016/S0140-6736(16)30173-8
2. Taylor, P. C., Keystone, E. C., van der Heijde, D., Weinblatt, M. E., Del Carmen Morales, L., Reyes Gonzaga, J., ... & Fleischmann, R. (2017). Baricitinib versus placebo or adalimumab in rheumatoid arthritis. *New England Journal of Medicine*, 376(7), 652–662. https://doi.org/10.1056/NEJMoa1608345
3. Fleischmann, R., Schiff, M., van der Heijde, D., Elewaut, D., Breedveld, F., Furst, D. E., ... & Keystone, E. (2012). Placebo-controlled trial of tofacitinib monotherapy in

ISSN: 2053-3578 I.F. 12.34

rheumatoid arthritis. *New England Journal of Medicine*, 367(6), 495–507. https://doi.org/10.1056/NEJMoa1112525

4. Burmester, G. R., Blanco, R., Charles-Schoeman, C., Wollenhaupt, J., Zerbini, C., Benda, B., ... & Kavanaugh, A. (2018). Tofacitinib (CP-690,550) in combination with methotrexate in patients with active rheumatoid arthritis: a randomized phase 3 trial. *Arthritis & Rheumatology*, 70(4), 535–546. https://doi.org/10.1002/art.40322
5. Singh, J. A., Saag, K. G., Bridges, S. L., Akl, E. A., Bannuru, R. R., Sullivan, M. C., ... & McNaughton, C. (2016). 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis & Rheumatology*, 68(1), 1–26. https://doi.org/10.1002/art.39480