Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 31s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Therapeutic Advances In Rheumatoid Arthritis: A Comprehensive Review On The Role Of Dmards And Biologic Agents

Jacintha Abisha Angel.S[1], Surendhar Amargeeth[1], Hepsiba Selva Kuamri[2], Keerthiga[3], Shathika[4], Hensha[5], Dr. Karthickeyan Krishnan[6*]

[1*]Pharm D Intern, Department Of Pharmacy Practice, Vistas,
Email Id: *Jacinthaangel285@Gmail.Com*
[1]Pharm D Intern, Department Of Pharmacy Practice, School Of Pharmaceutical Science, Vistas,
Email Id: *Suredhar.Clinicalresearchar@Gmail.Com,* Orcid No: 0009-0004-7392-6290
[2]Pharm D, Department Of Pharmacy Practice, School Of Pharmaceutical Science, Vistas,
Email Id: *Hepsibakrishnamoorthy@Gmail.Com*
[3]Pharm D, Department Of Pharmacy Practice, School Of Pharmaceutical Science, Vistas
Email Id: *Keerthigajaisankar@Gmail.Com*
[4]Pharm D, Department Of Pharmacy Practice, School Of Pharmaceutical Science, Vistas
Email Id: *Shathikaj2001@Gmail.Com*
[5]Pharm D, Department Of Pharmacy Practice, School Of Pharmaceutical Science, Vistas
Email Id: *Hensha2003@Gmail.Com*
[6]Head Of The Department, Department Of Pharmacy Of Practice ,School Of Pharmaceutical Scienece,Vistas Chennai
***Corresponding Author-**
Dr. Karthickeyan Krishnan
Head Of The Department, Department Of Pharmacy Of Practice ,School Of Pharmaceutical Scienece,Vistas Chennai

Cite this paper as: Jacintha Abisha Angel.S, Surendhar Amargeeth, Hepsiba Selva Kuamri, Keerthiga, Shathika, Hensha, Dr. Karthickeyan Krishnan (2025) Therapeutic Advances In Rheumatoid Arthritis: A Comprehensive Review On The Role Of Dmards And Biologic Agents. *Journal of Neonatal Surgery*, 14 (31s), 951-957.

ABSTRACT

Background: Rheumatoid arthritis (RA) is a long-lasting autoimmune inflammatory disease that causes gradual joint damage, pain, and disability. In recent years, treatment methods have shifted from simply managing symptoms to using targeted immune therapies with disease-modifying antirheumatic drugs (DMARDs) and biologics.

Objective: This review aims to evaluate recent advancements in RA treatment, focusing on conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs), and biologic disease-modifying antirheumatic drugs (bDMARDs). It will highlight their mechanisms, effectiveness, and safety.

Methods: A narrative literature review was conducted by searching PubMed, Scopus, and Google Scholar for articles published between 2000 and 2024. The keywords used were “Rheumatoid Arthritis,” “DMARDs,” “biologics,” and “JAK inhibitors.” We prioritized randomized controlled trials, meta-analyses, and clinical guidelines from EULAR and ACR.

Results: Methotrexate is still the mainstay of csDMARD therapy and effectively controls disease activity. JAK inhibitors like tofacitinib and baricitinib offer effective oral options with quick symptom relief. Biologic agents, including TNF inhibitors and non-TNF biologics (tocilizumab, rituximab), have improved outcomes for patients with hard-to-treat RA. Using combinations and starting aggressive therapies early increases remission rates. Safety issues, such as the risk of infection, liver toxicity, and heart events, require careful monitoring of patients.

Conclusion: Recent advances in DMARDs and biologics have changed how RA is managed, allowing for targeted and personalized treatments. A strategy focused on treating to target, which includes early intervention and the involvement of clinical pharmacists, is crucial for achieving optimal outcomes. Future developments in biosimilars and therapies guided by biomarkers promise even more improvements

Keywords: Rheumatoid Arthritis, DMARDs, Biologics, Methotrexate, JAK Inhibitors, Autoimmune Disease, Targeted Therapy

1. INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterized by persistent inflammation in the lining of the joints. [1] It leads to joint damage and worsening disability. Worldwide, about 0.5 to 1% of adults have RA, primarily women, with most cases starting between the ages of 30 and 50. [2] The disease significantly impacts quality of life and poses substantial economic challenges, including lost productivity and increased healthcare costs. [3]

substances, including tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1 (IL-1). [5] These substances lead to ongoing inflammation and joint damage. Early treatment is essential to avoid permanent damage and loss of function.

In the past, RA treatment mainly focused on relieving symptoms with nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, but these medicines do not stop the disease from getting worse. [6] The arrival of disease-modifying antirheumatic drugs (DMARDs) changed how RA is treated by addressing the immune system problems and inflammation. Conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), especially methotrexate, are central to treatment because they effectively suppress the immune system and are relatively affordable. [7]

Recent progress includes the development of biologic disease-modifying antirheumatic drugs (bDMARDs) that specifically target specific cytokines or immune cells, such as TNF inhibitors, IL-6 receptor blockers, and B-cell-depleting agents. [8] Additionally, targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs), such as Janus kinase (JAK) inhibitors, provide oral treatments that modulate signaling pathways within cells. [9] These new options have led to better results for patients with moderate to severe RA who do not respond well to traditional treatments.

This review aims to give an overview of recent advancements in RA treatment, focusing on the drug profiles, effectiveness, and safety of DMARDs and biologics. It also highlights current treatment guidelines and discusses future directions for improving patient care.

Pathophysiology of Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterized by persistent inflammation of the synovial joints. This leads to the destruction of cartilage, erosion of bone, and joint deformities. [10] The cause of RA involves a complex mix of genetic, environmental, and immune system factors.

Genetically, specific alleles like the HLA-DRB1 “shared epitope” raise the risk of developing RA. [11] Environmental factors, such as smoking and infections, can trigger autoimmune reactions in those who are genetically inclined. [12]

The disease starts with the activation of antigen-presenting cells, which stimulate autoreactive CD4+ T cells in the synovium. These T cells release pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6), which drive the inflammatory process. [13] B cells also play a role by producing autoantibodies, especially rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPAs). These autoantibodies form immune complexes that worsen joint damage. [14]

Activated synovial macrophages and fibroblast-like synoviocytes create matrix metalloproteinase (MMPs) and other enzymes that break down cartilage and bone. The activation of osteoclasts, driven by the receptor activator of nuclear factor-kappa B ligand (RANKL), results in bone resorption and erosions. [15]Chronic inflammation can also lead to the formation of new blood vessels and pannus. This process replaces normal synovium with invasive granulation tissue, which further accelerates joint destruction. [16] Systemic effects of RA can include cardiovascular disease, osteoporosis, and fatigue due to ongoing inflammation.

Understanding how the immune system is involved in RA has been crucial to developing targeted treatments that block specific cytokines or immune cells associated with the disease.

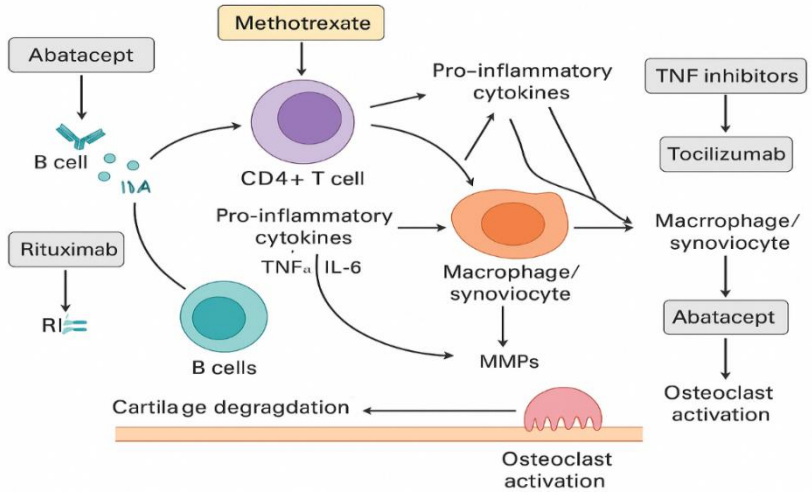

Figure 1. Pathogenesis of rheumatoid arthritis and therapeutic targets of DMARDs and biologics. CD4+ T cells, B cells, and macrophages are key contributors to inflammation and joint damage, with targeted interventions shown at various checkpoints.

Conventional Synthetic DMARDs (csDMARDs)

Conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) are essential for the initial treatment of rheumatoid arthritis (RA), particularly in early and moderate cases. These drugs aim to reduce inflammation in the joints caused by the immune system and slow or stop disease progression. [17]

Methotrexate

Methotrexate (MTX) is well-known as the "anchor drug" in RA treatment because of its effectiveness, safety, and cost. [18] It acts as a folate analog, blocking dihydrofolate reductase, which disrupts DNA synthesis and cell replication. MTX mainly decreases lymphocyte growth and the production of pro-inflammatory cytokines, exerting its immunosuppressive effects on joint inflammation. [19]

Treatment usually starts at 7.5–15 mg per week and can be increased to 25 mg per week, either orally or by injection, based on the patient's response. Healthcare providers generally recommend folic acid to lessen gastrointestinal and blood toxicity. [20] Common side effects include nausea, mouth sores, liver damage, and rare but serious complications like lung inflammation or low blood cell counts. Regular monitoring of liver and kidney function, as well as complete blood counts, is necessary. [21]

Sulfasalazine

Sulfasalazine (SSZ) combines sulfapyridine and 5-aminosalicylic acid, exhibiting immunomodulatory and anti-inflammatory effects. It likely inhibits the production of prostaglandins, neutrophil movement, and cytokine production. [22] SSZ is often used with other csDMARDs for early or mild RA.

Typical dosages start at 500 mg per day and can be increased to 2–3 g per day. Side effects may include gastrointestinal issues, rashes, and reversible low sperm counts. It is not safe for patients with sulfa allergies. [23]

Hydroxychloroquine

Hydroxychloroquine (HCQ) is an antimalarial medication that also exhibits immunomodulatory effects, primarily by blocking specific receptors and inhibiting antigen presentation. Although it is less potent than MTX, it is frequently used for mild RA or as part of combination therapies. [24]

HCQ is generally well-tolerated, with rare side effects like maculopathy. Long-term use requires annual eye exams because of the risk of permanent eye damage. [25]

Leflunomide

Leflunomide inhibits dihydroorotate dehydrogenase, a crucial enzyme in pyrimidine synthesis, thereby reducing the proliferation of activated T lymphocytes. [26] It effectively decreases disease activity and slows down radiographic progression.

The standard dose is 20 mg once daily. The most common side effects include gastrointestinal issues, liver damage, and high blood pressure. Because of its long half-life and potential to cause congenital disabilities, a cholestyramine washout is needed for rapid removal from the body. [27

Triple Therapy and Combination Strategies

Combining csDMARD therapies has shown better results than using a single drug in several studies. The most researched approach is triple therapy, which includes MTX, SSZ, and HCQ. This combination is similarly effective as some biologic treatments but costs much less. [28]

Combination strategies are especially beneficial for patients with severe disease activity and poor prognostic factors. They provide better disease control while postponing the need for more expensive biologic agents. [29]

Targeted Synthetic DMARDs (tsDMARDs)

Janus Kinase (JAK) Inhibitors: Tofacitinib, Baricitinib, Upadacitinib

JAK inhibitors are a group of oral disease-modifying antirheumatic drugs (DMARDs) that target signaling pathways inside cells involved in the development of RA. The most studied and approved JAK inhibitors are Tofacitinib, Baricitinib, and Upadacitinib. [30]

Tofacitinib mainly inhibits JAK1 and JAK3. This interferes with the signaling of several cytokines, including IL-2, IL-6, and interferon-γ.[31]

Baricitinib selectively inhibits JAK1 and JAK2. It has been found to improve disease activity scores in patients who do not respond well to csDMARDs or biologics.[32]

Upadacitinib is a selective JAK1 inhibitor. It is more effective than adalimumab in specific direct comparison trials for

moderate to severe RA.[33]

Mechanism of Action and Clinical Use

JAK inhibitors block the JAK-STAT (Signal Transducer and Activator of Transcription) pathway. This pathway is essential for transmitting signals from pro-inflammatory cytokines from the cell membrane to the nucleus. Inhibition reduces T-cell activation, B-cell differentiation, and cytokine production. [34]

These drugs are effective in inducing remission and improving patient function in those with moderate-to-severe RA, especially in patients who do not respond to traditional DMARDs.[35] Their oral form is more convenient than injectable biologics, resulting in improved patient compliance.

Safety and Monitoring

Common side effects include infections, especially herpes zoster, higher liver enzymes, high cholesterol levels, and low blood cell counts.[36] Rare but serious side effects include blood clots, cancers, and gastrointestinal perforation.[37] It's essential to monitor CBC, liver enzymes, and lipid levels at baseline and periodically. Patients should also be screened for latent tuberculosis and hepatitis B before starting treatment.[38

Biologic DMARDs (bDMARDs)

Biologic DMARDs are proteins made from living cells that target specific parts of the immune system involved in RA development. They are often given to patients who do not respond well to csDMARDs or tsDMARDs.

TNF-alpha Inhibitors: Adalimumab, Infliximab, Etanercept

TNF-α is a key cytokine in the inflammatory process of RA. TNF inhibitors bind to and neutralize TNF-α, thereby lowering inflammation and slowing disease progression. [39]

Adalimumab is a fully human monoclonal antibody given as a subcutaneous injection every two weeks.

Infliximab is a chimeric monoclonal antibody that is delivered through an intravenous infusion.

Etanercept is a fusion protein that acts as a TNF receptor and is given subcutaneously once or twice a week.

These treatments significantly improve ACR20/50/70 responses and reduce radiographic progression, whether used alone or in combination with methotrexate. [40]

Non-TNF Biologics

IL-6 Inhibitors (e.g., Tocilizumab)

Tocilizumab is a monoclonal antibody that targets the IL-6 receptor. IL-6 is involved in systemic inflammation, joint damage, and anemia from chronic disease. Tocilizumab improves clinical, laboratory, and imaging results, especially in patients who do not respond to TNF inhibitors. [41]

CD20 Inhibitors (e.g., Rituximab)

Rituximab is a chimeric monoclonal antibody that targets CD20+ B cells, which are involved in producing autoantibodies. It is administered as two infusions, two weeks apart, and repeated every 6 to 12 months. It is beneficial for patients with seropositive RA. [42]

T-cell Co-stimulation Modulators (e.g., Abatacept)

Abatacept is a fusion protein that stops T-cell activation by blocking the interaction between CD80/86 and CD28. It comes in both intravenous and subcutaneous forms and has a lower risk of tuberculosis and serious infections compared to other biologics. [43]

Table 1. TNF vs Non-TNF Biologics

Class	Drug Names	Target	Dosing Route	Special Considerations
TNF Inhibitors	Adalimumab, Etanercept, Infliximab	TNF-α	SC or IV	Risk of TB reactivation, injection site rxn
IL-6 Inhibitors	Tocilizumab	IL-6 receptor	SC or IV	Elevated cholesterol, liver enzymes
CD20 Inhibitor	Rituximab	CD20 (B cells)	IV	Requires premedication, PML risk

T-cell Modulator	Abatacept	CD80/CD86	SC or IV	Fewer serious infections vs others

As shown in Table 1, biologics differ based on their molecular targets and safety profiles, with non-TNF agents offering additional options in cases of TNF refractoriness.

Comparative Efficacy and Safety of DMARD Classes

The effectiveness of csDMARDs, tsDMARDs, and bDMARDs has been studied extensively in randomized controlled trials and meta-analyses. Methotrexate, when used alone, is effective at achieving remission or low disease activity in nearly 30% to 40% of patients. [44] However, combination csDMARD therapy, such as triple therapy, provides similar clinical benefits to biologic treatment for many patients with early RA. [45]

JAK inhibitors, such as upadacitinib and baricitinib, have demonstrated that they are at least as effective, and in some cases more effective, than TNF inhibitors in direct comparisons. [46] Biologic DMARDs, particularly TNF inhibitors and IL-6 inhibitors, have demonstrated effectiveness in the long-term control of disease and in preventing radiographic progression. Non-TNF biologics, such as rituximab and abatacept, are preferred for patients who cannot use TNF inhibitors or who are seropositive. [47]Regarding safety, csDMARDs are usually well-tolerated, with side effects that can be observed and managed. However, bDMARDs and tsDMARDs have a higher risk for serious infections, herpes zoster, and rare complications like venous thromboembolism, particularly in older patients or those with other health issues. [48] Assessing risks and benefits is crucial in choosing a treatment.

Table2. Comparison of csDMARDs, tsDMARDs, and bDMARDs in RA Management

Parameter	**csDMARDs**	**tsDMARDs (JAK inhibitors)**	**bDMARDs**
Examples	Methotrexate, Leflunomide, Hydroxychloroquine, Sulfasalazine	Tofacitinib, Baricitinib, Upadacitinib	Adalimumab, Infliximab, Tocilizumab, Rituximab, Abatacept
Mechanism of Action	Broad immunosuppression	JAK-STAT pathway inhibition	Cytokine inhibition or immune cell targeting
Administration	Oral	Oral	Subcutaneous or intravenous
Time to Onset	4–8 weeks	1–2 weeks	2–4 weeks
Monitoring	LFT, CBC, renal profile	CBC, LFT, lipids, and infection screening	CBC, LFT, infection screening
Cost	Low	Moderate to high	High
Common Side Effects	GI upset, hepatotoxicity	Infections, cytopenia, thrombosis	Infections, infusion reactions
Use in Monotherapy	Yes (methotrexate)	Yes	Some (e.g., tocilizumab)

Table 2 summarizes the comparative pharmacologic and clinical characteristics of csDMARDs, tsDMARDs, and bDMARDs, highlighting their utility in various disease stages.

Role of Clinical Pharmacists in RA Management

Clinical pharmacists are assuming a more significant role in RA management by ensuring patients adhere to their medication regimens, providing patient education, monitoring drug safety, and adjusting drug levels as needed. They help identify side effects early, reinforce safety checks such as liver function tests and blood counts, and support transitions to biosimilars. Their participation leads to better treatment results and reduces hospital visits and disease flare-ups. [49]

Future Perspectives in RA Treatment

New developments in RA treatment are focusing on personalized medicine by incorporating biomarkers, pharmacogenomics, and biosimilars. New drugs targeting GM-CSF, Bruton's tyrosine kinase (BTK), and TLR inhibitors are progressing through clinical trials. In addition, digital health tools and remote monitoring may alter how we track diseases and support patient

adherence in the post-pandemic era.

2. CONCLUSION

The treatment landscape for RA has undergone significant changes with the introduction of DMARDs and biologics. The best results are achieved through early, aggressive, and personalized treatment approaches tailored to disease activity. While csDMARDs remain essential, tsDMARDs and bDMARDs have broadened treatment options. Collaborative care, which includes clinical pharmacists, and ongoing research into new targets, will continue to enhance the quality of life for patients with RA.

REFERENCES

1. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. Lancet. 2016;388(10055):2023-2038.
2. Alamanos Y, Drosos AA. Epidemiology of adult rheumatoid arthritis. Autoimmun Rev. 2005;4(3):130-136.
3. Cross M, Smith E, Hoy D, et al. The global burden of rheumatoid arthritis: estimates from the Global Burden of Disease 2010 study. Ann Rheum Dis. 2014;73(7):1316-1322.
4. McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis. N Engl J Med. 2011;365(23):2205-2219.
5. Firestein GS. Evolving concepts of rheumatoid arthritis. Nature. 2003;423(6937):356-361.
6. Kirwan JR. The effects of glucocorticoids on joint destruction in rheumatoid arthritis. N Engl J Med. 1995;333(3):142-146.
7. Weinblatt ME. Methotrexate in rheumatoid arthritis: a quarter century of development. Trans Am Clin Climatol Assoc. 2013;124:16-25.
8. Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological DMARDs: 2019 update. Ann Rheum Dis. 2020;79(6):685-699.
9. O'Shea JJ, Kontzias A, Yamaoka K, Tanaka Y, Laurence A. Janus kinase inhibitors in autoimmune diseases. Ann Rheum Dis. 2013;72 Suppl 2:ii111-5.
10. McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis. N Engl J Med. 2011;365(23):2205–2219.
11. Gregersen PK, Silver J, Winchester RJ. The shared epitope hypothesis. An approach to understanding the molecular genetics of susceptibility to rheumatoid arthritis. Arthritis Rheum. 1987;30(11):1205–1213.
12. Källberg H, Padyukov L, Plenge RM, et al. Gene–environment interaction between HLA-DRB1 shared epitope and smoking in anti–cyclic citrullinated peptide–positive rheumatoid arthritis: results from a population-based case–control study. Arthritis Rheum. 2007;56(6):1662–1669.
13. Firestein GS, McInnes IB. Immunopathogenesis of rheumatoid arthritis. Immunity. 2017;46(2):183–196.
14. van der Woude D, van der Helm-van Mil AHM. Update on the epidemiology, risk factors, and disease outcomes of rheumatoid arthritis. Best Pract Res Clin Rheumatol. 2018;32(2):174–187.
15. Schett G, Gravallese E. Bone erosion in rheumatoid arthritis: mechanisms, diagnosis and treatment. Nat Rev Rheumatol. 2012;8(11):656–664.
16. Bartok B, Firestein GS. Fibroblast-like synoviocytes: key effector cells in rheumatoid arthritis. Immunol Rev. 2010;233(1):233–255.
17. Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological DMARDs: 2019 update. Ann Rheum Dis. 2020;79(6):685–699.
18. Weinblatt ME. Methotrexate in rheumatoid arthritis: a quarter century of development. Trans Am Clin Climatol Assoc. 2013;124:16 25.
19. Cronstein BN. Low-dose methotrexate: a mainstay in the treatment of rheumatoid arthritis. Pharmacol Rev. 2005;57(2):163–172.
20. Visser K, Katchamart W, Loza E, et al. Multinational evidence-based recommendations for the use of methotrexate in rheumatic disorders. Ann Rheum Dis. 2009;68(7):1086–1093.
21. Ranganath VK, Maranian P, Elashoff DA, et al. Comorbidities are associated with poorer outcomes in community patients with rheumatoid arthritis. Rheumatology (Oxford). 2013;52(10):1809–1817.
22. O'Dell JR, Mikuls TR, Taylor TH, et al. Therapies for active rheumatoid arthritis after methotrexate failure. N Engl J Med. 2013;369(4):307–318.
23. van Ede AE, Laan RFJM, Rood MJ, et al. Effect of folic or folinic acid supplementation on the toxicity and efficacy of methotrexate in rheumatoid arthritis: a forty-eight-week, multicenter, randomized, double-blind, placebo-controlled study. Arthritis Rheum. 2001;44(7):1515–1524.

24. Wallace DJ. The history of antimalarials. Lupus. 1996;5(Suppl 1):S2–S7.
25. Marmor MF, Kellner U, Lai TY, et al. Recommendations on screening for chloroquine and hydroxychloroquine retinopathy. Ophthalmology. 2016;123(6):1386–1394.
26. Strand V, Cohen S, Schiff M, et al. Treatment of active rheumatoid arthritis with leflunomide compared with placebo and methotrexate. Arthritis Rheum. 1999;42(9):1870–1878.
27. Wiese MD, Boey W, Heffernan M, et al. Leflunomide in rheumatoid arthritis: recommendations for use. Intern Med J. 2012;42(12):1361–1369.
28. O'Dell JR. Therapeutic strategies for rheumatoid arthritis. N Engl J Med. 2004;350(25):2591–2602.
29. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of DMARDs and biologic agents in the treatment of RA. Arthritis Care Res (Hoboken). 2012;64(5):625–639.
30. O'Shea JJ, Kontzias A, Yamaoka K, Tanaka Y, Laurence A. Janus kinase inhibitors in autoimmune diseases. Ann Rheum Dis. 2013;72(Suppl 2):ii111–ii115.
31. van der Heijde D, Tanaka Y, Fleischmann R, et al. Tofacitinib in patients with rheumatoid arthritis: a meta-analysis. Clin Rheumatol. 2013;32(5):583–592.
32. Taylor PC, Keystone EC, van der Heijde D, et al. Baricitinib versus placebo or adalimumab in rheumatoid arthritis. N Engl J Med. 2017;376(7):652–662.
33. Fleischmann R, Pangan AL, Song IH, et al. Upadacitinib versus placebo or adalimumab in rheumatoid arthritis. Lancet. 2019;393(10188):2303–2311.
34. 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;16(12):843–862.
35. Smolen JS, Genovese MC, Takeuchi T, et al. Safety of baricitinib in patients with rheumatoid arthritis: an integrated analysis. Lancet Rheumatol. 2020;2(10):e553–e565.
36. Cohen S, Tanaka Y, Mariette X, et al. Long-term safety of tofacitinib up to 9.5 years: integrated analysis of the global clinical trial programme in rheumatoid arthritis. Ann Rheum Dis. 2020;79(7):1039–1046.
37. US FDA Drug Safety Communication. FDA warns about increased risk of blood clots and death with higher doses of tofacitinib in rheumatoid arthritis patients. [Internet]. 2019. Available from: https://www.fda.gov
38. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Rheumatol. 2016;68(1):1–26.
39. Feldmann M, Maini RN. Anti-TNF therapy, from rationale to standard of care: what lessons has it taught us? J Immunol. 2010;185(2):791–794.
40. Emery P, Breedveld FC, Hall S, et al. Comparison of methotrexate monotherapy with a combination of methotrexate and etanercept in active early rheumatoid arthritis. Arthritis Rheum. 2008;58(2):295–308.
41. Jones G, Sebba A, Gu J, et al. Comparison of tocilizumab monotherapy versus methotrexate monotherapy in patients with moderate to severe rheumatoid arthritis. Arthritis Rheum. 2010;62(4):1005–1015.
42. Edwards JC, Szczepanski L, Szechinski J, et al. Efficacy of B-cell-targeted therapy with rituximab in patients with rheumatoid arthritis. N Engl J Med. 2004;350(25):2572–2581.
43. Genovese MC, Becker JC, Schiff M, et al. Abatacept for rheumatoid arthritis refractory to tumor necrosis factor α inhibition. N Engl J Med. 2005;353(11):1114–1123.
44. Singh JA, Cameron C, Noorbaloochi S, et al. Comparative effectiveness of biologics in rheumatoid arthritis: a network meta-analysis. Cochrane Database Syst Rev. 2020;5(5):CD012095.
45. O'Dell JR, Mikuls TR, Taylor TH, et al. Therapies for active rheumatoid arthritis after methotrexate failure. N Engl J Med. 2013;369(4):307–318.
46. Fleischmann R, Mysler E, Hall S, et al. Efficacy and safety of upadacitinib vs adalimumab in patients with rheumatoid arthritis. Arthritis Rheumatol. 2019;71(11):1788–1800.
47. van Vollenhoven RF, Emery P, Bingham CO, et al. Long-term safety of rituximab in rheumatoid arthritis: 9.5-year follow-up. Rheumatology (Oxford). 2020;59(6):1293–1301.
48. Curtis JR, Xie F, Chen L, et al. Real-world comparative risks of herpes zoster and serious infection in tofacitinib vs TNF inhibitors. Ann Rheum Dis. 2021;80(2):269–277.
49. Eades CE, Ferguson JS, O'Carroll RE. Public health roles for pharmacists in RA: A systematic review. Br J Clin Pharmacol. 2011;72(5):837–846.