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EDITORIAL

Janus Kinase (JAK) Inhibitors in Rheumatoid Arthritis

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Janus kinase (JAK) and signal transducer and activator of transcription (STAT) signalling has been established to have pathophysiological role in multiple disease states, such as myeloproliferative neoplasms, rheumatoid arthritis, inflammatory bowel disease and multiple immune-driven dermatological diseases etc. [1]

JAK inhibitors are low-molecular-weight compounds, which exert anti-rheumatic effects by suppressing the action of JAK, an intracellular tyrosine kinase. JAK inhibitors are useful mainly in a variety of cases, including patients who inadequately responded to treatment with methotrexate and/or DMARDs. [2]

Tofacitinib and baricitinib are the first orally available, inhibitors of (JAK) enzymes to be approved for the treatment of RA. Tofacitinib is a selective JAK1, 3 inhibitor with less activity against JAK2 and TYK2. Tofacitinib 5 mg bd, was approved by the FDA in 2012 for the treatment of RA in patients who are intolerant or unresponsive to MTX. An extended release formulation of it for the treatment of RA was approved by FDA in 2016.

Baricitinib is a selective, oral JAK1, 2 inhibitor with moderate activity against TYK2 and significantly less activity against JAK3. In 2017 the European Medicines Agency approved tofacitinib 5 mg bd in combination with MTX and baricitinib 4 mg and 2 mg once daily for the treatment of moderate to severe active RA in adult patients who are intolerant or unresponsive to one or more conventional DMARDs. [3]

Harigai M *et al* [4] has shown that tofacitinib and baricitinib are as efficacious as biological DMARDs and are safe. Fundamentally, no difference in the screening, prevention, and monitoring of infections between JAK inhibitors and biological DMARDs exists. However, increased risk of herpes zoster is probably common to all JAK inhibitors. Till date no indication of increased risk for malignancy has been reported in patients with RA treated with JAK inhibitors. However, there is a need to evaluate risks of relatively rare serious adverse events such as thromboembolic events, gastrointestinal perforation, and interstitial lung disease in clinical settings and even Latent TB. [4]

A recent met analysis evaluating the efficacy of three approved JAK inhibitors (tofacitinib, baricitinib, and upadacitinib) as monotherapy or combination therapy among patients with moderate-to-severe RA who had inadequate response to conventional synthetic disease-modifying antirheumatic drugs suggested that all JAK inhibitors demonstrated significantly better efficacy than DMARD. The differences in efficacy measures were not statistically significant between the JAK inhibitors. The study found that upadacitinib 15 mg once daily had numerically higher efficacy in terms of ACR response and clinical remission among approved JAK combination therapies and monotherapies for DMARDs patients with RA. [5]

In India these approved JAK inhibitors use has been started recently by the rheumatologists however, real world evidence still remain to emerge from the rheumatology clinics. Thus, continuous pharmacovigilance activity is warranted to establish the safety of JAK inhibitors in patients with RA and other rheumatic diseases till real rheumatology clinic evidence and experience suggests them to be safe and efficacious option over DMARDs.

References

1. McLornan DP, Pope JE, Gotlib J, Harrison CN. Current and future status of JAK inhibitors. Lancet 2021 ;398(10302):803-16
2. Morinobu A. JAK inhibitors for the treatment of rheumatoid arthritis. Immunol Med 2020 ;43(4):148-55.
3. Taylor PC. Clinical efficacy of launched JAK inhibitors in rheumatoid arthritis. Rheumatology (Oxford) 2019 ;58(Suppl 1):i17-i26
4. Harigai M. Growing evidence of the safety of JAK inhibitors in patients with rheumatoid arthritis. Rheumatology (Oxford) 2019 ;58(Suppl 1):i34-i42
5. Pope J, Sawant R, Tundia N, Du EX, Qi CZ, Song Y, Tang P, Betts KA. Comparative Efficacy of JAK Inhibitors for Moderate-To-Severe Rheumatoid Arthritis: A Network Meta-Analysis Adv Ther 2020 ;37(5):2356-72.

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