New Drug Update

A novel approach in treatment of rheumatoid arthritis: Janus kinase inhibitors

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INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune joint disorder, affecting small joints of the body, leading to severe inflammation of joints’ lining which leads to severe pain, deformities, and disability. The principal treatment of RA comprised of analgesics like cyclo-oxygenase 2 inhibitors, anti-inflammatory agents like oral glucocorticoids, disease-modifying anti-rheumatoid drugs (DMARDs) like methotrexate, etc. Much research has been done to unfold the pathophysiology of RA, giving way to newer biological agents, which were used if patients did not respond to DMARDs. They included tumor necrosis factor alpha (TNFα) inhibitors (infliximab, adalimumab, etanercept etc.), anti-interleukin 1 (IL) therapy (Anakinra), anti CD20 therapy (rituximab) and anti-IL 6 receptor therapy (tocilizimab). These biological agents are usually given in the face of treatment failure by a DMARD or are given along with one of the DMARD for better response. They have to be injected, which decreases the compliance of patient.

Janus kinase (JAK) inhibitors are a new class of drugs, also known as “Jakinibs,” that inhibit JAK enzymes, which are the main signal transducers for majority of cytokines, growth factors, and interferons. These drugs work from inside the cell and are unique in a way that their action interrupts the signaling involved in the inflammation. They include drugs like ruxolitinib, tofacitinib, both of which have been US Food and Drug Administration (USFDA) approved, and many others which are currently under trials. Tofacitinib was approved by USFDA in November 2012 for oral use in patients suffering with moderate to severe rheumatoid arthritis and do not respond to methotrexate.

Keywords: Rheumatoid arthritis, Janus kinase inhibitors, Tofacitinib

ABSTRACT

Janus kinase (JAK) inhibitors are a new class of drugs that inhibit JAK enzymes, which are the main signal transducers for the majority of cytokines, growth factors, and interferons. These drugs work from inside the cell and are unique in a way that their action interrupts the signaling involved in the inflammation. They include drugs like ruxolitinib, tofacitinib, both of which have been US Food and Drug Administration (USFDA) approved, and many others which are currently under trials. Tofacitinib was approved by USFDA in November 2012 for oral use in patients suffering with moderate to severe rheumatoid arthritis and do not respond to methotrexate.

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ADVERSE EFFECTS

The most concerning adverse effect that is associated with JAK inhibitors is directly related to their mechanism of action. Since these drugs interfere with the immune response, there is increased the risk of infections (bacterial, viral, fungal etc.). At cellular level, the most common adverse effect is a decrease in the number of natural killer cells, which happens due to the inhibition of JAKs 1 and 3. Due to this, and additional inhibition of the action of IFN, there is markedly increased the risk of cancer. However, a meta-analysis showed that risk of infection with both JAK inhibitors and biological therapy is more or less the same. Tofacitinib can additionally cause adverse effects like urinary tract infection, diarrhea, nasopharyngitis and upper respiratory infections.

CONCLUSION

JAK inhibitors work from inside the cell; thereby provide a unique approach towards the management of RA. Since they interfere with downward signalling of various cytokines, they find their role in several other autoimmune disorders and even in renal transplant patients for providing immunosuppression. These novel drugs are oral, hence offer enhanced patient compliance and also their adverse effect pattern is similar to the already available biological therapies for RA. However, longer term trials are still needed, to completely rule out the risk of malignancy with these drugs. Tofacitinib’s approval for use in RA has given a new ray of hope to patients with severe RA, who were not responding to the available DMARDs, or were intolerant to them.

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REFERENCES
