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Biological Disease Modifying Anti-Rheumatic Drugs (bDMARDs)

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COLUMN ARTICLE

The bDMARDs target specific components of the immune response that are dysregulated and are thought to be the cause of the disease process. These components are called pro-inflammatory cytokines. Tumor necrosis factor (TNF), interleukin-1 (IL-1), interleukin-6 (IL-6) and others are the pro-inflammatory cytokines found in the rheumatoid synovium. Few other bDMARDs target B- and T-cells. These agents have considerable efficacy in the treatment of patients with rheumatoid arthritis and other systemic inflammatory disorders.

TNF-α blockers

Five TNF-α inhibitors are approved for the treatment of selected rheumatic disease by the United States Food and Drug Administration. These are adalimumab, etanercept, infliximab, golimumab and certolizumab.

A 2008 systematic review of synthetic and biologic DMARD therapy for rheumatoid arthritis concluded that anti-TNF monotherapy was similar in efficacy to treatment with methotrexate alone, while the combination of an anti-TNF agent with methotrexate reduced disease activity more and slowed radiographic progression to a greater extent than did anti-TNF monotherapy or methotrexate alone [1].

Most patients with rheumatoid arthritis respond to treatment with TNF inhibitors, with significant improvements in signs and symptoms of disease, significant decrease in radiographic damage and significant improvement in quality of life and functional status.

They have also proved to be highly effective in treating patients with ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease, and juvenile idiopathic arthritis. However, they were ineffective in patients with scleroderma or vasculitis.

Rituximab

Rituximab is a chimeric monoclonal antibody that binds to CD20 antigen and leads to B-cell inhibition [2]. It is an effective biologic therapy for rheumatoid arthritis with a greatest benefit in seropositive patients. If given as two infusions of 1 gram each, it slows the radiographic progression in rheumatoid arthritis.

Rituximab is considered as a safe drug in rheumatoid arthritis, but infusion reactions can occur; most are mild to moderate. Pre-medication with methylprednisolone, diphenhydramine and acetaminophen can reduce these reactions.

Rituximab therapy carries a risk of hepatitis B reactivation among patients who have positive hepatitis B surface antigen (HBsAg) or hepatitis B core antibody (anti-HBc). All patients should be screened for HBsAg and anti-HBc prior to starting treatment [3].

Abatacept

It is a fully human fusion protein that inhibits co-stimulation (an essential step in the induction of adaptive immune responses) and inhibits T-cell activity [4].

Abatacept can be used when sDMARDs and/or other biologic drugs have failed to control inflammatory arthritis. Infection risk with abatacept is higher compared to other biologics [4].

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It is administered as a 30-minute intravenous infusion that is usually achieved without complications. Subcutaneous administration is equally effective and is now approved.

Abatacept is used to treat rheumatoid arthritis and polyarticular juvenile idiopathic arthritis. Clinical trials on abatacept in psoriatic arthritis and scleroderma have shown promising results [5].

Tocilizumab

It is a humanized monoclonal antibody that antagonizes the cytokinetic effect of IL-6. It has been approved for treatment of rheumatoid arthritis [6] and systemic onset juvenile idiopathic arthritis. It was recently granted a breakthrough designation status by the United States Food and Drug Association for giant cell arteritis based on positive results from a phase 3 clinical trial [7].

A dose of 4 mg/kg is started initially, then increased to 8 mg/kg based on clinical response. It is administered intravenously every 4 weeks. Administration through the subcutaneous route is also available. It may cause dyslipidemia but is generally well tolerated. Periodic monitoring of lipid profile along with other routine investigation is required.

Ustekinumab

Ustekinumab is a humanized monoclonal antibody that binds to and interferes with the biological effects of IL-12 and IL-23. It is approved for the treatment of psoriatic arthritis and moderate to severe plaque psoriasis [8].

It is administered at a dose of 45 mg subcutaneously at week zero, followed by a second dose at week 4, then every 12 weeks. Nasopharyngitis, upper respiratory tract infections and nausea are common side effects.

Secukinumab

Secukinumab is a humanized IgG1 monoclonal antibody that selectively binds to IL-17A and inhibits its proinflammatory action. It is approved for the treatment of active ankylosing spondylitis, psoriatic arthritis, and moderate to severe plaque psoriasis [9].

Nasopharyngitis, upper respiratory tract infections and diarrhoea are common side effects. If administered with a loading dose, 150 mg subcutaneously is given at weeks 0, 1, 2, 3, and 4 followed by 150 mg every 4 weeks. Without a loading dose, 150 mg subcutaneously is administered every 4 weeks.

Biosimilar

The introduction of biologics to health care has had a tangible effect on patients, especially where these medications have provided the only available treatment for a disease [10,11]. The success of innovator biological products and their costs timed with patent expiries have led biopharmaceutical companies to develop biosimilar products [12]. In the last 5 years, the number of biosimilar mAb products and soluble protein receptor constructs (-cepts) in development for the treatment of immunologic diseases has greatly increased. As a relatively new phenomenon in rheumatology, > 80% of confirmatory studies (phase III) for biosimilars have been or were planned to be started from 2013 onward [13].

Biosimilar Product	Original Product
infliximab/Inflectra	infliximab/Remicade
etanercept/Erelzi	etanercept/Enbrel
adalimumab/Amjevita	adalimumab/Humira

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