Introduction

B cell targeted therapy: a new approach to the treatment of rheumatoid arthritis

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Although the pathogenesis of rheumatoid arthritis (RA) remains unclear, multiple exogenous and endogenous antigenic triggers, in the presence of a genetic predisposition, initiate many autoimmune responses in the synovial compartment. Many cell populations, including monocytes, macrophages, B cells, T cells, endothelial cells, and fibroblasts, contribute to the inflammatory process. In RA, B lymphocytes have been implicated in the pathogenesis of rheumatoid synovitis.

The precise role played by B cells in RA is not fully understood, but potential mechanisms include an antigen-presenting function, secretion of proinflammatory cytokines, production of rheumatoid factor, and co-stimulation of T cells. The chimeric monoclonal antibody rituximab, which targets the CD20 antigen on B lymphocytes, has been used extensively in the treatment of B cell malignancies. More than 300,000 patients with non-Hodgkin's lymphoma, chronic lymphocytic leukemia, and other B cell diseases have been treated with rituximab, and more recently the agent has emerged as a potential treatment for RA via selective B lymphocyte depletion.

Clinical experience in the oncology setting shows that rituximab is well tolerated, with mild-to-moderate infusion reactions – most often during the first infusion phase – being the most common adverse event. Rare serious adverse events do occur but, because they are often related to circulating tumor loads or to the disease itself, it can be expected that these events will arise to a lesser extent with RA.

B cell targeted therapies represent an innovative approach to the treatment of RA. Ongoing research continues to evaluate the critical roles of B cells in sustaining the chronic inflammatory process of RA. These findings have contributed to the development of other targeted therapies that delete B cells, such as belimumab, an inhibitor of B lymphocyte stimulation. In a phase I trial belimumab treatment significantly reduced $CD20^+$ levels in patients with systemic lupus erythematosus.

The ultimate therapeutic goal in the treatment of any disease is a cure. Until the pathophysiology/etiology of RA is better understood, treatment strategies must focus on disease management. Early diagnosis and treatment with disease-modifying antirheumatic drugs (DMARDs) are necessary to reduce early joint damage, functional loss, and mortality. However, choosing which patients should receive combination DMARDs, and which combinations, remains one of our major challenges in treating RA patients.

Many well controlled clinical trials demonstrate that methotrexate and other DMARDs, including the tumor necrosis factor-α inhibitors, have shown considerable efficacy in controlling the inflammatory process, but many patients continue to have active disease. Optimizing clinical response requires the use of a full spectrum of clinical agents with different therapeutic targets. Newer therapies, such as rituximab, that specifically target B cells have emerged as viable treatment options for patients with RA.

DMARD = disease-modifying antirheumatic drug; RA = rheumatoid arthritis.