TNF-alpha (tumor necrosis factor-alpha) is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. TNF-alpha plays an important role in rheumatoid arthritis, ankylosing spondylitis, psoriasis, and Crohn’s disease. Elevated concentrations of TNF-alpha have been found in the joints of rheumatoid patients and in the colons of Crohn’s patients. TNF-alpha also affects bone metabolism by stimulating osteoclast development and activity. Anti-TNF-alpha (etanercept, infliximab, adalimumab, etc.) binds to and, therefore, neutralizes the biological activity of the inflammatory cytokine, TNF-alpha. Anti-TNF-alpha is currently in use for treatment of inflammatory arthropathies, Crohn’s disease, and psoriasis.

Etanercept (Enbrel) is a dimeric fusion protein, consisting of the TNF-alpha receptor linked to IgG (immunoglobulin G). Etanercept binds to TNF-alpha and blocks its own interaction with cell surface TNF-alpha receptors. It is indicated for the treatment of patients with rheumatoid arthritis, ankylosing spondylitis, and psoriasis. Immunosuppressed patients taking this drug are at an increased risk for infections. Entanercept is administered in two 25 mg subcutaneous injections per week.

Infliximab (Remicade) is an IgG monoclonal antibody that binds to TNF-alpha. It neutralizes the biological activity of TNF-alpha by binding to it and inhibiting the binding of TNF-alpha to its receptors. Infliximab is indicated for the treatment of patients with rheumatoid arthritis and Crohn’s disease. Infliximab is administered intravenously 5 mg/kg every 8 weeks. There is an increased risk of infection in immunocompromised patients who are taking infliximab or etanercept.

Adalimumab (Humira) is an IgG monoclonal antibody specific for TNF-alpha, thereby blocking its interaction with cell surface TNF receptors. Adalimumab is indicated for the treatment of rheumatoid arthritis. Its primary adverse effect is an increased risk of infection, especially in immunocompromised patients. The dosage is one 40 mg subcutaneous injection administered every other week.

Several recent clinical studies assessing soluble bone turnover markers in patients taking anti-TNF-alpha have shown a significant decrease in bone resorption associated with a decrease in osteoclastic activity.1-4 In these investigations, markers, such as osteocalcin, deoxypiridinoline, telopeptide of type I collagen, and procollagen, were assayed before and after treatment with anti-TNF-alpha in patients with inflammatory conditions.

Recent radiological studies also have shown significant increases in spinal and femoral bone mineral density in patients taking anti-TNF-alpha for inflammatory conditions.1-3,5-10 Dual energy X-ray absorptiometry or quantitative ultrasound bone densitometry was used to measure bone density before and after a course of the drug.

A recent study showed that transgenic TNF-alpha null mice, crossed with Sh3bp2 mutants, did not have trabecular and cortical bone loss found in Sh3bp2 homozygotes.4-10 In a separate study, systemic anti-TNF-alpha antibody therapy prevented bone loss in mice through distinct mechanisms involving decreased bone resorption.12

TNF-alpha knock-out mice do not lose bone after an ovariectomy.13 Moreover, an increased production of TNF-alpha has been found in postmenopausal females with osteoporosis.13 Raloxifene inhibits osteoclast activity by reducing TNF-alpha synthesis.13

Anti-TNF-alpha, therefore, appears to be a new category
of drug that is efficacious in the treatment of osteoporosis, particularly in patients with poor tolerance for more standard methods of treatment.

Disclosure Statement
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