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Importance of Rotativity of Etanercepte administration sites for good Clinical response to treatment

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Abstract

The present work aims to demonstrate the importance of the rotation of the injection sites to maintain the response to treatment with Etarnecept, an immunobiological drug with anti TNF action, that is applied subcutaneously and is indicated in cases of psoriasis refractory to other treatments. This study shows a possible lack of response to the treatments after consecutive applications in the same anatomical site.

Introduction: Etanercept (Enbrel®; Amgen-Wyeth) is a fully human tumor necrosis factor (TNF) receptor that reduces the inflammatory response by inhibiting interactions between TNF and cell-surface TNF receptors. Currently three TNF antagonists (adalimumab, infliximab and etanercept) are approved by the US Federal Drug and Administration (FDA) for the treatment of plaque psoriasis. Adalimumab and etanercept are indicated in the treatment of moderate to severe plaque psoriasis, whereas infliximab is indicated for severe plaque psoriasis. Adalimumab and infliximab are monoclonal antibodies, while etanercept is a soluble receptor fusion protein. Etanercept is also FDA approved for rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis (JIA), and ankylosing spondylitis (AS).

Etanercept is an important therapeutic option in patients with moderate to severe plaque psoriasis. Studies have found it to have a high efficacy, favorable benefit to side-effects ratio, and safe long-term usage compared to other systemic treatments for psoriasis such as methotrexate, cycloporine, and PUVA. Effective treatment of psoriasis is needed because of the associated morbidity of psoriasis. Quality-of-life studies in patients with psoriasis attest to its significant impact on day to day activities and effect on personal relationships.

Patients with psoriasis have increased disease-related inability to work, and face significant discrimination with resulting financial difficulties and depression. Psoriasis has also been associated with several comorbid conditions including obesity and cardiovascular disease. These data have prompted an awareness and interest in more aggressive management of psoriasis including biologic agents.

Mechanism of action: Etanercept is a fully soluble, human dimeric fusion protein with a molecular weight of 150 kDa. It consists of two extracellular ligand-binding domains of the human 75 kDa TNF receptor linked to the Fc portion of human immunoglobulin G1 (IgG1) by three disulfide bonds. The protein is produced using recombinant DNA technology in a mammalian Chinese hamster ovarian cell line and consists of 934 amino acids. Despite the presence of an Fc region, etanercept does not promote complement-mediated cell lysis in vitro as opposed to the monoclonal antibodies that do exhibit this in vitro. Etanercept acts as a competitive inhibitor of TNF, a naturally occurring proinflammatory cytokine produced by many different cell types including activated T cells, fibroblasts, adipocytes, and keratinocytes. TNF acts as a key mediator of inflammatory processes in the pathogenesis of psoriasis and psoriatic arthritis.

Etanercept inhibits the activity of TNF by competitively binding it, thus antagonizing interactions with TNF receptors on cell surface, and preventing activation of the inflammatory cascade. It is unique among TNF blocking biologic agents for psoriasis in that it mimics the activity of naturally occurring soluble TNF receptors, and prevents binding of free, soluble, non-membrane-bound TNF. There are two distinct receptors for naturally-occurring TNF: p55, also known as TNF-β or lymphotoxin, and p75, which is TNF-α. Biological activity of TNF is modulated through these receptors.

Elevated levels of TNF-α have been found in fluid from patients with psoriatic arthritis, psoriatic skin lesions, and serum of patients with plaque psoriasis. TNF-α stimulates the production of chemokines and the expression of adhesion molecules by keratinocytes and vascular endothelial cells. The release of these signals cause recruitment of additional inflammatory cells into the plaque, amplifying the inflammatory process within psoriatic plaques. Treatment with etanercept has been shown to reduce several markers of inflammation within biopsied plaques. Moreover, serum and lesional TNF-α levels directly correlate with the severity of psoriasis, as measured by the psoriasis area and severity index (PASI) score. Additionally, the dimeric nature of etanercept protein allows the binding of TNF-α at an affinity that is 50 to 1000 times greater than in naturally occurring TNF-α receptors.

Etanercept may also weakly interact with the TNF-β receptor, which acts on B-cells, T-cells, NK-cells and lymphoid architecture to stimulate immunoreactivity. TNF-β inhibition has been shown to be effective in moderating the symptoms of psoriasis. However, onercept, a human recombinant soluble TNF-β receptor, was discontinued in April 2005 during Phase III clinical trials for moderate to severe psoriasis after two patients developed sepsis.