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Advances in Psoriasis Biological Agent

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ABSTRACT

Biological agents are proteins that have pharmacological activity, derived from living materials, either from humans, animals, or microorganisms, and can be synthesized in large quantities with the help of genetic engineering techniques (recombinant DNA techniques). Biological agents are divided into three types: monoclonal antibodies in humanized, primatized, fully human, chimeric; cytokines or recombinant human cytokines growth factors; and 3) fusion proteins. The nomenclature for receptor fusion proteins and monoclonal antibodies follows the rules established by the International Nonproprietary Names of the World Health Organization (WHO). The suffix "-cept" is used as a code to identify a drug as a receptor molecule, and "-mab" is used as a code for a monoclonal antibody. The origin of the antibody is indicated by the code "-u-" for fully human origin (e.g., secukinumab). Antibodies derived from humans and mice are humanized, code named "-Zu-" (e.g., ixekizumab or chimeric, "-xi-" (eg, infliximab).

1. Introduction

Biological agents are proteins that have pharmacological activity, derived from living material, whether from humans, animals, or microorganisms, and can be synthesized in large quantities with the help of recombinant DNA techniques. Biological agents are divided into three types, namely: monoclonal antibodies in the form of humanized, primatized, fully human, chimeric; cytokines or recombinant human cytokines growth factors; and fusion proteins.[1, 2] The nomenclature for receptor fusion proteins and monoclonal antibodies follows the rules established by the International Nonproprietary Names of the World Health Organization (WHO). The suffix "-cept" is used as a code to identify a drug as a receptor molecule, and "-mab" is used as a code for a monoclonal antibody. The origin of the antibody is indicated by the code "-u-" for fully human origin (e.g., secukinumab). Antibodies derived from humans and mice are humanized, coded "-zu-" (eg, ixekizumab or chimeric, "-xi-" (e.g., infliximab). Past and current therapies The group of prior biologic therapeutic agents includes molecules that target T cell activation and migration, namely alefacept and efalizumab.[3,4]

Alefacept

Alefacept was approved in January 2003 by the FDA for the treatment of moderate to severe psoriasis.

Alefacept is a fully human LFA-3/IgG1 fusion protein that blocks the interaction of LFA-3 on antigen-presenting cells with CD2 on T cells. The IgG1 domain of alefacept interacts with FcγIII receptors on accessory cells, such as macrophages and natural killer cells, to induce selective apoptosis of memory-effector T lymphocytes. Alefacept is administered intramuscularly at a dose of 15 mg weekly for 12 weeks. A phase III trial by Mark et al. in 507 patients with chronic plaque psoriasis found a significant reduction in PASI in patients receiving alefacept compared to placebo. Patients receiving intramuscular alefacept therapy at a dose of 15 mg weekly had a reduction in PASI of at least 75% at week 14, i.e. two weeks after stopping the 12 weeks of alefacept dosing. Patients with at least 50% improvement in PASI showed statistically significant improvements in Dermatology Life Quality Index (DLQI) compared to placebo. Alefacept is not indicated for patients with below-normal CD4 T-lymphocyte counts or in HIV-infected patients because of the potential for disease aggravation resulting from an alefacept-induced reduction in CD4 T-lymphocyte counts. In pregnancy, alefacept falls into category B.8 As more biologic agents appear, alefacept becomes inferior in treating psoriasis. [4-7]

Efalizumab

Efalizumab was approved by the FDA in the same year as alefacept, and was the first biologic agent to be approved in the United States and Europe. Efalizumab is a humanized monoclonal antibody that directly fights CD11a, the subunit of LFA-1. Efalizumab induces a blocking interaction between LFA-1 and intracellular adhesion molecule 1 (ICAM-1). The LFA-1/ICAM-1 binding is involved in cellular interactions at several sites, thereby interfering with T lymphocyte activation in lymph nodes, lymphocyte extravasation, T-cell reactivation by cutaneous antigen presenting cells, and interaction of activated T lymphocytes with keratinocytes. With this, it is suspected that the pathogenesis of psoriasis in the form of abnormal cytokine production, hyperproliferation of keratinocytes, and abnormal keratinocyte differentiation can be corrected.

Efalizumab is administered subcutaneously with an initial dose of 0.7 mg/kgBW, followed by 1 mg/kgBW (maximum 200 mg) weekly. Several phase III trials have found 27% to 39% of patients have at least 75% improvement in PASI after 12 weeks of efalizumab therapy. A meta-analysis of randomized controlled trials by Brimhall et al in 2007 showed that efalizumab has higher efficacy than alefacept, but lower than other biologic agents, such as etanercept, and infliximab. Efalizumab is contraindicated in patients with a history of malignancy, tuberculosis or other severe infections, as well as in immunocompromised patients. In 2009, efalizumab was withdrawn from the market because of an association between long-term treatment with efalizumab and the incidence of progressive multifocal leukoencephalopathy.[4,5]

Etanercept

Etanercept was approved by the FDA for the treatment of moderate to severe psoriasis, psoriatic arthritis, rheumatoid arthritis, and ankylosing spondylitis in 2004. Etanercept is a recombinant human TNF receptor fusion protein, consisting of two extracellular domains of the human soluble TNF receptor unit that binds TNF-α, both soluble and membrane-bound, and the Fc fragment of human IgG that stabilizes the molecule. As a dimeric molecule, etanercept can bind to two TNF- molecules and act as a competitive inhibitor of endogenous TNF.[7,8]

Etanercept is administered subcutaneously at a dose of 50 mg, twice weekly for 12 weeks, followed by 50 mg weekly. A phase III trial by Stephen et al showed that subcutaneous etanercept therapy at a dose of 50 mg twice weekly gave at least 75% improvement in PASI (PASI 75) in 47% of patients compared to placebo in 5% of patients. week

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increased PASI 75 response. At week 24, PASI 75 response was found in 59% of patients. Mild to moderate skin reactions at the injection site occurred in 37% of patients receiving etanercept therapy, generally not requiring discontinuation of the drug. The average duration of a skin reaction is 3 to 5 days. This reaction generally occurs in the first month of drug administration and then subsides. The needle cover for injecting etanercept contains latex so etanercept should not be used in latex sensitive patients. Another contraindication to etanercept is sepsis.[9,10]

2. Conclusion

Biological agents are divided into three types, namely: monoclonal antibodies in the form of humanized, primatized, fully human, chimeric; cytokines or recombinant human cytokines growth factors; and fusion proteins.

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