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Pharmaceutical Sciences **REVIEW ARTICLE ……!!!**

IMMUNOADHESIONS - A MINIREVIEW

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ABSTRACT

Currently protein based therapies remains the mainstay of treatment for malignancies, autoimmune diseases and infectious disease. Though they exhibit specific action and enhanced pharmacokinetic stability, the high cost, proper diagnosis to prior use and severe adverse effects warrants cautious clinical use. This review focuses on immunoadhesion that are currently used for treatment or in clinical development.

INTRODUCTION:

Immunoadhesions are fusion protein that consists of extracellular domains of transmembrane proteins with human immunoglobulin constant domain. They competitively inhibit the binding of a ligand to its specific receptor and thereby prevent downstream effects. [1] Advantages of immunoadhesion include specificity, enhancement of host immune function and low immunogenicity. Currently bispecific immunoadhesion are used that can attach to two different proteins at the same time thus binding cancer cells and immune cells together to initiate cytotoxicity. [2] The current review aims to discuss immunoadhesion that are currently used for treatment or in clinical development.

Abatacept

Molecules that prevent T cell co-stimulation have emerged as promising immunomodulatory agents. One such is abatacept and is composed of a human cytotoxic T-lymphocyte associated antigen-4 (CTLA4) protein joined to a human immunoglobulin. It inhibits of T-cell activation by blocking interaction of CD80/CD86 receptors to CD28. It is highly efficacious for T cell-mediated autoimmune disorders. [3]The common adverse effects are severe hypersensitivity and anaphylactic reactions, infections, neurologic, musculoskeletal, and connective tissue effects. [4]

Belatacept

Belatacept consists of CTLA4 fused with the Fc constant region of human immunoglobulin and blocks antigen presenting T cells stimulation, thereby inhibiting the immune response. [5] It used for primary maintenance of immunosuppressant in kidney transplant recipients. The most common adverse reactions with belatacept include anaemia, diarrhoea, urinary tract infection, edema, constipation, hypertension, pyrexia, cough, nausea, vomiting, headache, leukopenia, lymphoproliferative disorder and progressive multifocal leukoencephalopathy. [6]

Baminercept

Baminercept is a lymphotoxin-β receptor (LTBR) and immunoglobulin fusion protein that leads to reduced activation of T cells, dendritic cells and vascular endothelium. The most common adverse event in patients receiving baminercept was headache.

Briobacept

It is a recombinant B cell- activating factor (BAFF) fusion protein linked to the Fc domain of human immunoglobulin. It decreased B-cell numbers in the periphery and lymphoid organ. Pre-clinical studies showed that it decreased anti-DNA antibodies, proteinuria and ameliorated glomerular changes. Clinical trials show promising reports for treatment of autoimmune diseases such as systemic lupus erythematous, rheumatoid arthritis and Sjogren syndrome. [1]

Atacicept

Atacicept is a CD267 fusion protein that binds to and blocks the receptor for both BAFF and a proliferation- inducing ligand (APRIL). It diminished plasma cell survival and antibody production in mice and humans. [8] It has shown promising results in clinical trials of treatment of autoimmune diseases. [9,1] Serious adverse events related to immunosuppression such as serious infections and relapsing fever has been reported. [10]

Aflibercept

Aflibercept contains the extracellular domains of vascular endothelial growth factor receptor (VEGFR1 and VEGFR2). [11] It inhibit the activity of vascular endothelial growth factor subtypes VEGF-A and VEGF-B, as well as to placental growth factor (PGF), inhibiting the growth of new blood vessels in the capillaries or the tumour. They are currently being evaluated in Phase 3 clinical studies to treat ovarian cancer. Adverse effects like reduced blood cell count, diarrhoea, abdominal pain and fatigue and hypertension has been reported.

Alefacept

Alefacept was the first biologic approved for treatment of psoriasis. [12] Alefacept is a human lymphocyte function-associated antigen (LFA)-3 fused with human immunoglobulin. It binds to CD2 molecules on the surface of activated T-cells, and thereby blocks co-stimulation of T-cells by the antigen presenting cell and also depletes memory T-cells. The most common symptoms reported by patients undergoing therapy were flu like symptoms such as headaches, rhinitis, and fatigue. [13]

Though biologicals have improved therapy due to greater efficacy and tolerability they are associated with rare adverse events and are expensive. Hence, these agents should be used with cautiously clinical settings.

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