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Reports on Scientific Meetings

Optimizing treatment of plaque psoriasis with biologics

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Psoriasis has long been a challenge in the daily practice of dermatology and worldwide over 80 million people were affected. In Australia, the prevalence is about 2-3% with a male-to-female ratio of 1:1. The average age of onset is about 20 years. With advances in molecular biology, the pathogenesis of psoriasis is better understood. Current understanding of psoriasis is that it is a T-cell mediated autoimmune disorder. There is a persistent T-cell stimulation to drive abnormal keratinocyte proliferation and differentiation. Both innate and adaptive immunity are involved.

Increase in severity of psoriasis is associated with increased co-morbidities. Psoriasis was shown to be associated with increased prevalence of hypertension, hyperlipidaemia, arthritis and anxiety. Psoriasis was also shown to have a significant negative emotional impact on patients and be associated with a decrease in quality of life.

Traditional therapy for psoriasis consists of topical agents, phototherapy and systemic drugs. These regimens are able to provide adequate disease control in most patients. However this is achieved with significant long term side effects. Examples are topical-steroid-induced skin atrophy and Cushing's syndrome, PUVA-induced skin malignancy, methotrexate-related hepatotoxicity, cyclosporin-related nephrotoxicity, as well as teratogenicity associated with systemic retinoids. To minimise the cumulative toxic effects of various treatments, dermatologists have developed strategies including combination, sequential and intermittent regimens. However these strategies are inconvenient and may create frequent relapses.

Under the circumstance of long term adverse effects and inconvenience of traditional therapy, the development of an effective and safe regimen suitable for continuous long term use is deemed necessary. Biologic therapy that targets specific steps and cells in the pathogenesis of psoriasis has thus been developed. It has gained significant importance in the treatment of psoriasis in recent years. Biologics are mainly divided into T-cell inhibitors such as efalizumab and alefacept, and tumour necrosis factor (TNF) inhibitors such as etanercept, infliximab and adalimumab. These agents are recombinant proteins, monoclonal antibodies or fusion proteins.

There are 4 main strategies for the biologics to work in the pathogenesis of psoriasis: (1) Deplete T-cell: alefacept, (2) Block T-cell activation:

efalizumab, (3) Induce immune deviation and (4) Inhibit cytokine (anti-TNF-α): infliximab, etanercept.

Alefacept is a fully humanised fusion protein. It inhibits the activated T-cell and depletes CD4+ T-cell. However it has a relative slow onset of action. Monitoring of CD4+ T-cell during treatment is recommended.

Efalizumab is a recombinant humanised monoclonal IgG-1 antibody targeting CD11a, the alpha subunit of lymphocyte function associated antigen-1 (LFA-1), that inhibits multiple T-cell mediated events involved in the pathogenesis of psoriasis. These include the process of T-cell activation, T-cell trafficking to sites of cutaneous inflammation and T-cell reactivation. Multiple phase III clinical trials have demonstrated the efficacy, safety, and health-related quality of life benefit of 1-2 mg/kg/week, three and six months of efalizumab regimen in patients with moderate to severe chronic plaque psoriasis. In an open-label trial to evaluate the efficacy, safety and tolerability of continuous efalizumab up to three years, there is sustained efficacy at 36 months with no cumulative toxicity and end organ damage. Seventy-three percent of patients were able to achieve Psoriasis Area and Severity Index (PASI) 75 and 55% achieved PASI 90.

Infliximab is the prototype for anti-TNF-α agent. It is a chimeric murine monoclonal antibody. It has a rapid onset of action at a dose of 5 mg/kg with good therapeutic response for psoriasis. Adverse effects include fulminant sepsis, pancytopenia, hepatitis, heart failure, demyelination, lupus-like disease, and malignancy. Neutralizing antibodies may occur on prolonged use and may require dose increment.

Etanercept is a fusion protein consists of human TNF receptor and Fc region of human IgG-1. A higher dose at 50 mg twice/week was more effective than 25 mg twice/week. Moreover PASI 75 continued to increase at week 24 compared to week 12 in the course of treatment.

Learning points:

Biologics have become increasingly important in the management of psoriasis. Different classes of biologics have different efficacy, rate of onset of action, and adverse effect profile. Efalizumab was shown to be effective and safe in long term therapy for psoriasis.