Biologic therapy: the dawn of a new age for psoriasis patients

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The prevalence of psoriasis is 2-3% in developed nations. About 80% of these patients were of the chronic plaque type. Both genetic and environmental factors were important in its pathogenesis. There is a profound reduction of quality of life due to physical symptoms and psychosocial impairment. Psoriasis is among those major medical illnesses such as cancer, myocardial infarction and hypertension in terms of worse patient-reported physical and mental outcomes. In the EUROPSO study, what bothered patients regarding treatment included: time consumption, ineffectiveness, expense, and side effects. The status quo treatment options include topical agents, phototherapy, and systemic agents. All these have their own merits and disadvantages. Various co-morbid conditions also limit the choice of treatment options. Clinical challenges will also arise from alcohol and drug interactions (acitretin, methotrexate, NSAIDs and cyclosporin), metabolic conditions (hyperlipidaemia and diabetes), joint involvement, and pregnancy. In an International Consensus Conference, there were several unmet needs in psoriasis identified: (1) long-term safety profiles, (2) therapies for patients of all ages and life stages, (3) treatments with less frequent or less invasive monitoring, (4) effective monotherapy, (5) greater convenience, and (6) treatment that improves patients' quality of life.

Biologics seem to be able to put promise into practice. They specifically target on the psoriatic immune response. Two groups of drug actions are nowadays the mainstream: (1) biologics that block interaction (efalizumab: CD11a/LFA-1; alefacept: LFT-3/CD2); (2) anti-TNF-alpha (infliximab: human/mouse monoclonal TNF-antibody; adalimumab: humanised monoclonal TNF-alpha antibody; etanercept: p-75-human-TNF-receptor). Infliximab is EMEA/FDA approved for psoriatic arthritis. In the SPIRIT study by Gottieb AB et al, the PASI 75 response at week 10 was 71.1% for infliximab 3 mg/kg intravenous group and 87.9% for 5 mg/kg group. The overall percentage of serious infections through week 30 was 0.5%, infusion reaction 20%, antinuclear antibodies 24%, antibody versus infliximab 23% and anti-DNA 4%.

Adalimumab was EMEA/FDA approved for use in treating psoriatic arthritis. It directs specifically against TNF and is humanised. It can be administered in combination with methotrexate or as monotherapy. It is well tolerated, with low incidence of allergic reactions (<1%). The half-life is about 14 days. In the ADEPT study using adalimumab 40 mg every other week, the percentage achieving PASI 50 was 75%, PASI 75 59% and PASI 90 90%. The noticeable adverse

events in patients taking adalimumab were serious infections (2.41 in 4-year follow-up of 2327 patient-years). Among these were pneumonia (0.52), urinary tract infection (0.26), septic arthritis (0.13%), and tuberculosis (0.04).

Efalizumab was approved by EMEA and FDA for psoriasis. It is a humanised monoclonal antibody to CD11a, a subunit of LFA-1. It acts by inhibiting trafficking of T-cells to the dermis and epidermis, T-cell reactivation in these areas and Cd11c+ dendritic cells. However, it did not meet the primary endpoint in psoriatic arthritis trial. The approved dosage was 1 mg/kg. Study had shown that 2 mg/kg did not give significant difference. In a long-term, open-label study, maintenance treatment with efalizumab gave a sustained effect in 45% of patients with PASI 75. The incidences of adverse events of efalizumab were (%, placebo/efalizumab): headache (22/32), chills (4/13), nausea (7/11), pain (5/10), myalgia (5/8), fever (3/7), and infection (26/29). Safety data and case study reports showed that 18% could have rebound after withdrawal of the drug.

Etanercept was EMEA/FDA-approved for treating psoriasis and psoriatic arthritis. It is the only soluble TNF receptor antagonist. It is a fully human protein with low immunogenicity. There is no pharmacokinetic interaction with methotrexate. There is significant improvement in PASI score as early as week 2. In patients with initial PASI response less than 50, continued treatment till week 24 showed 75% improvement in the PASI score. Re-treatment at a later stage showed similar response in PASI after discontinuation of the drug. The median time to relapse was 85 days for 25 mg biweekly regimen and 91 days for 50 mg biweekly regimen. There was no rebound psoriasis, no increase in neutralising antibody and no allergic side effects in re-treatment. Study showed that dose step-down after week 12 had sustained PASI 75 response. It significantly improves joint pain at week one and it inhibits structural damage. Therefore, one can aim at maximising the response by first going high then going low. There was statistically significant improvement in Dermatology Life Quality Index (DLQI) as early as week 1, improvement of depressive symptoms and nail lesions. Etanercept was generally well tolerated in several studies. There were no reports of opportunistic infections or tuberculosis and no routine laboratory monitoring specific for it is required.

The International Consensus Conference gave consensus for biologic therapy as an effective treatment for psoriasis. It is relatively safe in the short to medium term, while long-term safety and efficacy need to be observed. It demands fewer monitoring requirement, and is more effective than current therapies as monotherapy. It can be used for significant periods of time and it improves multiple facets of quality of life. Therefore, it can be one of systemic treatment options for moderate-to-severe psoriasis.

Learning points:

Biologic therapy is a new option for treating moderate-to-severe psoriasis. Its safety and efficacy in the short-to-medium term have been intensively studied, though its long term effect still needs to be established.