

## Observations

At present, treating patients with biological drugs – especially infliximab – is laborious. You need more time, nurses, space and money. The number of our patients treated with biologics is small, so it is difficult to draw any conclusions about long-lasting procedures, results and side-effects. Efalizumab and etanercept are administered by the patients themselves, but still require careful monitoring of infections and other side-effects, which takes costly time.

As we already know, biologics have many side-effects: infections, malignancies,

hypersensitivity reactions, lupus-like or multiple sclerosis (MS)-like syndromes, etc. Tumour necrosis factor-alpha (TNF- $\alpha$ ) regulates cytokine production in the body. Some scientists have also associated TNF- $\alpha$  with major depression. According to Tying et al. (Lancet 2006, Jan 7), reducing the effects of the some cytokines in the brain may relieve depressive symptoms. Furthermore, we know that new effective antidepressive drugs may add to the suicidal feelings of some depressive patients, especially at the beginning of the treatment (BMJ 2005, May).

Psoriasis is a complex biopsychosocial condition. We need new safe treatments to improve quality of life of our psoriasis patients. In addition, we need more studies and information about the central nervous system (CNS) side-effects of biologics. Antidepressive side-effects are, of course, desirable for patients. Still, in my opinion, patients with severe long-lasting psoriasis require more careful monitoring for psychiatric disorders, especially at the start of biological treatments.

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## Clinical Experience with Biological Agents at the Department of Dermatology, Aarhus University Hospital

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To provide the best possible therapy for patients with severe psoriasis, we have tried to gain experience with all the available biological agents, even before they became licensed for this indication. This means that we have clinical experience with more than 100 patients, some of whom have been treated for more than 3 years.



Remicade® is used for severe and unstable psoriasis, including pustular psoriasis. Enbrel® is selected for severe psoriasis, particularly in patients with associated arthropathy. Raptiva® is prescribed mainly for moderate to severe, stable plaque-type psoriasis without arthropathy. Humira®, which is still not approved for psoriasis, is

given to patients who do not respond to the other biologicals. Screening for tuberculosis is mandatory for the anti-TNF- $\alpha$  antagonists. For Raptiva® only patients considered to be at risk of tuberculosis are screened.

Our experience is longest for Remicade® (infliximab), which is extremely effective early on. However, in a significant number of patients the effect is reduced over time. To avoid this loss of efficacy, we try to use Remicade® in combination with methotrexate. Infliximab is also effective in other immune-mediated inflammatory skin diseases. Thus, we have obtained excellent results in refractory cases of pityriasis rubra pilaris, Behcet's disease, pyoderma gangrenosum, vasculitis, dermatomyositis and sarcoidosis. Some patients have

withdrawn from Remicade® treatment because of side-effects, including tuberculosis, severe pneumonia and infusion reaction. Also, we have seen 2 cases of atopic dermatitis-like eczema. Both had a history of atopy, but had not experienced eczema previously. Because there are similar reports with tumour necrosis factor (TNF) antagonists in the literature, we recommend that patients with a history of atopy are monitored closely during anti-TNF- $\alpha$  therapy.

Initially Enbrel® is usually less effective than Remicade®. Therefore, all patients are treated at first on the higher dose, 50 mg twice weekly, and then reduced after 3 months to 50 mg once a week. In most patients the improvement can be maintained on this doseregimen. However, some patients experience a partial recurrence when the Enbrel® dose is lowered. This may lead to up dosing or discontinuation, depending on the circumstances. Because we observe a rather rapid recurrence of psoriasis upon stopping Enbrel® therapy, we continue therapy when the disease is under control. The clinically significant side-effects observed during Enbrel® therapy are mainly of an infectious nature, including bronchitis, pneumonia, urinary tract infection and erysipelas. In patients with such infections, Enbrel® is continued or temporarily discontinued. However,

in a few severe cases Enbrel® is discontinued permanently.

Patients selected for Raptiva® therapy have stable plaque-type psoriasis without a history of arthropathy. Used in this way we have obtained a good clinical response in the majority of patients. Although controlled clinical studies indicate that the risk of infection is not increased during Raptiva® therapy, we have had patients with infections such as pneumonia, dental root abscess, mastitis, urinary tract infection and impetigo. We have observed only 1 or 2 patients with a papular eruption, which seems to be particular to Raptiva®. Two patients who developed arthropathy were found to have a history of that condition. Unfortunately 3 patients had a worsening of their psoriasis with widespread papules. Although uncommon, this worsening requires special attention because it may be difficult to control even with Sandimmune® and other biological agents. We do not know which patients are at risk of developing this paradoxal reaction to Raptiva®. Nevertheless, we try to avoid Raptiva® in patients with unstable psoriasis.

Humira® is approved for psoriatic arthritis, but still not for psoriasis. Therefore, we have limited the use of Humira® to patients who fail to

respond to the other biologicals. So far, the results look promising.

Because a single biological agent is not ideal for all patients with severe psoriasis, it is important that dermatologists who use this type of therapy become familiar with all available agents. This is also important due to the fact that patients who become resistant to one biological agent often respond to another biological agent.

In my opinion too few psoriasis patients are offered biological therapy. This is partly due to high cost and uncertainties about long-term safety. A contributing factor may be a conservative attitude among dermatologists who do not fully appreciate the suffering of many psoriasis patients.

Although we still wait for safe and effective treatments for the majority of patients with psoriasis, the introduction of biological agents has already changed my clinical practice. Patients who never had their disease under control can now enjoy a normal life, and our department has almost completely stopped using messy and stigmatizing tar treatment. As a consequence we have been able to decrease the number of beds in our inpatient service.