Biologics in Private Practice – Alternatives to Methotrexate and Ciclosporine

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The introduction of biological drugs in dermatology for the treatment of moderate to severe psoriasis is still a recent event, in which, as so often before, our speciality has been runner-up to the field of rheumatology. The products registered in Scandinavia, are, with few exceptions, based on a similar "crude" technology, in which more or less human or humanized antibodies are raised towards mediators of inflammation. This era of engineered antibodies will probably be of relatively transient duration, and will be replaced before long, when more sophisticated technologies launching synthetic and stable orally active compounds are introduced, and when more specific mediators of disease are identified. Thus, the use of TNF-inhibitors for the treatment of psoriasis is still a relatively crude technology, rather like shooting a sparrow out of a tree with a pump-gun, where you are sure to get the bird, but also half the crown of the tree. This is the inevitable cost of blocking one of the "main-switches" of the immune system, namely the TNF-dependent immune-mediator cascade.

Biological drugs are, however, undoubtedly effective, and they appear to improve quality of life for many psoriasis patients. Some of the products have now also been released for use in private practice, and we introduced them in our clinic during 2005. The rules as to which patients qualify for treatment (these rules having been introduced for socio-economic reasons) still limits their use, and thereby the possibility of obtaining hands-on experience with the biologics. However, we find the therapies convenient to handle and monitor in private practice, and they are in no way more tedious to use than other conventional therapies, such as methotrexate and cyclosporine. On the other hand, I do not find the biologics to be more effective than methotrexate or cyclosporine, but experience them rather as a reasonable alternative when traditional therapies for some reason are not an option.

Whenever a dermatologist is introduced to a new medication, she or he is sure (at some point) to test it on other skin disorders, so-called "off-label use". Thus, we and others are using Enbrel® for the treatment of Behcet's disease, and we have had apparent success treating a patient with severe adult atopic dermatitis using the CD11a-blocking agent Raptiva®. This patient had previously tried most other known conventional therapies, as well as cyclosporine, azathioprine and photopheresis, either without success or with unacceptable side-effects. This particular atopic dermatitis patient tolerates the treatment well and is experiencing a significant reduction in itching. Also, the dermatitis is partly cleared. Such cases remind us that there are still development possibilities for a novel use of these new potent therapies. Hospital clinics should be given resources and more freedom from bureaucracy to spearhead this development, and the private clinics should be encouraged to adapt the already established therapies. In addition, new molecular targets should be identified. Dr Øystein Grimstad, from the department of dermatology at the Norwegian University of Science and Technology, has recently spent a year of research at the University of Tokyo, where he confirmed that the cytokine IL-31 indeed appears to deserve its name as the "itch-cytkine". Thus, Dr Grimstad, for the first time in an animal disease model, described IL-31 to be an important mediator for the development of itching – in this case a model of atopic dermatitis. This means that IL-31 could be a new and attractive target for the reduction, and thereby treatment, of one of the key symptoms of T-cell mediated inflammation of the skin, namely itching.

All in all, the new generation of biological drugs recently made available for the treatment of psoriasis are, for several reasons, not the ideal treatment of psoriasis, but they deserve their place as visitors in time and as templates for next generation of psoriasis treatments, which are yet to come.

Biological Therapy Provides New Possibilites for Combination Therapy for Serious and Previously Therapy-resistent Psoriasis

Experiences from the Department of Dermatology at St. Olavs Hospital, Trondheim, Norway.

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In Norway, infliximab (Remicade®) and etanercept (Enbrel®) are approved for treating moderate to serious plaque psoriasis and psoriatic arthritis, while adalimumab (Humira®) is approved for psoriatic arthritis. Efalizumab (Raptiva®) is approved for severe plaque psoriasis. In Norway, the patient must apply to the National Office for Social Insurance before each separate treatment occasion in order to get a referral for treatment using biological therapy. Relatively strict indication exists: the patient must have moderate to serious plaque psoriasis, which has not responded to or is intolerant to other systemic treatment, including cyclosporine, methotrexate and/or PUVA, or where such treatment is contraindicated. Norway has about 4,5 million inhabitants. 2–3% of the population has psoriasis, and roughly 25% of the psoriasis patients are serious cases. If 10% of those with serious psoriasis have a therapy-resistant form of psoriasis and in need of biological therapy, we would have about 2500–3000 Norwegian patients in need of such treatment.

At the Department of Dermatology in Trondheim, we began biological treatment using infliximab for a patient with serious plaque psoriasis in August 2001, our first patient treated using biological therapy. He still uses infliximab (3 mg/kg) combined with methotrexate 4.5 years after starting treatment, and we have seen a continued positive effect of this treatment. Since then, we have treated 22 patients with severe plaque psoriasis using infliximab. Etanercept has now also been approved for treatment of plaque psoriasis, and we have 25 patients who have begun treatment with etanercept for psoriasis. During the last year, we have also begun treatment using efalizumab of 11 patients with widespread plaque psoriasis. Adalimumab has recently been used for 3 patients with psoriasis at our department, and for the time being, this is the therapeutical agent with which we have the least amount of experience.

Patients who come into question for treatment using biological therapeutics are often patients who have a long treatment history, and who are difficult to treat successfully. They have already tried light treatment, including PUVA, methotrexate, cyclosporine, and often also systemic retinoids. Biological therapeutics make an important addition to the treatment options available for these patients. However, that does not mean that biological treatment works equally well for all patients with severe psoriasis. We have the impression that those of our patients who come into question for this type of therapy have a more active/severe form of psoriasis than patients who have participated in large international studies. Even though our patient numbers are small, this may explain