

ORIGINAL ARTICLE

Efalizumab for severe refractory atopic eczema: retrospective study on 11 cases

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Abstract

Background Efalizumab is a recombinant humanized murine monoclonal antibody against CD11a, approved for the treatment of plaque psoriasis. However, recent reports suggest that it also may be effective in the treatment of severe atopic dermatitis (AD).

Objective To evaluate the clinical effect of efalizumab in AD.

Methods A systematic retrospective study of the medical files of patients treated with efalizumab for AD in Danish dermatology departments. Positive outcome was defined as improvement of the disease registered in the patient's file over a period exceeding 6 months.

Results Two of eleven patients had a positive outcome. Nine patients stopped treatment due to progression of AD or lack of effect.

Limitations Retrospective study.

Conclusions Only a minority of patients with severe AD responded to efalizumab treatment in a standard dose.

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Keywords

atopic dermatitis, atopic eczema, biologics, Efalizumab

Conflict of Interest

None declared.

Management of severe atopic dermatitis is a major challenge to patients and dermatologist.^{1,2} The general principles of treatment are to preserve and restore the stratum corneum skin barrier and to eliminate inflammation and infection of the skin. This is usually done by the treatment with moisturizers, topical steroids or topical immunomodulators. Phototherapy may be effective for mild or moderate atopic dermatitis, but in more severe cases, there is a need of systemic immunomodulatory and immunosuppressive agents such as corticosteroids, cyclosporin, azathioprine, methotrexate, mycophenolate mofetil or interferon- α . There is a lack of randomised controlled studies describing the effect of systemic therapy in atopic dermatitis.³ Recent case reports have suggested that Efalizumab may be effective in patients with atopic dermatitis. Efalizumab (Raptiva[®]) is a recombinant humanized murine monoclonal antibody against CD11a, a subunit of lymphocyte function associated antigen (LFA-1) and a leucocyte cell surface protein. The proposed mechanism of action in the treatment of atopic dermatitis is inhibition of T lymphocytes binding to endothelial cells resulting in less trafficking of T lymphocytes

to the skin without an associated depletion of T cells. Other hypothetical mechanisms include inhibition of T-lymphocyte activation and decreased CD-25 expression.⁴⁻⁶ A total of 14 cases of atopic dermatitis patients with a positive response to treatment with efalizumab have been published.⁷⁻¹⁰ In most cases, onset of the effect was gradual, and best results were reported after long-term treatment (6–9 months).

The aim of this study was to identify all cases of atopic dermatitis treated with efalizumab in dermatological departments in Denmark, and to assess effect and side-effects of the treatment.

Material and methods

All five dermatological departments in Denmark were contacted in order to identify all cases of atopic dermatitis treated with efalizumab in the period from the drug was first registered in Denmark in 2006 until March 2008. In each department, the person responsible for efalizumab therapy was contacted. Two departments did not report any cases, and three departments had a total of 11 cases. The medical records of the patients were

Table 1 Eleven patients treated with Efalizumab for severe refractory atopic eczema. A description of age and sex, dosage regimen, duration of therapy, reason of discontinuation, side effects and concomitant therapy

Case no.	Age and sex (years/sex)	Dosage of efalizumab (mg/kg/week)	Duration of efalizumab therapy (months)	Treatment discontinued due to	Side effects	Concomitant therapy
1	43/Male	1	6 (2 weeks pause)	Progression in AD	Otitis externa	None Topic steroid
2	71/Female	1	4 (5 weeks pause)	Progression in AD	Fever and enlarged lymph nodes after 6 and 12 weeks of therapy	Cyclosporine Topic pimecrolimus
3	65/Female	1	3	Progression in AD	None	Cyclosporine
4	28/Female	1	4	No visible improvement in AD	None	Azathioprine
5	23/Female	1	12 (3 weeks pause)		Lymphocytosis Gingivitis	Prednisolone Topic steroid
6	25/Female	1	10	Progression in AD*	Headache after first injection pruritus	Prednisolone Topic steroid
7	38/Female	1	5	No visible improvement in AD and persisting lymphocytosis	Lymphocytosis (anaplastic large cell lymphoma?) Fluelike symptom Headache	Topic steroid
8	19/Female	1	3	No visible improvement in AD	None	Topic steroid
9	35/Female	1	3	Progression in AD	Headache Tiredness	Topic steroid
10	35/Male	1	2	No visible improvement in AD	None	Topic steroid
11	56/Male	1	6	No visible improvement in AD	Nausea, Chills Tiredness	Cyclosporine Topic steroid

*Treatment was discontinued after 10 months of Efalizumab therapy.
AD, atopic dermatitis.

reviewed and relevant data extracted. Since no scoring of disease severity was systematically used, a positive outcome of efalizumab treatment was considered when improvement of disease, as assessed by less erythema, less scaling and less pruritus, was registered in the medical record of the patient, and the treatment was continued for more than six months.

Results

Clinical presentation of cases is summarized in Table 1. The median age of the patients was 40 years (range, 19–71 years) with a predominance of women (8 of 11 patients). Common for all patients, except one, was a lifelong history of severe atopic dermatitis and presence of multiple allergies. All patients had a generalized eczema and severe head and neck dermatitis with several annual episodes of superinfection. All patients had previously been treated with topical and systemic corticosteroids, phototherapy, and other topical and systemic immunomodulating agents such as azathioprine, cyclosporin and mycophenolate mofetil. Two patients had been treated with photopheresis and one patient with plasmapheresis. A standard regimen of efalizumab treatment was given (0.7 mg/kg initially followed by 1 mg/kg weekly) in all cases. Within 8 weeks of efalizumab therapy, a slight improvement in atopic dermatitis was observed in four patients (case 1, 2, 6 and 7), and in one patient (case 5), improvement was seen within 12 weeks. However, only two of these patients (case 5 and 6) had a sustained effect of efalizumab lasting from 10 to more

than 12 months, although one (case 6) continually suffered from pruritus regardless the treatment. The mean length of efalizumab therapy was 5 months (range, 2–12 months). Previously reported side-effects of efalizumab in patients with atopic dermatitis were viral infection, rebound phenomenon, *Staphylococcus aureus* infections and thrombocytopenia.^{9,11} In our material, disease severity progressed in 5 patients, and in one case, the progression was severe, which led to drug discontinuation and supplementary therapy with systemic steroids and cyclosporin. Impetigo occurred in 6 of the 11 cases (1, 4, 7, 8, 9 and 11) and was treated with dicloxacillin, within a mean period of 5 weeks after initialization of efalizumab (range, 2–10 weeks), and one patient (case 5) was treated with topical fucidic acid after 12 weeks of efalizumab therapy. One patient (case 2) was treated with systemic itraconazole due to *Pityrosporum ovale* infection of the scalp after 13 weeks of efalizumab therapy. This patient developed fever and enlarged lymph nodes in the neck region after 6 weeks and fever after 12 weeks of therapy. Both episodes were related to catharralia and were not further commented in the medical file. Three patients developed lymphocytosis, which was an expected finding and was not considered of clinical importance. One patient, a 38-year-old female patient (case 7), developed fatal anaplastic large cell lymphoma 9 months after discontinuation of efalizumab. Review of the patient's records revealed that she had had intermittent lymphocytosis, enlarged lymph nodes and elevated lactate dehydrogenase prior to efalizumab therapy; therefore, her

lymphoma was unlikely to be caused by efalizumab. As a minor side-effect, headache was reported in four patients after the first injections of efalizumab. None of the included patients in our study developed thrombocytopenia.

Six patients (case 2–6 and 11) continued with other systemic immunomodulating agents (cyclosporin, prednisolone and azathioprine) simultaneously throughout efalizumab therapy.

Discussion

Fourteen cases of successful off-label treatment with efalizumab in patients with severe atopic dermatitis have been reported in the literature.^{7–10} In this systematic retrospective study, including all patients from Danish dermatological departments treated with efalizumab for severe atopic dermatitis, 2 of 11 patients had a positive outcome defined as improvement of disease and continuation of treatment for more than 6 months.

The two patients (case 5 and 6), who benefited from efalizumab therapy, were treated for 10 and 12 months, respectively, and a gradual improvement was observed within 12 weeks of the therapy, which is in good agreement with previously reported successfully treated cases in the literature.^{7–10} This supports previous findings that in non-responders efalizumab should be administered for a longer time in order to have a positive therapeutic effect. In two cases (1 and 2) efalizumab was paused for 2 and 5 weeks due to serious flare up in atopic dermatitis, which may naturally have impaired the possible efficacy of the treatment. However, progression of disease (flare up) may also be seen as a side-effect to efalizumab.

All included patients had been treated with a standard regimen of efalizumab optimized for the treatment of psoriasis vulgaris. It cannot be excluded that different dosing schedule would be more appropriate for the treatment of atopic dermatitis. The strength of this study is, that, compared to single cases, where there is a tendency to positive reporting bias, this is a systematic study including all cases of efalizumab-treated atopic dermatitis patients in the Danish

hospital system. The weakness of the study is that data are retrospectively evaluated, and no scoring system was systematically used for assessment of the extent and severity of atopic dermatitis.

Conclusion

In this systematic retrospective study of efalizumab for treatment of severe atopic dermatitis, we found that 2 out of a total of 11 patients had a positive outcome defined as improvement and continuation of treatment for more than 6 months. Only the standard dose of efalizumab recommended for psoriasis was used, and no conclusion can be drawn on other treatment regimes.

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