

Efficacy of omalizumab in the treatment of atopic dermatitis: A pilot study

Lee E. Sheinkopf, M.D.,* Asif W. Rafi, M.D.,# LanAnh T. Do, M.D.,# Roger M. Katz, M.D.,# and William B. Klaustermeyer, M.D.*

ABSTRACT

Omalizumab is a unique biologic therapeutic drug approved for treating atopic patients with moderate to severe persistent allergic asthma with a serum IgE ranging from 30 to 700 IU/mL. This study was performed to examine the efficacy of omalizumab for the treatment of atopic dermatitis (AD), a disease with significant morbidity. A prospective analysis was performed to assess the efficacy of omalizumab in 21 patients with moderate to severe persistent allergic asthma and AD. Patients were stratified into the following groups: very high IgE (>700 IU/mL), high IgE (186–700 IU/mL), and normal IgE (0–185 IU/mL). AD severity was assessed at 0, 1, 3, 6, and 9 months via an Investigator Global Assessment index. Twenty-one patients (14–64 years old) were evaluated. Pretreatment IgE levels ranged from 18.2 to 8396 IU/mL, (mean IgE level was 1521 IU/mL). All 21 patients showed clinical and statistically significant improvement of their atopic dermatitis ($p < 0.00052$). In conclusion, this study indicates that omalizumab is effective in treating AD in patients with moderate to severe persistent allergic asthma.

(Allergy Asthma Proc 29:530–537, 2008; doi: 10.2500/aap.2008.29.3160)

Key words: Anti-IgE, asthma, atopic dermatitis, biologic therapeutic, IgE, investigator global assessment, omalizumab, prospective, treatment

Atopic dermatitis (AD) is a chronic and relapsing inflammatory skin disease affecting >10% of children and 1–3% of adults, with increasing prevalence and significant morbidity.^{1,2} It often precedes the occurrence of asthma, allergic rhinitis, and food allergy, otherwise known as the atopic march.^{3,4} Although AD is commonly associated with elevations in serum IgE, the diagnosis of AD is also clinical. It is based on findings of pruritic dermatitis, facial and extensor eczema in infants and children, flexural eczema in adults, and chronic or relapsing dermatitis.¹ The pathophysiological mechanisms behind AD involve a complex interplay of many different components of the immune system in addition to environmental and genetic factors, which makes the treatment of AD such a challenging task. The treatment mainly includes skin hydration, allergen and irritant avoidance, and topical corticosteroids. Topical steroids help abate the inflammation in AD but may have adverse

local effects such as dermal atrophy and risk of deleterious systemic side effects such as hypothalamic-pituitary-adrenal axis suppression.^{5–9} Systemic corticosteroids, cyclosporine A, mycophenolate mofetil, methotrexate, and azathioprine are agents for recalcitrant AD; however, they are associated with the risk of systemic toxicity. The topical calcineurin inhibitors, tacrolimus and pimecrolimus, are also treatments for AD. These agents have a good safety and efficacy profile.^{10–16}

AD involves many different components of the immune system. In the acute phase, there is emphasis of a Th2 immune response leading to the production of IL-4 and IL-13 (triggering production of IgE by B lymphocytes), IL-5 (important for recruitment and activation of eosinophils), and IL-6. Chronic AD is characterized by a switch from Th2 cells to Th1 cells with the subsequent up-regulation of interferon (IFN) γ and IL-5.^{17,18} Various antigen-presenting cells are also involved in this immunologic interplay, *viz.*, Langerhans cells, dendritic cells, and macrophages. Langerhans cells are increased in number in chronic AD lesions,^{19,20} express Fc ϵ RII and Fc ϵ RI (high affinity) IgE receptors, and have been found to be carrying IgE antibodies.^{21,22} When IgE binds to Fc ϵ RI, there is antigen presentation and a cascade of Th2 cell events.²³ Dermal dendritic cells and inflammatory dendritic epidermal cells also have an affinity to anti-Fc ϵ RI α receptors.²³ Other important cells known to be involved in AD include atopic keratinocytes, monocytes, macrophages, and mast cells.

From the *VA Greater Los Angeles Healthcare System/University of California, Los Angeles, Department of Allergy and Immunology, Los Angeles, California, and #Allergy Asthma Care Center, Inc., 11500 West Olympic Boulevard., Suite 630, Los Angeles, California

Presented at the annual meeting of the American College of Allergy, Asthma, and Immunology, Philadelphia, Pennsylvania, 2006

This study involved human subjects and was Institutional Review Board (Quorum IRB) approved

Address correspondence and reprint requests to Lee E. Sheinkopf, M.D., VA Greater Los Angeles Healthcare System/University of California, Los Angeles, Department of Allergy and Immunology, 11301 Wilshire Boulevard 111R, Los Angeles, CA 90073
Copyright © 2008, OceanSide Publications, Inc., U.S.A.

The possible role of IgE in AD has motivated much investigation into the molecular processes involved within the pathogenesis of AD. Recent investigation has led to therapies that target IgE, possibly adding to the arsenal of therapeutics for AD. Omalizumab (Xolair; Genentech, South San Francisco, CA) is a recombinant humanized monoclonal anti-IgE antibody, which blocks the interaction of IgE with high-affinity FcεRI and down-regulates dendritic cell, basophil, and mast cell FcεRI expression. It reduces free IgE in the serum and blocks the initial antigen presentation, the additional production of IgE, and also reduces the numbers of inflammatory cells such as eosinophils, B lymphocytes, and T-helper and T cytotoxic lymphocytes, as shown in patients with asthma^{24–26} and allergic rhinitis.^{24,27} It has also been shown to be efficacious and it has been Food and Drug Administration approved for the treatment of patients who are ≥12 years of age with moderate to severe persistent allergic asthma whose symptoms are not optimally controlled on asthma controller medications and with serum IgE ranging from 30 to 700 IU/mL. It is given subcutaneously every 2–4 weeks and dosing is based on serum IgE and body weight. It has been found to be effective in the treatment of other allergic disorders such as allergic rhinitis and peanut food allergy.²⁸ Few studies have investigated the use of omalizumab in treatment of AD,^{23,29–32} which is part of the atopic diathesis including asthma and allergic rhinitis. The primary objective of this study was to examine the efficacy of omalizumab for the treatment of AD in 21 patients aged 14–64 years with IgE levels ranging from 18 to 8396 IU/mL, with the majority of patients having food allergy as the trigger for their AD. Our pilot data has shown that omalizumab is effective in treating AD in patients with a broad range of serum IgE levels. In addition, this efficacy was seen relatively early in treatment and in patients with refractory disease.

METHODS

We conducted a prospective analysis on the therapeutic potential and efficacy of omalizumab in patients with AD, from the fall of 2003 through the winter of 2006. This was done at our investigational research center at The Allergy Asthma Care Center in Santa Monica, CA. Our study was Institutional Review Board (Quorum IRB) approved. Omalizumab was given subcutaneously (150 or 300 mg dosed every 2 weeks based on pretreatment serum IgE levels and body weight in kilograms) in 21 patients with moderate to severe persistent allergic asthma and a diagnosis of AD based on Hanifin and Rajka's criteria.³³ Our research team made an arbitrary decision to not dose above 300 mg every 2 weeks. All patients or their guardians (for patients <18 years old) signed the IRB-proved in-

formed consent agreement before participation. Pretreatment serum IgE levels were measured in all patients before starting omalizumab.

Twelve female and nine male patients ranging from 14 to 64 years old (mean age, 43 years) with mild, moderate, and severe AD were evaluated in a private practice setting with a mean pretreatment IgE level of 1521 IU/mL (range, 18.2–8396 IU/mL) over a period of 1–3 years. Patients were stratified into subgroups based on their pretreatment serum IgE level. Six patients were classified as very high IgE (>700 IU/mL), 10 patients were classified as high IgE (186–700 IU/mL), and 5 patients were classified as normal IgE (<186 IU/mL). Patients who entered the study were noted to have a diagnosis of AD for at least 24 months; however, this was not one of the inclusion criteria.

Major inclusion criteria included patients with moderate to severe persistent allergic asthma not optimally controlled on asthma controller medications, ages ≥12 years, diagnosis of AD, and showed IgE-mediated hypersensitivity to allergens. Major exclusion criteria included previous treatment with omalizumab, previous adverse reaction to omalizumab, age <12 years, patients taking immunosuppressive agents, and pregnancy. Patients were on concurrent medications during treatment with omalizumab including inhaled corticosteroids, inhaled β-agonists, antihistamines, antileukotrienes, topical steroid creams/ointments, and emollients or moisturizers. In addition, two patients were on immunotherapy before the study. Two patients were consistently taking oral corticosteroids for their severe persistent asthma (Table 1). IgE-mediated diseases included AD, oral allergy syndrome, allergic asthma, allergic rhinoconjunctivitis, urticaria, angioedema, latex allergy, and food allergy (which was a trigger for AD in all 17 patients with food allergy). Food-allergic patients were instructed to continue avoiding identified allergenic foods. Other related comorbidities included chronic rhinosinusitis, gastroesophageal reflux disease, and migraine headaches (Table 1). Once enrolled, patients were closely monitored at their routine visits and with routine phone calls every 2 weeks. All patients were observed for 60 minutes after injection. All patients were dispensed an Epi-Pen (Meridian Medical Technologies, Inc., Columbia, MD) and instructed how to use it should anaphylaxis occur. Assessment of clinical changes and any adverse effects were conducted at every patient visit. These assessments included a full physical examination, vital signs, and a detailed patient history of adverse effects at each visit before their subsequent injection. Quality of life measurements were completed using Juniper Quality of Life measurements at each visit interval. An Investigator Global Assessment (IGA), based on a modified Scoring Atopic Dermatitis (SCORAD) index,^{34,35} was used to calculate the sever-

Table 1 Patient demographics

Patient	Gender	Age (yr)	IgE*	IgE-Mediated Diseases	Initial Omalizumab Dose
1	M	47	6981	Asthma, allergic rhinitis, AD, food allergy (fish, shellfish, wheat, cow milk, and egg white)	300 mg every 2 wk
2	F	62	18	AD, asthma, contact dermatitis	150 mg every 4 wk
3	F	48	4237	Asthma, urticaria, food allergy (avocado, peanut, shellfish, and tree nuts), latex allergy, contact dermatitis, AD	300 mg every 2 wk
4	F	48	1918	Asthma, AD, food allergy (chicken, asparagus, cantaloupe, fish, and shellfish)	300 mg every 2 wk
5	M	62	209	Asthma, allergic rhinitis, food allergy (avocado), AD	150 mg every 2 wk; after 6 months 300 mg every 4 wk
6	M	14	599	Asthma, AD, food allergy (wheat, nuts)	300 mg every 2 wk
7	M	34	355	Moderate persistent asthma, allergic rhinitis, AD, food allergy (soy, shellfish, fish, peanut, and wheat)	300 every 2 wk
8	M	28	288	Moderate persistent asthma, allergic rhinitis, AD	300 mg every 4 wk
9	M	47	189	Persistent asthma, acute/chronic urticaria, food allergy, AD	150 mg every 2 wk
10	M	22	5278	Asthma, AD, food allergy (seafood, peanut, wheat, nut, cow milk)	300 mg every 2 wk
11	F	54	50	Asthma, latex allergy, AD, urticaria, food allergy (seafood)	300 mg every 4 wk
12	F	55	53	AD, gastroesophageal reflux disease, angioedema (after eating nuts, fish, shellfish, egg, tea, and raspberry), persistent asthma, vocal cord dysfunction, allergic rhinitis	150 mg every 4 wk
13	F	28	301	Persistent asthma, AD, food allergy, allergic rhinitis, gastroesophageal reflux disease, Crohn's disease	300 mg every 2 wk
14	F	56	450	Steroid-dependent asthma, AD, food allergy (apple, melons, mango, orange, and papaya), gastroesophageal reflux disease, chronic sinusitis/migraine headaches, urticaria	300 mg every 2 wk
15	F	64	503	Asthma, AD, allergic urticaria and angioedema after eating apples or rye, sensitive to pears, oranges, melons	300 mg every 2 wk
16	M	55	56	AD (face), steroid-dependent persistent asthma, gastroesophageal reflux disease	150 mg every 4 wk
17	M	47	204	Asthma, urticaria, AD, allergic rhinoconjunctivitis, migraine headaches	300 mg every 4 wk
18	F	27	516	asthma, AD, food allergy (orange, carrot, celery)	300 mg every 2 wk
19	F	20	618	Asthma, AD, food allergy (celery, peanuts, banana, and cantaloupe: all flare this patient's AD)	300 mg every 4 wk
20	F	45	716	Asthma, AD, food allergy (peanut, fish, shellfish, nuts, and legumes)	150 mg every 2 wk
21	F	37	8396	Asthma, AD	300 mg every 4 wk

*Initial IgE (IU/mL); mean IgE, 1525.

AD = atopic dermatitis.

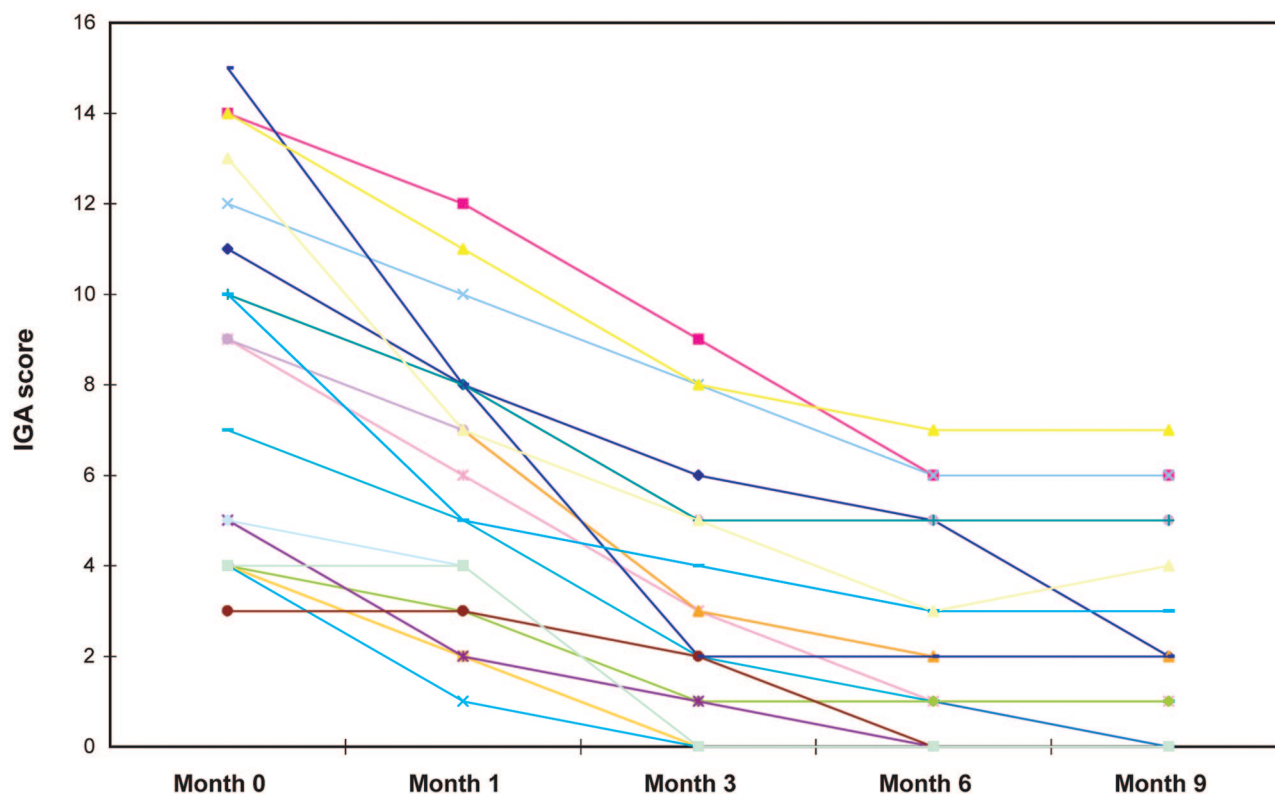


Figure 1. Efficacy of omalizumab on score for atopic dermatitis (SCORAD) scores with time. IGA, investigator global assessment.

ity of AD in each patient. These scores were calculated at months 0, 1, 3, 6, and 9 after starting omalizumab. The SCORAD was scored by the same investigator to prevent interobserver variability. Six markers of intensity—erythema or darkening, edema or papulation, oozing or crusting, excoriations, lichenification or prurigo, and dryness of uninvolved skin—were assessed to define the severity of AD lesions. Each marker of intensity ranged from 0 to 3 points (0 = none, 1 = mild, 2 = moderate, and 3 = severe). A final modified IGA score ranged from 0 to 18 (1–6 = mild AD, 7–12 = moderate AD, 13–18 = severe AD).

Statistical Analysis

A one-way analysis of variance (ANOVA) was performed to assess the statistical significance of the improvement of IGA scores. An ANOVA was calculated for the entire group of patients (21 patients) and within the five groups/correlated samples (months 0, 1, 3, 6, and 9).

RESULTS

All 21 patients completed the study. All IgE subgroups included patients with mild, moderate, and severe AD, except for the normal IgE subgroup, which did not include severe AD patients. All 21 (100%) patients showed clinical and statistically significant improvement of their AD over time based on

their IGA scores. When examining all 21 patients, statistical improvement was noted between mean IGA scores from month 0 to months 1, 3, 6, and 9 ($p < 0.01$). Statistical significance was also noted from month 1 to months 3, 6, and 9 ($p < 0.01$); month 3 to months 6 and 9; and month 6 to month 9 ($p < 0.01$; Fig. 1 and Table 2). We next examined the efficacy of omalizumab in different IgE subgroups (Table 2). Statistical significance was found within in all three IgE subgroups over time. Although improvement was noted in all three subgroups, a more profound improvement in SCORAD scores was noted in those patients with lower pretreatment serum IgE levels compared with those patients with high or very high IgE levels.

However, statistical significance was only shown between the patients with a normal IgE and patients with a very high IgE ($p < 0.05$). This is important because those patients with lower pretreatment serum IgE levels did not necessarily have less severe AD. Overall, one patient stopped their omalizumab after 6 months because of itching that was not related to their AD (Table 2). Interestingly, this patient's AD lesions did not relapse, during the last 3 months of the study, after stopping the omalizumab. In addition, two patients were not fully compliant with their interval dosing. These two patients obtained their omalizumab every 2–3 months when they were required to be dosed every

Table 2 IGA scores

Patient	IgE (IU/mL)	Month					
		0	1	3	6	9	12
1	6981	11	8	6	5	2	2
2	18	13	7	5	3	4	3
3	4237	9	6	3	1	1	—
4*	1918	9	7	5	5	5	—
5	209	3	3	2	0	0	0
6	599	7	5	2	1	1	1
7	355	14	11	8	7	7	6
8	288	5	2	1	0	0	0
9#	189	15	8	2	2	2	—
10	5278	12	10	8	6	6	5
11	50	4	4	0	0	0	0
12	53	5	4	0	0	0	0
13	301	4	1	0	0	0	0
14	450	13	7	3	2	2	2
15	503	4	2	0	0	0	0
16	56	10	5	4	3	3	3
17	204	10	8	5	5	5	4
18	516	4	3	1	1	1	0
19	618	4	3	2	1	0	0
20	716	4	3	2	2	2	—
21#	8396	14	12	9	6	6	6

*Patient stopped omalizumab dosing after 5th dose.

#Patient was very irregular with dosing intervals and received omalizumab every 2–3 mo instead of every 2–4 wk.

IGA = Investigator global assessment.

2 or 4 weeks (Table 2). These patients noted dramatic improvement of their AD lesions and continued to note significant improvement of their AD lesions even at 9 months, despite obtaining their omalizumab at longer than recommended intervals. Among the 17 patients with food allergy, on repeated accidental or intentional ingestion of the identified food, 4 patients reported no exacerbation of their AD (Tables 1 and 3). The two patients with AD associated with latex sensitivity also noted no exacerbation of their AD on repeated exposure to latex after having been on omalizumab for at least 6 and 9 months. The reexposure to foods and latex was not part of the study protocol; however, these outcomes were noted from patient reports at the interval visits.

DISCUSSION

We have examined the effects of omalizumab on moderate to severe allergic asthmatic patients with AD and have found significant and promising results. Our pilot data showed substantial clinical improvement of AD over time with a maximum omalizumab dose of 300 mg every 2 weeks. However, given the frequent monitoring of patients in this study, it is important to

take into account a possible placebo effect on the results.

Our study population of 21 patients is likely why we had variations in IgE values and severity of AD. Not all patients with AD, particularly severe AD, have elevated IgE levels, and this was seen in our study. In addition, those patients with severe and refractory AD were on maximal medical therapy for at least 12 months. There were six patients with a pretreatment serum IgE above 700 IU/mL. According to dosing calculations, the adjusted appropriate dose of omalizumab for these six patients would either be 300 mg every month or 375 mg every 2 weeks depending on body weight. If a patient is above 132 lb with an IgE over 700 IU/mL, dosing is not recommended. Doses above 375 mg are not endorsed by the Food and Drug Administration for the treatment of moderate to severe persistent allergic asthma and raise fears of adverse effects. The recommended total IgE levels for treatment ranges from 30 to 700 IU/mL, and this creates much uncertainty and hesitation in treating patients with levels above 700 IU/mL (as they may require a higher dose of omalizumab) moved and integrated into the results section.

Table 3 Notable clinical improvements while on omalizumab

Patient	Improvement
1	AD Improved after 1st dose. Patient able to eat shellfish after 9th dose without AD exacerbation
2	AD improved
3	Latex allergy improved after 1st dose; able to eat peanut after 3rd dose without AD symptoms, and avocado after 11th dose without AD symptoms
4	Improved AD after 4th/5th dose of Xolair
5	Improvement noted after 1st-2nd injection
6	AD improved after 4th dose
7	AD improved after 2nd dose
8	AD improved
9	AD improved
10	AD improved after 2nd dose
11	AD and latex allergy markedly improved after 11th dose; AD cleared after 16th dose
12	AD cleared after 2nd-3rd dose; able to eat nuts and coconut without any side effects (angioedema or AD) after 2nd dose; GERD symptoms cleared after 3rd dose
13	AD improved
14	AD improved
15	AD markedly cleared after 5th dose; food sensitivities decreased as well especially to tomato, potato, and oranges, and eventually no symptoms after 8th dose; able to eat all food after 9th dose
16	AD markedly cleared by 4th-5th dose
17	AD markedly cleared after 5th dose; AR/AC also cleared markedly after 5th dose
18	AD markedly cleared after 3rd- 4th dose
19	Improved AD after 1st dose of Xolair
20	AD improved mildly; major improvement of itching after 4th dosage
21	AD improved

AD = atopic dermatitis; AR = allergic rhinitis; AC = allergic conjunctivitis; GERD = gastroesophageal reflux disease.

In one study by Krathen and Hsu, three patients with chronic severe lichenified AD and other atopic comorbidities who were followed for 4 months on 450 mg of

omalizumab dosed every 2 weeks had no clinical response at 4 months.³¹ It was noted that these patient's pretreatment serum IgE levels ranged from 5440 to 24,000 IU/mL. It is possible that at such high pretreatment IgE levels there may need to be a higher dose used for clinical improvement. However, these high serum IgE levels may indicate another disease process, which may explain the lack of clinical response in these patients. On the other hand, as seen in our study, even at a pretreatment IgE level as high as 8396 (the highest IgE of all enrolled patients), there was still clinical improvement using a maximum dose of 300 mg every 2 weeks. In addition, clinical improvement was seen as early as 1 month in our study. This was noted in patients with IgE levels as high as 6000–8396 IU/mL (Table 2). In one pilot study, favorable clinical results were seen in patients with IgE levels up to 34,000 who were dosed at 150 mg of omalizumab every 2 weeks for 20 weeks. It was highlighted in this study that only a small amount of IgE was bound by omalizumab in these patients, and that this may suggest another immunologic alteration from this drug.³⁶

Administration of omalizumab and improvement in severity of AD was seen in a case series of three non-asthmatic patients aged 10–13 years old, presented by Lane *et al.*³² In Lane's study, three patients with refractory AD were followed. Their pretreatment serum IgE levels ranged from 1990 to 6120 IU/mL. This study showed clinical improvement in severity of AD with dosing of omalizumab as high as 450 mg given every 2 weeks over a 22-week period. These patients were already on additional therapy such as TMP-SMX, tacrolimus, topical steroids, antihistamines, and montelukast. Pretreatment IgE levels were high, although not exceedingly high, as seen in the two studies previously mentioned. Interestingly, in Lane's study, the AD of one patient (IgE = 2890 IU/mL) responded very well to omalizumab dosed at 300 mg every 2 weeks, which was the maximum dose given in our study. However, the AD of two other patients (IgE = 1990 and 6120 IU/mL) did not improve at doses of omalizumab lower than 450 mg every 2 weeks.

It is interesting to note how soon clinical improvement is seen in AD patients treated with omalizumab and if frequent dosing intervals are necessary to achieve this effect. In a study by Vigo *et al.*, seven patients with AD and asthma, aged 7–58 years old, were followed for 7 months.³⁰ The highest pretreatment serum IgE level was 2020 IU/mL, and the highest omalizumab dose used was 375 mg given every 2 weeks. An IGA score was used to assess AD severity. In this study, clinically significant results were noted at 3 months into therapy. However, statistical significance was only established from 0 to 7 months of therapy. Our study showed clinical improvement as soon as 1 month into therapy ($p < 0.05$) and AD lesions

continued to improve with the most pronounced results seen at 9 months into therapy. Two patients had missed injections. They received omalizumab at 2- to 3-month intervals and reported clinical improvement of their AD, with the best overall improvement at 9 months into therapy. This suggests that monthly or biweekly dosing may not be necessary to achieve clinical benefit.

The variation of serum IgE levels, dosing intervals, and dosing of omalizumab in the treatment of AD and the success of this therapy as seen in the aforementioned studies as well as our study poses the following question: How and why is omalizumab effective? With very elevated IgE levels in some patients, the efficacy of omalizumab in treating AD seems to be improbable based on its known mechanism of action, but clinical results are seen. As outlined by Soresi and Togias, immunomodulatory properties of anti-IgE may exist. An example is the down-regulation of IFN- α production by the cross-linking of IgE receptors on plasmacytoid dendritic cells and how anti-IgE might modulate IFN- α production. Other examples include anti-IgE recognition of membrane-bound IgE on B lymphocytes leading to opsonization of B lymphocytes or down-regulation of IgE production.³⁷ This was a mechanism also discussed by Belloni *et al.* whereby omalizumab may promote reduced IgE mRNA production. Could this therapy alter other immunologic pathways involved with AD even at very low doses and regardless of serum IgE levels? Perhaps only a small amount of high-affinity receptor down-regulation is required to promote further down-regulation of these receptors or inhibition of their production. Therefore, the removal of free IgE may not be the primary goal for therapeutic use of omalizumab in AD or other allergic disorders.

It is important to note that although asthma and allergic rhinoconjunctivitis control was not one of our primary outcome measures, all patients showed clinical improvement, subjectively and objectively, with respect to these atopic diseases. In addition, two patients had AD associated with latex sensitivity, and treatment with omalizumab controlled their AD despite continued reexposure to latex. Therefore, omalizumab may prevent the further exacerbation of AD by blocking the allergic response from latex exposure. Interestingly, this clinical correlation was also seen by Leynadier and colleagues. Their study showed the efficacy of omalizumab in allergic ocular and skin manifestations (dosed at 150–750 mg/month) in a double-blind, randomized, placebo-controlled study of health care workers with occupational latex allergy.³⁸ We also noted improvement of AD in those patients with peanut allergy and peanut reexposure. The efficacy for omalizumab and peanut allergy has already been shown in patients with systemic reactions. In a double-blind, randomized, placebo-controlled, dose-ranging

trial in 84 patients with a history of immediate hypersensitivity to peanuts, anti-IgE therapy had been shown to increase the threshold of sensitivity to peanuts on oral food challenge.²⁸

Clinical improvement of AD lesions as well as lack of clinical manifestations of food hypersensitivity were also seen in patients with other food allergies, besides peanut allergy, who were treated with omalizumab. Although not part of the study protocol and not recommended outside a controlled setting, these patients accidentally or intentionally reintroduced themselves to these foods while on omalizumab (Tables 1 and 3).

It has been shown that omalizumab displays a good safety profile when used for the treatment of asthma in adults and children.^{39–42} The most frequent adverse events include local reactions at the site of injection (45%) and viral infections (23%). Rare adverse events include rash, gastrointestinal events, and bleeding. Severe events include malignancy (0.5%) and anaphylaxis (0.1%).^{41,43–45} There is no evidence of immune complex disease or development of anti-omalizumab antibodies.⁴⁰ Given these possible adverse events, it is important to note that there were no major adverse events in our group of patients while on therapy, except for injection site irritation and minor local reactions. One patient discontinued omalizumab due to itching, and this was not related to their AD.

Long-term double-blind randomized placebo-controlled studies involving large numbers of patients solely with AD are necessary to define the efficacy of omalizumab in the treatment of this allergic disorder in patients with varying levels of IgE. In addition, dosing and dosing intervals still remain to be completely elucidated.

REFERENCES

1. Leung DY, Nicklas RA, Li JT, et al. Disease management of atopic dermatitis: an updated practice parameter. Joint Task Force on Practice Parameters, representing the American Academy of Allergy, Asthma, and Immunology, the American College of Allergy, Asthma, and Immunology, and the Joint Council of Allergy, Asthma, and Immunology. Work Group on Atopic Dermatitis. *Ann Allergy Asthma Immunol* 93:1–21, 2004.
2. Schultz-Larsen F, and Hanifin JM. Epidemiology of atopic dermatitis. *Immunol Allergy Clin North Am* 22:1–24, 2002.
3. Boguniewicz M, and Leung DY. Atopic dermatitis. *J Allergy Clin Immunol* 117(suppl):S475–S480, 2006.
4. Leung DY, Boguniewicz M, Howell M, et al. New insights into atopic dermatitis. *J Clin Invest* 113:651–657, 2004.
5. Boguniewicz M, Eichenfield LF, and Hultsch T. Current management of atopic dermatitis and interruption of the atopic march. *J Allergy Clin Immunol* 140(suppl):S140–S150, 2003.
6. Ellison JA, Patel L, Ray DW, et al. Hypothalamic pituitary-adrenal function and glucocorticoid sensitivity in atopic dermatitis. *Pediatrics* 105:794–799, 2000.
7. Lutgemeier MD, and Lubach D. Development and regression of dermal corticosteroid atrophy. 4. Concentration dependence of the skin thinning effect of triamcinolone acetonide. *Derm Beruf Umwelt* 35:55–57, 1987.

8. Oikarinen A, and Autio P. New aspects of the mechanism of corticosteroid-induced dermal atrophy. *Clin Exp Dermatol* 16: 416–419, 1991.
9. Hardie RA, Waring AJ, and Barnetson RS. Atrophic skin striae following the use of clobetasol propionate ointment. *Practitioner* 219:376–378, 1977.
10. Boguniewicz M. Update on atopic dermatitis: Insights into pathogenesis and new treatment paradigms. *Allergy Asthma Proc* 25:279–282, 2004.
11. Kapp A, Papp K, Bingham A, et al. Long-term management of atopic dermatitis in infants with topical pimecrolimus, a non-steroid anti-inflammatory drug. *J Allergy Clin Immunol* 110: 277–284, 2002.
12. Wahn U, Bos JD, Goodfield M, et al. Efficacy and safety of pimecrolimus cream in the long-term management of atopic dermatitis in children. *Pediatrics* 110:e2, 2002.
13. Ho VC, Gupta A, Kaufman R, et al. Safety and efficacy of non-steroid pimecrolimus cream 1% in the treatment of atopic dermatitis in infants. *J Pediatr* 142:155–162, 2003.
14. Chapman MS, Schachner LA, Bereneman D, et al. Tacrolimus ointment 0.03% shows efficacy and safety in pediatric and adult patients with mild to moderate atopic dermatitis. *J Am Acad Dermatol* 53(suppl):S177–S185, 2005.
15. Schachner LA, Lamerson C, Sheehan MP, et al. Tacrolimus ointment 0.03% is safe and effective for the treatment of mild to moderate atopic dermatitis in pediatric patients: Results from a randomized, double-blind, vehicle-controlled study. *Pediatrics* 116:e334–e342, 2005.
16. Hanifin JM, Paller AS, Eichenfield L, et al. Efficacy and safety of tacrolimus ointment treatment for up to 4 years in patients with atopic dermatitis. *J Am Acad Dermatol* 53(suppl):S186–S194, 2005.
17. Worm M. Novel therapies for atopic eczema. *Curr Opin Investig Drugs* 3:1596–1603, 2002.
18. Leung DY, and Soter NA. Cellular and immunologic mechanisms in atopic dermatitis. *J Am Acad Dermatol* 44:S1–S12, 2001.
19. Hanifin JM, and Chan S. Biochemical and immunologic mechanisms in atopic dermatitis: New targets for emerging therapies. *J Am Acad Derm* 41:72–77, 1999.
20. Uno H, and Hanifin JM. Langerhans cells in acute and chronic epidermal lesions of atopic dermatitis, observed by L-Dopa histofluorescence, glycol methacrylate thin section, and electron microscopy. *J Invest Dermatol* 75:52–60, 1980.
21. Bruynzeel-Koomen CA, Van Wichen DF, Toonstra J, et al. The presence of IgE molecules on epidermal Langerhans cells in patients with atopic dermatitis. *Arch Dermatol Res* 278:199–205, 1986.
22. Bieber T, de la Salle C, Wollenberg A, et al. Human Langerhans cells express the high-affinity receptor for immunoglobulin E. *J Exp Med* 175:1285–1290, 1992.
23. Novak N, and Bieber T. The role of dendritic cell subtypes in the pathophysiology of atopic dermatitis. *J Am Acad Dermatol* 53:S171–S176, 2005.
24. Peters S. The impact of comorbid atopic disease on asthma: Clinical expression and treatment. *J Asthma* 44:149–161, 2007.
25. Djukanovic R, Wilson SJ, Kraft M, et al. Effects of treatment with anti-immunoglobulin E antibody omalizumab on airway inflammation in allergic asthma. *Am J Respir Crit Care Med* 170:583–593, 2004.
26. Noga O, Hanf G, and Kunkel G. Immunological and clinical changes in allergic asthmatics following treatment with omalizumab. *Int Arch Allergy Immunol* 131:46–52, 2003.
27. Plewako H, Arvidsson M, Petruson K, et al. The effect of omalizumab on nasal allergic inflammation. *J Allergy Clin Immunol* 110:68–71, 2002.
28. Leung DY, Sampson HA, Yunginger JW, et al. Effect of anti-IgE therapy in patients with peanut allergy. *N Engl J Med* 348:986–993, 2003.
29. Forman SB, and Garrett AB. Success of omalizumab as monotherapy in adult atopic dermatitis: Case report and discussion of the high-affinity immunoglobulin E receptor, FcεRI. *Cutis* 80:38–40, 2007.
30. Vigo PG, Girgis KR, Pfuetze BL, et al. Efficacy of anti-IgE therapy in patients with atopic dermatitis. *J Am Acad Dermatol* 55:168–170, 2006.
31. Krathen RA, and Hsu S. Failure of omalizumab for treatment of severe adult atopic dermatitis. *J Am Acad Dermatol* 53:338–340, 2005.
32. Lane JE, Cheyney PA, Lane TN, et al. Treatment of recalcitrant atopic dermatitis with omalizumab. *J Am Acad Dermatol* 54: 68–72, 2006.
33. Hanifin JM, and Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol (Stockh) Suppl* 92:44–47, 1980.
34. Kunz B, Oranje AP, Labrèze L, et al. Clinical validation and guidelines for the SCORAD index: Consensus report of the European Task Force on Atopic Dermatitis. *Dermatology* 915: 10–19, 1997.
35. Pucci N, Novembre E, Cammarata MG, et al. Scoring atopic dermatitis in infants and young children: Distinctive features of SCORAD index. *Allergy* 60:113–116, 2005.
36. Belloni B, Ziai M, Lim A, et al. Low-dose anti-IgE therapy in patients with atopic eczema with high serum IgE levels. *J Allergy Clin Immunol* 120:1223–1225, 2007.
37. Soresi S, and Togias A. Mechanisms of action of anti-immunoglobulin E therapy. *Allergy Asthma Proc* 27(suppl 1):S15–S23, 2006.
38. Wu AC, Paltiel D, Kuntz KM, et al. Cost-effectiveness of omalizumab in adults with severe asthma: Results from the asthma policy model. *J Allergy Clin Immunol* 120:1146–1152, 2007.
38. Leynadier F, Doudou O, Gaouar H, et al. Effect of omalizumab in health care workers with occupational latex allergy. *J Allergy Clin Immunol* 113:360–361, 2004.
39. Dodig S, Richter D, Cepelak I, et al. Anti-IgE therapy with omalizumab in asthma and allergic rhinitis. *Acta Pharm* 55:123–138, 2005.
40. Ayres JG, Higgins B, Chilvers ER, et al. Efficacy and tolerability of anti-immunoglobulin E therapy with omalizumab in patients with poorly controlled (moderate-to-severe) allergic asthma. *Allergy* 59:701–708, 2004.
41. Vignola AM, Humbert M, Bousquet J, et al. Efficacy and tolerability of anti-immunoglobulin E therapy with omalizumab in patients with concomitant allergic asthma and persistent allergic rhinitis: SOLAR. *Allergy* 59:709–717, 2004.
42. Milgrom H, Berger W, Nayak A, et al. Treatment of childhood asthma with anti-immunoglobulin E antibody (omalizumab). *Pediatrics* 108:E36(1–10), 2001.
43. Nayak A, Casale T, Miller SD, et al. Tolerability of retreatment with omalizumab, a recombinant humanized monoclonal anti-IgE antibody, during a second ragweed pollen season in patients with seasonal allergic rhinitis. *Allergy Asthma Proc* 24: 323–339, 2003.
44. Weber RW. Adverse reactions to biological modifiers. *Curr Opin Allergy Clin Immunol* 4:277–283, 2004.
45. Walker S, Monteil M, Phelan K, et al. Anti-IgE for chronic asthma in adults and children. *Cochrane Database Syst Rev* 3:CD003559, 2004. □

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.