

but sustained disease activity at lower level at the end of treatment. In 3 patients, increase of dosage to 30 mg showed no advantage over 15 mg. There was no correlation between disease duration and treatment response, nor did cases that were readily put under pioglitazone fare better than those with many failed treatment trials before PPAR- γ rescue.

Our result is in line with later oral communications on October 27, 2011 from P. Mirmirani, MD, and from W. Bergfeld, MD, both in undisclosed numbers of patients.³ They report improvement in 50%, respectively 67% of cases, rather than remission. Baibergenova and Walsh⁴ studied 24 other patients and observed remission in 5 and some improvement in half of them. In our view the negative outcome in most cases challenges the treatment rationale and questions the usefulness of pioglitazone for LPP. Improvement in a minority of patients may be the result of a partial rescue of lost PPAR function, being only one in a spectrum of pathogenetic pathways; its restoration may be insufficient in most patients to repair all hits onto the follicle. Alternatively, it may reflect that tumor necrosis factor- α overexpression in LPP induces PPAR- γ down-regulation and that the positive result from pioglitazone is merely an anti-inflammatory effect. Not excluded in responders is a spontaneous halt of disease activity, LPP being self-limited over time. In fact, a more recent gene expression analysis in patients with LPP failed to reproduce deficient PPAR- γ expression.⁵

Philipp Spring, MD,^a Zoi Spanou, MD,^b and
Pierre A. de Viragh, MD^{a,b,c}

Dermatology University Clinic, Centre Hospitalier
Universitaire Vaudois (CHUV), Lausanne^a;
Dermatology University Clinic, Inselspital, Bern^b;
and private practice, Zurich,^c Switzerland

Funding sources: None.

Conflicts of interest: None declared.

Correspondence to: Pierre de Viragh, MD,
Schanzeneggstr. 1, 8002 Zurich/Switzerland

E-mail: pierre.deviragh@bin.ch

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<http://dx.doi.org/10.1016/j.jaad.2013.04.066>

Anti-IgE therapy and severe atopic dermatitis: A pediatric perspective

To the Editor: Omalizumab is a humanized monoclonal anti-IgE antibody that limits the release of mediators of the allergic response by reducing the surface-bound IgE on its high-affinity receptor on mast cells and basophils, and also by reducing high-affinity IgE receptor expression on basophils and tracheobronchial submucosal gland cells.¹ Its efficacy and safety has been proven in the treatment of atopic-related disease in the adult population.¹ Despite initial reports showing a lack of benefit from omalizumab in mild and moderate atopic dermatitis (AD), there is a growing body of evidence for benefit in severe disease.²⁻⁵ This evidence is mostly limited to the adult population with only 3 patients younger than 12 years included in previous case series.²⁻⁴

We report our experience with omalizumab in pediatric patients with severe AD. The criteria used at

Table 1. Criteria for omalizumab therapy for childhood atopic dermatitis at Sainte-Justine Hospital, Montréal, Quebec, Canada

Inclusion criteria

- 1) Atopic dermatitis onset before age 2 y
- 2) History of allergic rhinitis, asthma, or food allergy
- 3) Proven allergic sensitization as shown by skin prick tests or measure of serum-specific IgE for food or airborne allergens
- 4) SCORAD⁴ index >50, despite our standard treatment, defined as regular use of second-generation antihistamine, cysteinyl leukotriene receptor antagonist, and topical combination of emollients, high-potency corticosteroids, and calcineurin inhibitors
- 5) Elimination diet for specific food allergens has been attempted without benefit
- 6) Flow cytometry shows normal levels of lymphocyte subgroups
- 7) If clinically relevant, negative STAT-3 and DOCK-8 mutation analysis to rule out hyper-IgE syndrome

DOCK, Dedicator of cytokinesis; SCORAD, Scoring Atopic Dermatitis; STAT, Signal Transducer and Activator of Transcription.

Table II. Clinical details of 7 children with atopic dermatitis treated with omalizumab

Patient	Age, y/sex	Comorbidities	Positive tests*	Systemic therapy (before omalizumab)	Omalizumab dose (every 2 wk)	Treatment duration, mo	Serum IgE [§] , IU/L	SCORAD index (after 12 mo of treatment)
1	6F	Food allergies Asthma Allergic rhinitis 7 Skin infections	8 Aeroallergens 15 Food allergens [†]	Cyclosporin IVIG Azathioprine	225 mg or 0.001 mg/kg/IU	67	17,190 → 727	81.9 → 16.2
2	6F	Food allergies Asthma Allergic rhinitis 3 Skin infections	9 Aeroallergens 16 Food allergens [†]	None	225 mg or 0.003 mg/kg/IU	12	7520 → 1695	81.2 → 40.6
3	6M	Food allergies Asthma Allergic rhinitis 2 Skin infections	7 Aeroallergens 22 Food allergens [†]	Cyclosporin MMF	300 mg or 0.005 mg/kg/IU	12	8126 → 4527	53 → 21.5
4	11M	Food allergies Asthma Allergic rhinitis 6 Skin infections	9 Aeroallergens 12 Food allergens [†]	Cyclosporin	375 mg or 0.002 mg/kg/IU	15	10,291 → 4998	71.5 → 34.4
5	11M	Food allergies Asthma Allergic rhinitis 3 Skin infections	10 Aeroallergens 29 Food allergens [†]	Azathioprine MMF	375 mg or 0.001 mg/kg/IU	68	24,082 → 5457	69 → 27 [‡]
6	15M	Food allergies Asthma Allergic rhinitis 8 Skin infections	11 Aeroallergens 25 Food allergens [†]	Cyclosporin	375 mg or 0.002 mg/kg/IU	13	9051 → 5161	75 → 43
7	19F	Food allergies Asthma Allergic rhinitis 8 Skin infections	11 Aeroallergens 11 Food allergens [†]	None	375 mg or <0.001 mg/kg/IU	18	35,790 → 23,925	96.2 → 28

F, Female; IVIG, intravenous immunoglobulins; M, male; MMF, mycophenolate mofetil; SCORAD, Scoring Atopic Dermatitis.

*Determined by prick testing or IgE-specific analysis.

[†]Includes food with history of immediate allergic reactions, and sensitization to tolerated or unintroduced food.

[‡]Exception: SCORAD index measured only after 36 mo of treatment.

[§]Determined by Immulite (Siemens Medical Solutions, Malvern, PA).

our center for receiving anti-IgE therapy are listed in Table I. Omalizumab dosage was calculated according to the patient's mass and baseline serum IgE titers per manufacturer's guidelines, but never exceeded 375 mg by subcutaneous injection every other week. Oral antihistamines, cysteinyl leukotriene receptor antagonist, topical treatment with an emollient, calcineurin inhibitor, and corticosteroid preparation were continued but systemic therapy ceased at least 1 month before starting omalizumab (Table II).

Seven patients (aged 6-19 years) with severe AD were treated with omalizumab in the studied period (Table II). At baseline, AD was qualified as severe with a mean initial Scoring Atopic Dermatitis (SCORAD) index of 75.4 (53-96.2). All patients had high serum IgE levels with a mean value of 16,007 IU/L (7520-35,790 IU/L) (Table II). The mean equivalent dose of omalizumab administered was 0.0021 mg/kg/IU.

The first objective clinical improvement was observed after 3 to 6 months of treatment. The mean SCORAD index after 12 months was 30.0 (16.2-43), a mean improvement of 45.6 (31.6-59.6; $P < .0005$) (Table II). In patient 5, for whom the SCORAD index was not available at 12 months, a good clinical response was noted at 3 months and the SCORAD index decreased from 69 at baseline to 27 after 36 months of treatment (Table II). Over the follow-up period, the total serum IgE levels of all patients decreased to a mean level of 6610 IU/L; a mean reduction of 60.5% ($P = .007$) (Table II). After a mean follow-up period of 30 months of therapy, no adverse events were reported, with only 1 patient discontinuing omalizumab for scheduling reasons despite a good clinical response. Over this period, no patient needed other systemic treatment for AD control and the use of topical corticosteroids and calcineurin inhibitors decreased.

Our study is limited by the absence of a placebo control group. Placebo-controlled prospective trials are needed to clarify the role and efficacy of anti-IgE therapy in this patient population.

Jonathan Lacombe Barrios, MD,^{a,c} Philippe Bégin, MD,^{a,c} Louis Paradis, MD,^{a,c} Afshin Hatami, MD,^b Jean Paradis, MD,^a and Anne Des Roches, MD^c

Department of Medicine, Service of Allergy and Clinical Immunology, Centre Hospitalier de l'Université de Montréal^a; and Department of Pediatrics, Services of Dermatology^b and Allergy and Clinical Immunology,^c Centre Hospitalier Universitaire Sainte-Justine, Montréal, Quebec, Canada

Funding sources: None.

Disclosure: Drs Des Roches and Louis Paradis have received in the last 5 years an honorarium from Novartis Canada as investigators for a previous study. Drs Lacombe Barrios, Bégin, Jean Paradis, and Hatami have no conflicts of interest to declare.

Correspondence to: Anne Des Roches, MD, Centre Hospitalier Universitaire Sainte-Justine, 3175, Ch de la Côte-Sainte-Catherine, Montréal, Quebec, Canada H3T 1C5

E-mail: a.des.roches@umontreal.ca

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<http://dx.doi.org/10.1016/j.jaad.2013.05.035>

A pilot study evaluating the efficacy of botulinum toxin A in the treatment of Raynaud phenomenon

To the Editor: Raynaud phenomenon is characterized by severe vasospasm leading to pain, digital ulceration, and compromise in daily activities.¹ Efficacy of existing treatments is not uniform. Recent case series describe the use of onabotulinum toxin A (BTX) in the treatment of vasospastic episodes associated with Raynaud.^{2,3} We investigated BTX against placebo in the treatment of Raynaud-associated vasospasm.

After Emory Institutional Review Board approval, 10 patients with severe Raynaud (ie, history of digital infarcts or ulcerations, standard therapy failure, or impending digital amputation) were recruited from dermatology and rheumatology clinics. Exclusion criteria included pregnancy, BTX allergy, mild Raynaud, and myasthenia gravis.

Patients were randomized to receive BTX injections into either the left or right hand, while the contralateral hand was injected with saline. The patient and the assessor were both blinded to the randomization scheme. A 100-U vial of BTX was diluted with 2 mL of 0.9% sodium chloride. BTX was