and assist families in understanding the rationale for a particular medication regimen to increase compliance and decrease exacerbations.

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Theresa A. Bingemann, MD
Rochester, NY

IMMUNOTHERAPY, IMMUNOMODULATION, PREBIOTICS/PROBIOTICS

A Randomized Controlled Study of Peanut Oral Immunotherapy: Clinical Desensitization and Modulation of the Immune Response

Varshney P, Jones SM, Scurlock AM, et al. *J Allergy Clin Immunol.* 2011;127(3):654–660

PURPOSE OF THE STUDY. To determine if peanut oral immunotherapy (OIT) was safe and effective in inducing desensitization in peanut-allergic children. Previous studies on peanut OIT did not include a placebo control.

STUDY POPULATION. Studied were 28 children aged 1 to 16 with peanut allergy defined by clinical history of reaction after ingestion, an elevated peanut immunoglobulin E (IgE) level of >15 kU/L, or an IgE level of >7 kU/L if a significant reaction had occurred within the previous 6 months. All subjects had had a positive skin-prick test result to peanut.

METHODS. Subjects began with an initial dose escalation, with build-up visits every 2 weeks, until a maintenance dose of 4000 mg was reached. Home dosing was continued daily between build-up visits. An oral food challenge (OFC) to peanut occurred around week 48, after at least 1 month of maintenance. Skin-prick testing, cytokine production, and peanut IgG_4 and IgE and T-regulatory cell levels were assessed during treatment.

RESULTS. Peanut OIT significantly increased the amount of peanut tolerated at the OFC compared with placebo (mean: 5000 vs 280 mg, respectively; $P < .001$). Three peanut OIT-treated subjects withdrew because of adverse allergic effects. The peanut-OIT group showed a reduction in skin-test size and interleukin 5 and interleukin 13 levels and increases in peanut IgG_4, and IgE, and T-regulatory cell levels.

CONCLUSIONS. The results of this study clearly showed that peanut OIT induces desensitization as well as marked changes in the immune response in subjects with peanut allergy.

REVIEWER COMMENTS. This study is novel in that it is the first placebo-controlled study of peanut OIT. The study found dramatic efficacy for OIT in inducing desensitization to peanut, as well as concomitant immunologic changes. If OIT is going to become a mainstay of therapy for food allergy, future research will need to address adverse effects of OIT, the optimal duration of OIT, and the efficacy of OIT in inducing long-term tolerance. The sublingual route of immunotherapy for peanut was evaluated in a companion study reported on in the same issue and also showed promise for efficacy and safety (Kim EH, Bird JA, Kulis M, et al. *J Allergy Clin Immunol.* 2011;127[3]:640–646).

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Jessica Savage, MD
Corinne Keet, MD
Baltimore, MD

Immunologic Effects of Sublingual Immunotherapy: Clinical Efficacy Is Associated With Modulation of Programmed Cell Death Ligand 1, IL-10, and IgG_4

Piconi S, Trabattoni D, Rainone V, et al. *J Immunol.* 2010;185(12):7723–7730

PURPOSE OF THE STUDY. To evaluate an optimal treatment regimen for sublingual immunotherapy (SLIT) and investigate the underlying mechanism.

STUDY POPULATION. There were 62 Italian patients aged 19 to 60 years enrolled from a clinic in Milano, Italy, between February and September 2009. Inclusion criteria were a clinical history that suggested ragweed sensitization, a positive skin-prick-test result to ragweed pollen, and a clinical report of asthma and/or rhinoconjunctivitis.

METHODS. The patients were randomly assigned to 1 of 4 treatment arms: preseasonal SLIT (5 months); seasonal SLIT (3 months); prolonged SLIT (5 months × 3 years); or no SLIT. Subjects on SLIT were treated with a median Amba1 (major ragweed allergen) dose of 120 mg/day. Clinical outcomes were recorded in daily diaries by the subjects during pollen season. Immunologic outcomes were assessed just before the initiation and completion of the SLIT regimen in the treatment groups and at the beginning and end of the study in the control groups. Clinical efficacy was evaluated with a visual analog scale. Lymphocyte subsets were evaluated by flow cytometry. Peripheral blood mononuclear cells were isolated and incubated with and without Amba1, and their cytokine profiles were analyzed by flow cytometry. Amba1-specific immunoglobulin G_4 (IgG_4) was measured by an enzyme-linked immunosorbent assay.

RESULTS. Clinical outcomes improved in all SLIT regimens compared with controls. This improvement was significantly better in the prolonged-SLIT (5 months × 3 years) compared to the other SLIT regimens. Cytokine analysis of $CD4^+$ T lymphocytes, $CD19^+$ B lymphocytes, and $CD14^+$ monocytes revealed the following: interleukin 4 (IL-4)–producing cells were reduced in all SLIT regimens compared with controls, and IL-10–producing cells were

increased in all SLIT regimens compared with controls. These results were statistically significant compared with controls in all but $CD4^+$ IL-4–producing cells, and the results were similar across all treatment arms. All SLIT regimens resulted in an increase in Amba1-specific IgG_4, and this increase was most impressive in the prolonged-SLIT treatment arm.

CONCLUSIONS. Although all SLIT regimens resulted in an improvement in clinical efficacy, prolonged SLIT was the most effective. The reduction in IL-4 and increase in IL-10 production is consistent with observations from subcutaneous immunotherapy studies and provides insight into the mechanism of SLIT. These cytokine changes might serve as an objective marker of efficacy of SLIT for patients on treatment.

REVIEWER COMMENTS. Further evaluation of SLIT is of particular importance in the pediatric population because of its less invasive method of administration compared with injection immunotherapy and its improved safety profile. However, more studies are needed before the therapy makes it to US practice.

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Erika Torjusen, MD
Elizabeth C. Matsui, MD, MHS
Baltimore, MD

Efficacy and Safety of Timothy Grass Allergy Immunotherapy Tablets in North American Children and Adolescents

Blaiss M, Maloney J, Nolte H, Gawchik S, Yao R, Skoner SP. *J Allergy Clin Immunol.* 2011;127(1):64–71, 71.e1–71.e4

PURPOSE OF THE STUDY. To investigate the efficacy and safety of timothy grass allergen immunotherapy (AIT) treatment using sublingual tablets in children and adolescents with grass pollen–induced allergic rhinoconjunctivitis (ARC).

STUDY POPULATION. Three hundred forty-five subjects, aged 5 to 17 years, with a clinical history of physician-diagnosed grass pollen–induced ARC with or without asthma were studied.

METHODS. This was a double-blind, randomized, placebo-controlled, parallel-group, multicenter, phase III study. Subjects were randomly assigned (1:1) to once-daily sublingual grass AIT treatment (2800 bioequivalent allergen units; 15 μg of Phlp5) or placebo. Treatment began ~16 weeks before the grass pollen season (GPS) and continued through the entire GPS for a total treatment period of 23 weeks. The total combined score was a summation of the daily symptom score and daily medication score, which were predefined. Immune parameters were measured over time. Safety was measured on the basis of reported adverse events.

RESULTS. The mean total combined scores for the entire GPS were significantly less in the grass-AIT group than in the placebo group by 26% ($P = .001$). The mean daily symptom score was significantly less in the grass-AIT group than the placebo group by 25% ($P = .005$). The improvements in scores for ocular and nasal symptoms were 28% and 23%, respectively, were noted in the AIT group ($P = .003$). The median daily medication score was significantly reduced in the grass-AIT group by 81% ($P = .006$). There was a significant improvement in quality of life in the AIT group that was greatest at the peak of the season (38%) when compared with the entire season (18%). Treatment with grass AIT did not significantly reduce asthma symptom scores. Levels of Phlp5-specific immunoglobulin G_4 (IgG_4)- and IgE-blocking factor were similar between the 2 groups at baseline and increased over time in the grass-AIT group ($P < .001$). Grass AIT was generally well tolerated, but 82% experienced some adverse events, primarily oral and throat pruritus and/or irritation. One subject in the AIT group received epinephrine for dose-related angioedema, dysphagia, and cough.

CONCLUSIONS. Allergen immunotherapy using sublingual grass pollen tablets is effective in the treatment of grass pollen–induced ARC with anticipated and acceptable adverse effects.

REVIEWER COMMENTS. This is the first North American study to show effective symptom control and an acceptable safety profile in children and adolescents with grass pollen–induced ARC by using a sublingual tablet for dose delivery. There was no increase in the outcome of asthma attacks, and there was improvement in quality of life at the peak of the allergy season. These results show promise for future therapy targeting children and adolescents for immunotherapy using an effective, safe, and easy-to-deliver alternative to traditional subcutaneous injection immunotherapy.

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Rohit D. Divekar, MD, PhD
Stacie M. Jones, MD
Little Rock, AR

Prevention of Allergy in Infants of Allergic Mothers by Probiotic *Escherichia coli*

Lodinová-Zádníková R, Prokesová L, Kocourková I, Hrdý J, Zizka J. *Int Arch Allergy Immunol.* 2010;153(2):201–206

PURPOSE OF THE STUDY. To study the effect of after-birth oral colonization by a probiotic *Escherichia coli* strain in infants of allergic mothers to reduce occurrence of allergy later in life.

Immunologic Effects of Sublingual Immunotherapy: Clinical Efficacy Is Associated With Modulation of Programmed Cell Death Ligand 1, IL-10, and IgG_4

Erika Torjusen and Elizabeth C. Matsui

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