Abstract and Introduction

Abstract

Specific allergen immunotherapy has been practiced for allergic rhinoconjunctivitis for over 100 years and is the only treatment option that is disease modifying. In the USA, immunotherapy is usually administered via subcutaneous injection; this is the only route with a US FDA-approved formulation. There is growing interest in developing US-standardized formulations for the sublingual route, but up until recently there have been few US trials. Most of the experience with sublingual immunotherapy (SLIT) comes from Europe, where it is widely used and there is a large body of literature supporting its use. The purpose of this review is to summarize recent adult and pediatric clinical trials of SLIT in the USA. Most of the trials are for inhalant allergies, but there is some early work on SLIT as a novel therapy for food allergies.

Introduction

Presently, only subcutaneous immunotherapy is approved by the US FDA for inhalant and stinging insect allergies in the USA. Sublingual immunotherapy (SLIT) has been used with increasing frequency in Europe and is being viewed with increased interest by US allergists as an alternative to subcutaneous immunotherapy.

The first published double-blind, placebo-controlled, randomized clinical trial (DBPC-RCT) with inhalant SLIT came from London, UK in 1986. This was followed by numerous studies from Europe in the last two decades, which confirmed the efficacy and safety of SLIT. Some novel studies include the first DBPC-RCT on allergoid SLIT tablets in 1998 and the first DBPC-RCT of SLIT successfully treating atopic dermatitis in dust mite-sensitized children.

Important work has also gone into elucidating the underlying mechanism of SLIT. The current thought is that tolerogenicity is induced by oral dendritic cells, which reside on the uppermost layers of oral tissue and in the context of SLIT, capture allergen and produce IL-10 and IL-12 cytokines. This thereby promotes a tolerogenic pathway and a T-cell shift from a Th2 to a Th1 and Treg phenotype. Treg cells further propagate the Th1 pathway by producing IL-10 and TGF-β that negatively feedback on Th2 cytokines and subsequently cause a decrease in IgE levels and an increase in IgG4 levels.

In the USA, there was early work performed on SLIT for cat allergy in 1993; however, this aside, there were no other published DBPC-RCTs until the past few years. Renewed interest may be, in part, due to the advent of two SLIT grass pollen tablets – Grazax® and Oralair®, approved for use in Europe in the late 2000s. These SLIT tablets are currently undergoing trials in the USA. Here we review those and other recent US clinical trials for inhalant and food SLIT.

US SLIT Trials for Inhalant Allergies

In 2008, the first steps toward establishing US-standardized sublingual allergenic extracts were made with a Phase I safety and dosing trial of timothy grass (*Phleum pretense*), short ragweed (*Ambrosia artemisiifolia*), house dust mite (*Dermatophagoides farinae*), and cat hair extracts administered via a metered dose pump with a sublingual actuator. A total of 91 adults 18–50 years of age with allergic rhinitis were enrolled (nine timothy grass, 25 dust mite, 25 ragweed and 32 cat hair). Approximately a third had concurrent asthma and participants underwent a single-session dose-escalation regimen followed by an 8-week, open label daily self-administered course of SLIT. Treatment was administered outside of the peak allergy season. Adherence to the therapy in patients who completed the study averaged approximately 80%. Most patients reached monthly cumulative doses equivalent to 10–100-times the recommended subcutaneous immunotherapy doses.

The dose-escalation procedure was shown to be safe, eliciting only mild to moderate symptoms. During the treatment phase, local symptoms were the most common, accounting for 90.9% of all adverse events and were mostly characterized by rhinoconjunctivitis and oral-mucosal itching and irritation. Systemic adverse effects, such as those involving the lungs or skin, accounted for 9.1% of all adverse events. There were 14 withdrawals (four due to noncompliance, seven due to adverse events during the 8-week treatment period, three due to adverse events during the single-session dose escalation). No epinephrine was used, although one patient with cat allergy who owned a cat did go to the emergency department for anaphylaxis (increased rhinitis symptoms, chest discomfort and shortness of breath...
These initial ragweed and house dust mite SLIT studies highlight the fact that polysensitization is often a factor in monotherapy studies; patients with aphthous ulcers and gastrointestinal conditions may be more vulnerable to adverse effects from SLIT. 

A patient with irritable bowel syndrome noted increased diarrheal symptoms while receiving the low-dose SLIT. The authors suggested that oral aphthous ulcer experienced localized swelling and pruritus at the site after receiving the initial dose of the high-dose vaccine. One increased asthma symptoms of moderate severity that lasted for 3 months and required occasional use of albuterol. One patient with an escalation, one in the low dose SLIT group for nausea and diarrhea during dose escalation, and two in the placebo group). Adverse events increased at 6 months and at the end of the study (12–18 months). In the high dose SLIT group there was a significant increase in the bronchial threshold to allergen challenge.

There were four possible treatment-related withdrawals (one in the high dose SLIT group for abdominal cramps and diarrhea during escalation, one in the low dose SLIT group for nausea and diarrhea during dose escalation, and two in the placebo group). Adverse events, particularly mouth and throat irritation, were common in both treatment groups. One subject in the high-dose group experienced increased asthma symptoms of moderate severity that lasted for 3 months and required occasional use of albuterol. One patient with an oral aphthous ulcer experienced localized swelling and pruritus at the site after receiving the initial dose of the high-dose vaccine. One patient with irritable bowel syndrome noted increased diarrheal symptoms while receiving the low-dose SLIT. The authors suggested that patients with aphthous ulcers and gastrointestinal conditions may be more vulnerable to adverse effects from SLIT.

These initial ragweed and house dust mite SLIT studies highlight the fact that polysensitization is often a factor in monotherapy studies;
Patients were randomized to once-daily 2800 bioequivalent allergen units of timothy SLIT tablet (approximately 15 µg of Phl p 5 daily, which is approximately 30-times the standard subcutaneous immunotherapy dose) as monotherapy, or the same dose of timothy extract plus nine additional pollen extracts (other tree and weed pollens) regardless of whether they were sensitive to the extract. SLIT was then administered for 10 months, the first 4 weeks of which were a build-up phase, and the last 2 months of which coincided with the following grass season. Dose adjustments were allowed at visits. The SLIT was administered initially with a dropper bottle, but later was switched to pump glass bottles.

Fifty three of the 58 subjects completed the study (reasons for withdrawal were noncompliance: two, adverse event: one, other: two), all of whom reached the highest allowed dose. Overall compliance was approximately 80%. For the primary outcomes, there was no significant difference in the symptom or medication scores among the three groups. This may have been due to record low rainfall in the region leading to 2008 grass pollen counts that were much lower than in the observational season of 2007; thus, all the three groups had improved medication and symptom scores during the second grass pollen season.

Although no effect in the primary outcome was detected, differences in multiple relevant secondary outcomes suggested a positive effect. Subjects who were treated with timothy monotherapy had significantly improved nasal challenge results and increased timothy-specific IgG4 compared with placebo. Both the timothy monotherapy group and the multiallergen group had significantly improved titrated skin prick test results and increased timothy-specific IgE compared with placebo. This pattern suggests that timothy SLIT monotherapy has a positive immunomodulatory effect, but the effect is lost when coadministered with multiple allergens. The reason for this is not clear.

In terms of adverse events, in the timothy monotherapy group, 84% of subjects experienced adverse events and in the multiallergen group, 65% of subjects experienced adverse events compared with placebo (6%). Most of the adverse events were mild in nature and included itching, burning, irritation, numbness and tingling sublingually or in the mouth. Other side effects included swelling of the sublingual area or mouth, sore throat, cold sores, hay fever symptoms, heartburn and nausea. None of the subjects experienced urticaria, bronchoconstriction or other systemic symptoms during the study. One subject dropped out of the multiallergen group because of adverse effects of persistent lip and mouth swelling.

The studies described up to this point applied the sublingual-swallow method of SLIT. This involves keeping the allergy extract drops under the tongue for approximately 2 min then swallowing. An alternative to this delivery method is the allergy immunotherapy tablet, which dissolves quickly under the tongue. Nelson et al. studied 438 adults aged 18–65 years with allergic rhinitis in a Phase III DBPC-RCT of timothy grass SLIT tablet in Canada and USA. Although most patients (85%) were polysensitized, they were excluded if they had allergies to overlapping, noncross-reactive allergens. Asthma was a coexisting condition in approximately a quarter of the patients. There was an observational period before and during the 2008 grass pollen season. Patients were randomized 1:1 to once-daily 2800 bioequivalent allergen units of timothy SLIT tablet (15 µg Phl p 5) or placebo. There was no build-up dosing, the first three doses were administered on-site, and the remaining doses were home-administered. Dosing started approximately 16 weeks before the anticipated 2009 grass pollen season and continued through its duration.

A total of 367 patients completed the study (reasons for withdrawal were adverse event: 19, noncompliance: 24, other: 28). There was a 20% improvement in the primary outcome of mean total combined daily symptom and daily medication score during the peak and entire season. There was also a 24% improvement in total asthma symptom score and asthma medication score, although overall the asthma symptom/medication score was low. Phl p 5-specific IgG4 and IgE blocking antibodies increased with treatment, which is consistent with a beneficial effect of immunotherapy. This trial was among the first to show effectiveness of timothy SLIT in adults in North America. The improvements in symptom and medication scores were comparable with results from Europe and Canada.

Similar to studies with SLIT drops, there was a high rate of local adverse events with the SLIT tablets (oral pruritus, throat irritation, ear pruritus, oral paresthesia, mouth edema and mouth erythema). There was one treatment-related asthma exacerbation that was moderate in severity. There were seven serious adverse events but only one assessed as possibly treatment related (abdominal pain in a placebo patient). Two subjects were administered epinephrine. One was in the treatment group and experienced dysphagia, uvular edema, pharyngeal edema, flush and chest discomfort within minutes of the first dose and was ultimately discontinued from the trial.

As a pediatric counterpart to this study, Blaiss et al. carried out a multicenter DBPC-RCT involving 41 American and eight Canadian sites to investigate clinical efficacy and safety of sublingual timothy grass tablets in children with grass pollen allergic rhinoconjunctivitis with or without asthma. This was a 2-year study that included an initial observation period followed by a treatment period of 23 weeks including preseasonal and seasonal time periods. The subjects were children 5–17 years of age. A total of 282 subjects completed the trial (140 in the placebo group and 142 in the grass treatment group). Approximately a quarter of patients had coexisting asthma.

Patients were randomized to once-daily 2800 bioequivalent allergen units of timothy SLIT tablet (approximately 15 µg of Phl p 5) or
placebo. The primary end point was total combined score (sum of daily symptom score plus daily medication score). Secondary end points were the combined average weekly scores of the validated Rhinoconjunctivitis Quality of Life Questionnaire.

With treatment, there was a 26% relative reduction in mean total combined score. Specifically, the improvement in mean daily symptom score (28%) was comparable to that seen in studies with European children despite the shorter duration of the grass pollen season.[16] There was also a 38% improvement in quality-of-life score at the peak of grass pollen season and 18% improvement averaged over the entire season. Unlike the aforementioned European study, there was no improvement in asthma symptoms, probably because children enrolled in the USA study had well-controlled asthma at baseline and the study was not powered to see a change in asthma improvement. Both Phl p 5-specific IgG4 and IgE-blocking factor levels increased, which is consistent with a beneficial immunomodulatory effect.

Adverse events were reported in both treatment (70%) and placebo (25%) groups. The most common reaction was oral pruritus and throat irritation. One patient in the treatment group had an asthma event related to the treatment but did not require further medical treatment. One patient reported lip angioedema, mild dysphagia and intermittent cough after the first dose of timothy SLIT on day 1 of the study. The symptoms resolved after investigator-administered epinephrine. Five subjects had serious adverse events, but none were considered treatment related. There were no reports of aspiration of tablets.

This was the first study to show that the timothy SLIT tablet was effective and safe in North American children after just one grass pollen season. There have been no other studies published yet on inhalant SLIT in US children, but there are at least 11 registered in the USA, currently in progress or completed,[101] for a variety of inhalant allergens including cockroach, grass pollen and house dust mite.

Preliminary data from two other large-scale multicenter DBPC-RCTs in the USA have been promising. The first is a Phase III trial of a sublingual tablet containing five grass pollen allergen extracts (cocksfoot, sweet vernal grass, rye grass, meadow grass and timothy). [17,18] A total of 437 adults aged 18–65 years with allergic rhinitis were randomized to receive daily 300 index of reactivity sublingual tablet (which corresponds to approximately 20 µg of the group’s five major allergens) or placebo starting 4 months before the pollen season and continuing through its duration. There were a high proportion of polysensitized patients, but overlapping allergens were excluded. Positive results were reported for total combined symptom and medication score as well as secondary efficacy end points, including individual symptom and medications scores and patient quality-of-life assessment. Adverse events were mostly mild to moderate, and included throat irritation, oral pruritus, ear pruritus, mouth edema and oral paresthesia. No serious drug-related adverse events occurred.

The second study, which is also promising, evaluates ragweed SLIT tablet. A total of 565 adults were randomized to daily ragweed SLIT tablet (6 or 12 Amb a 1-U) or placebo.[19–21] Treatment was initiated approximately 4 months before and continued throughout ragweed season. Both treatment groups showed significant mean improvement in total nasal and ocular scores compared to placebo during peak ragweed season. There were no reports of systemic allergic reactions. Based on the results of this ragweed SLIT tablet study and the three grass SLIT tablet studies mentioned previously, it appears that SLIT tablets will have a higher likelihood for FDA approval compared with the SLIT drops. See for a summary of the US trials for inhalant SLIT published to date.

Table 1. Summary of published randomized, double-blind, placebo-controlled US clinical trials for inhalant Sublingual immunotherapy in allergic rhinoconjunctivitis.

<table>
<thead>
<tr>
<th>Study (year)</th>
<th>Study population</th>
<th>Allergen/vehicle/maintenance dose</th>
<th>SLIT regimen/duration/timing of treatment</th>
<th>Clinical efficacy</th>
<th>Immunological change</th>
<th>Treatment-related adverse events</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skoner et al. (2010)</td>
<td>115 adults aged 18–50; &lt;10% with asthma; 18 withdrew</td>
<td>Ragweed/glycerol/medium dose: 4.8 µg Amb a 1 daily. High dose: 48 µg Amb a 1 daily</td>
<td>1-day rush dose-escalation then daily self-administration/17 weeks/preseasonal and co-seasonal</td>
<td>High dose: improved medication score during peak season. No difference in symptom scores</td>
<td>High dose: increase in sIgG. No difference in sIgE, sIgG4, sIgA, nasal provocation</td>
<td>Frequent oral-mucosal AE. Three withdrew due to gastrointestinal AE, one due to rash, one due to uvula swelling. No anaphylaxis</td>
<td>[11]</td>
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Frequent oral-
<table>
<thead>
<tr>
<th>Authors</th>
<th>Study Population</th>
<th>Study Design</th>
<th>SLIT Description</th>
<th>Symptoms/Signs</th>
<th>AE</th>
</tr>
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<tbody>
<tr>
<td><strong>Bush et al.</strong></td>
<td>31 adults aged 18–50; ten with asthma; ten withdrew</td>
<td>Dust mite/glycerol/low dose: 1 µg Der f 1 daily. High dose: 70 µg Der f 1 daily</td>
<td>4-week build-up then daily self-administration/12–18 months/no specific timing</td>
<td>No difference in symptom or medication scores</td>
<td>mucosal AE. Two withdrew due to gastrointestinal AE. One had increased asthma. No anaphylaxis</td>
</tr>
<tr>
<td><strong>Amar et al.</strong></td>
<td>58 adults aged 18–70; five with asthma; five withdrew</td>
<td>Timothy/glycerol/single allergen: 19 µg Phl p 5 daily. Multiallergen: 19 µg Phl p 5 plus nine additional allergens daily (trees, weeds)</td>
<td>4-week build-up then daily self-administration/15 months/preseasonal and co-seasonal</td>
<td>No difference in symptom or medication scores</td>
<td>Frequent oral-mucosal AE. One withdrew due to persistent lip and mouth swelling. No anaphylaxis</td>
</tr>
<tr>
<td><strong>Nelson et al.</strong></td>
<td>439 adults age 18–65; 23% with asthma; 391 included in intent-to-treat analysis</td>
<td>Timothy/tablet/15 µg Phl p 5 daily</td>
<td>No build-up, daily self-administration (first three doses observed on site)/23 weeks/preseasonal and co-seasonal</td>
<td>20% improvement in combined symptom and medication score (p = 0.005)</td>
<td>Increase in slgG4 and IgE-blocking factor. One asthma event. One event required epinephrine (dysphagia, uvular and pharyngeal edema and macular rash, chest discomfort)</td>
</tr>
<tr>
<td><strong>Blaiss et al.</strong></td>
<td>345 children age 5–17; 26% with asthma; 307 included in intent-to-treat analysis</td>
<td>Timothy/tablet/15 µg Phl p 5 daily</td>
<td>No build-up, daily self-administration (first three doses observed on site)/23 weeks/preseasonal and co-seasonal</td>
<td>26% improvement in combined symptom and medication score (p = 0.001)</td>
<td>Increase in slgG4 and IgE-blocking factor. Frequent oral-mucosal AE. One event required epinephrine (lip edema, dysphagia and cough)</td>
</tr>
</tbody>
</table>

AE: Adverse event(s); slgE: Specific IgE; slgG: Specific IgG; SLIT: Sublingual immunotherapy; tSPT: Titrated skin prick test.

**US SLIT Trials for Food Allergies**

Although most of the SLIT studies have focused on inhalant allergies, there is some early work on SLIT as a novel therapy for food allergy. Food allergy is a condition for which currently there is no treatment other than avoidance. Here the authors review well-described US pediatric trials of peanut SLIT,[22,23] and SLIT versus oral immunotherapy (OIT) for cow's milk allergy.[24]

A small US study investigated SLIT for peanut allergic children in a DBPC-RCT.[22] Eighteen children aged 1–11 years (median age 5.2 years) were studied over a 1-year period. The study consisted of 6 months of SLIT dose escalation followed by 6 months of maintenance,
Skin-prick reactivity to cow's milk decreased and cow's milk-specific IgG4 levels increased in all three groups. Basophil activity as there was evidence of immunological changes, but the data did not necessarily correlate with the clinical outcome of desensitization. There was evidence of immunological changes, but the data did not necessarily correlate with the clinical outcome of desensitization. After 60 weeks of maintenance dose, patients underwent an open food challenge with 8 g of cow's milk protein. The food challenge threshold increased in all patients: 40-fold for SLIT/SLIT, 54-fold for lower dose SLIT/OIT and 159-fold for the higher dose SLIT/OIT. One patient in the SLIT/SLIT group, four patients in the lower dose SLIT/OIT group, and three patients in the higher dose SLIT/OIT group required albuterol administration. There was no evidence of anaphylaxis in any patient. The data suggests that peanut SLIT can induce desensitization, which is defined as a temporary increase in the threshold dose of food allergen required to cause an allergic reaction. But long-term studies will be required to evaluate for oral tolerance, which is the permanent loss of allergic reactivity and the end point that allows for discontinuation of therapy. Another group compared SLIT to OIT for peanut allergic children in a DBPC-RCT.[23] Twenty one US children aged 7–13 years were randomized to active SLIT/placebo OIT or active OIT/placebo SLIT. After initial escalation, SLIT/OIT doses were increased biweekly or weekly to 3696 mg/day SLIT and 2000 mg/day OIT of peanut protein. A 10 g double-blind, placebo-controlled food challenge was performed after 6 months of maintenance. Prior to the study being unblinded, preliminary data was reported on nine children who had completed the 6-month food challenge. Results on the nine showed that there was a significant increase in median challenge threshold (246 mg) and significant changes in total and peanut-specific IgE, IgG4, and skin-prick-test wheal diameter. Symptoms elicited by the 4772 home doses included: 15.4% oropharyngeal, 10.2% gastrointestinal, 3.8% lower respiratory, 2.4% skin and 0.9% upper respiratory. Treatment included antihistamines (43.2% of doses), β2-agonists (1.3%) and epinephrine (one dose). Once the ongoing study is complete, the groups will be unblinded, and we will see if there is a difference in response between OIT and SLIT for peanut. Cow's milk has also come into consideration for SLIT. In an open label, randomized US trial of SLIT alone versus combined SLIT and OIT for cow's milk allergy, 30 children aged 6–17 years were evaluated.[24] Inclusion criteria were cow's milk-specific IgE level greater than 0.35 kUa/l, >3 mm wheal on skin prick test to cow's milk and a positive double-blind, placebo-controlled food challenge to cow's milk at baseline. Exclusion criteria included severe persistent asthma, history of intubation secondary to asthma exacerbation, or anaphylaxis due to cow's milk requiring intensive care unit admission. Twenty eight patients completed the study (two withdrew because of adverse events). Participants underwent a dose-escalation regimen with cow's milk SLIT, followed by randomization into one of three groups: crossover into OIT lower dose (target dose 1 g), crossover into OIT higher dose (target dose 2 g), or continuing with SLIT alone (target dose 7 mg cow's milk protein). The number of total adverse reactions was not different between groups, but the number of multisystem reactions was 11-times higher in the OIT groups, mainly because they received much higher cumulative doses owing to the volume and concentration restraints of SLIT. Epinephrine was given twice after patients receiving SLIT aspirated the dose and four times during OIT. After 60 weeks of maintenance dose, patients underwent an open food challenge with 8 g of cow's milk protein. The food challenge threshold increased in all patients: 40-fold for SLIT/SLIT, 54-fold for lower dose SLIT/OIT and 159-fold for the higher dose SLIT/OIT. One out of ten in the SLIT/SLIT group, six out of ten in the higher dose SLIT/OIT group, and eight out of ten in the lower dose SLIT/OIT group passed the 8 g milk challenge. Six out of the 15 subjects who passed the oral challenge went on to lose desensitization within 6 weeks of being off therapy (three required epinephrine). This study showed that OIT was superior to SLIT alone at inducing desensitization to cow's milk. Desensitization was lost as early as one week off therapy. There was evidence of immunological changes, but the data did not necessarily correlate with the clinical outcome of desensitization. Skin-prick reactivity to cow's milk decreased and cow's milk-specific IgG4 levels increased in all three groups. Basophil activity as...
measured by spontaneous histamine release decreased significantly in the SLIT/OIT groups only, but expression of basophil activation markers CD63 and CD203c did not significantly change. Cow's milk-specific IgE initially increased then decreased in the SLIT/OIT groups, but not the SLIT/SLIT group.

The same group did a post hoc study on the children from the SLIT/SLIT arm who, after 60 weeks of maintenance, reacted to less than 4 g of cow's milk protein on food challenge. They crossed these eight children over to OIT. Dose escalation was started at less than a quarter of the tolerated food challenge dose and escalated to 2 g daily for 1 year. Preliminary data showed that 24.4% had side effects on OIT. Overall, the two escalation time periods studied showed similar reaction rates (6 weeks of SLIT escalation before OIT vs 60 week SLIT escalation before OIT). However, there were fewer severe side effects and rescue medications used in OIT group after prolonged SLIT escalation treatment of 60 weeks. The rates of desensitization for this study have not yet been reported, but based on the improved safety profile the authors suggest that extending SLIT therapy before starting OIT may be a beneficial approach.

Expert Review & Five-year View

SLIT has been demonstrated in US studies to be efficacious and safe in the limited number of allergens evaluated so far. Hopefully this will lead to FDA approval for this treatment in the near future. It appears from the studies discussed that SLIT by tablet will have a higher likelihood of FDA approval compared with SLIT drops. We should see the development of other common allergens in tablet form for SLIT, including dust mites, tree pollen and cat hair over the next several years. Studies will need to be performed to determine if mixed unrelated allergens given together by the SLIT method will demonstrate clinical efficacy and safety. We may likely see further studies looking at the disease-modifying aspects of SLIT and whether early treatment with SLIT in children at risk for allergy and asthma may prevent their development. Food studies will continue to assess the role of SLIT versus OIT that will hopefully lead to better and safer means of inducing desensitization and tolerance to improve the lives of the increasing growing population of people with food allergy in the USA.

Sidebar

Key Issues

- Most of the sublingual immunotherapy (SLIT) data up until the latter part of this decade came from Europe. With the growing interest in developing US-standardized SLIT formulations, there is an increasing number of trials in progress or completed in the USA.

- Large, well-designed adult and pediatric US trials have shown that SLIT is generally safe and well-tolerated. Efficacy data have been mixed, but appear better for SLIT table than SLIT drops.

- Adverse events in the US SLIT trials are similar to those seen in the European trials. Most patients have some mild and local reactions that are tolerable and do not usually result in medication discontinuation. The rate of systemic effects is low.

- Questions remain with regards to the mechanisms of action of SLIT, treatment schedules, duration of treatment, optimal dose and delivery method, cost–effectiveness and safety profile in high-risk patients such as severe asthmatics.

- Early work in food SLIT suggests some benefit as to desensitization, but this has been limited to a few small trials.

References


   - A detailed, comprehensive review on Sublingual immunotherapy (SLIT) worldwide and discusses unmet needs.


• Shows that the grass SLIT tablet, Grazax®, has a sustained disease modifying effect.


• Shows that the grass SLIT tablet, Oralair™, has a sustained disease modifying effect.


•• The first study to demonstrate efficacy of grass SLIT tablet in US children.


• This is the first study to demonstrate efficacy of peanut SLIT in US children.


• This is the first study to compare the efficacy of oral immunotherapy versus SLIT for cow's milk allergy in children.


Website


Papers of special note have been highlighted as:

• of interest

•• of considerable interest