Homerton University Hospital NHS
NHS Foundation Trust

Immunotherapy for Severe Allergic Rhinitis & bee/wasp venom allergy

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bsaci
improving allergy care
through education, training and research

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BSACI GUIDELINES

Immunotherapy for allergic rhinitis

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Clinical & Experimental Allergy

Summary

Allergic rhinitis (AR) affects more than 20% of the population in the United Kingdom and western Europe and represents a major cause of morbidity that includes interference with usual daily activities and impairment of sleep quality. This guidance prepared by the Standards of Care Committee (SOCC) of the British Society for Allergy and Clinical Immunology (BSACI) is for the management of AR in patients that have failed to achieve adequate relief of symptoms despite treatment with intranasal corticosteroids and/or antihistamines. The guideline is based on evidence and is for use by both adult physicians and paediatricians practising allergy. During the development of these guidelines, all BSACI members were included in the consultation process using a web-based system. Their comments and suggestions were carefully considered by the SOCC. Where evidence was lacking, consensus was reached by the experts on the committee. Included in this guideline are indications and contraindications for immunotherapy, criteria for patient selection, the evidence for short- and long-term efficacy of subcutaneous and sublingual immunotherapy,

The Problem

- Tight" chest
- Wheezy chest
- Waking at night
- Blocked nose
- Runny nose
- Itchy, red eyes
- Itchy mouth, throat & ears
- Irritability
- Poor concentration
- Tiredness
- Poor performance at work or school
- Reduced quality of life

Conventional treatment

- Avoidance
- Physical barrier
- Close windows
- Stay in the house/change clothes/shower
- Antihistamines
- Topical corticosteroid spray
- Sodium cromoglycate eye drops
- Anti-leukotrienes

Immunotherapy

House of Lords Science & Technology Committee
Review and Recommendations on Allergy 2007

Key recommendation:

Immunotherapy is a useful resource in the prophylactic treatment of life threatening allergies or whose allergic disease does not respond to other medication

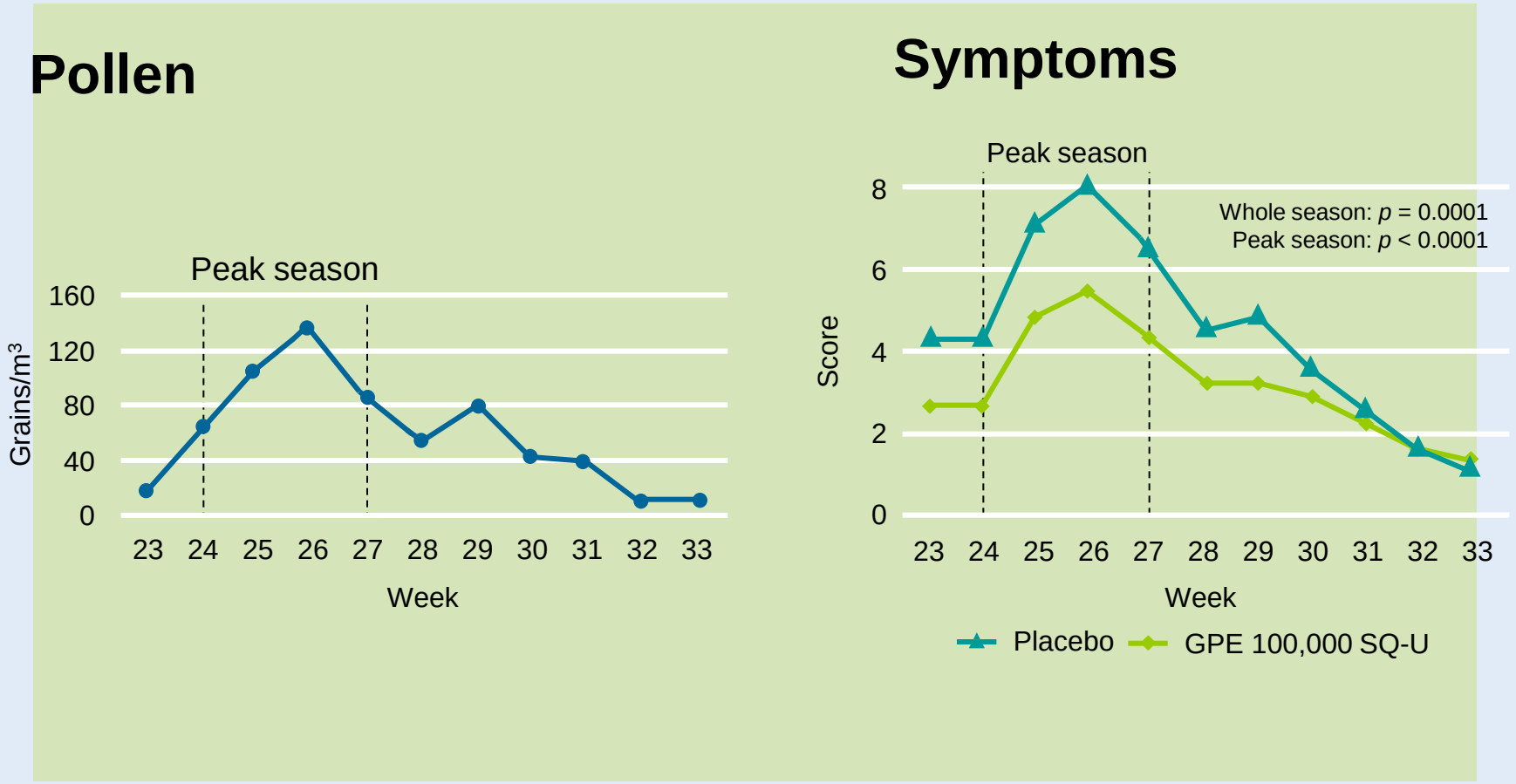
What is it?

- Allergen immunotherapy involves the repeated administration of allergen extracts with the aim of reducing symptoms on subsequent allergen exposure, improving quality of life (QoL) and inducing long-term tolerance.
- In the case of venom allergy this effect is potentially life saving.
- Can be given by injection or sublingual tablet/ drops

Does it work?

- Studies show a 30 – 58% decrease in symptoms for tree, grass & HDM treatments.
- Cochrane review +
- Category 1a evidence [grading according to Scottish Intercollegiate Guidelines Network (SIGN) www.sign.ac.uk/)] for efficacy in adults and children to support both SCIT and SLIT for allergic rhinitis.

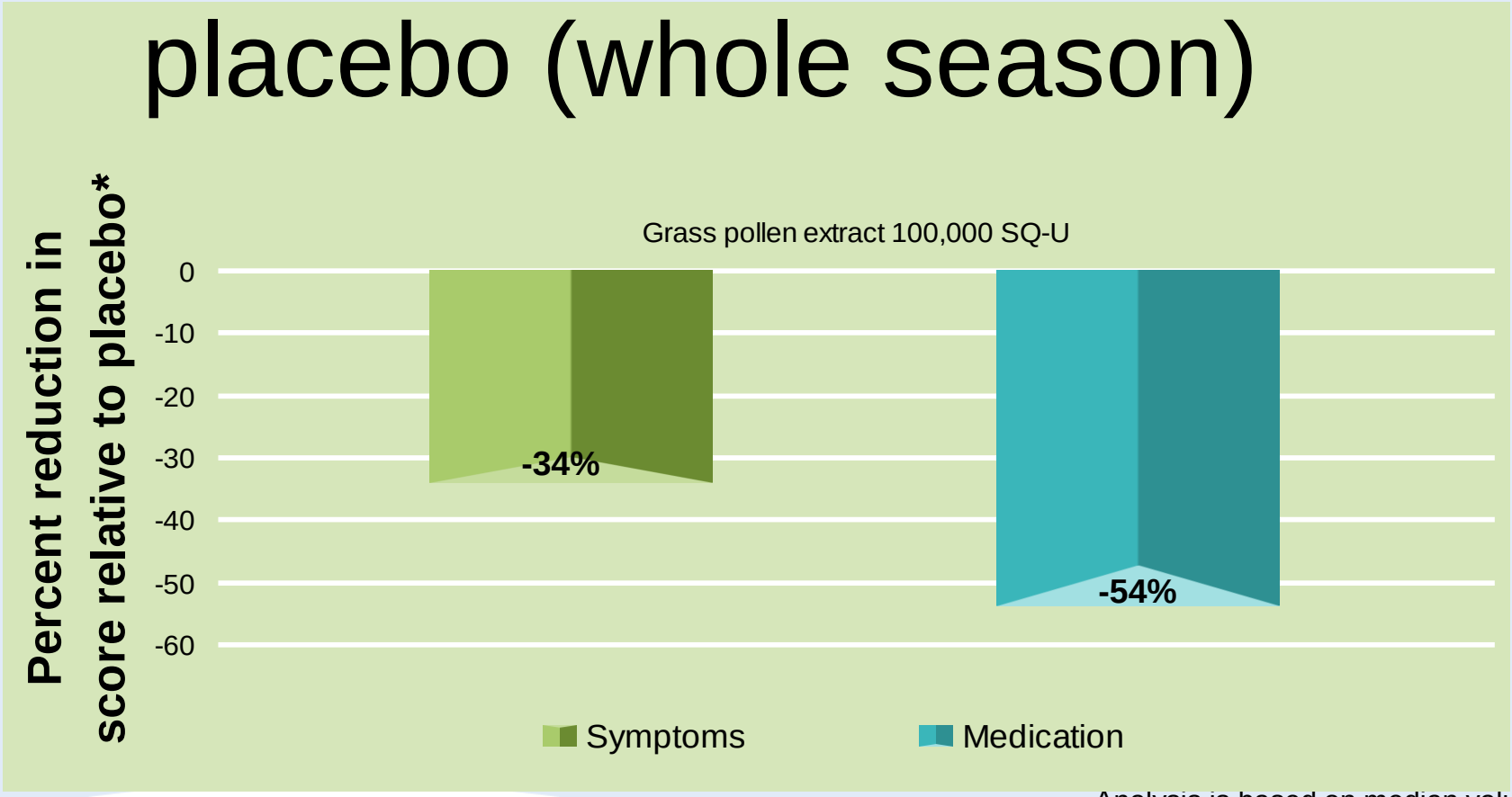
Pollen count and symptom scores during the pollen season (1 year)



GPE = grass pollen extract
= standardised quality units

Frew AJ *et al. J Allergy Clin Immunol* 2006;117:319-25

Reduction in symptom and medication scores relative to placebo (whole season)



*** Patients had access to symptomatic medications**

Analysis is based on median values
SQ-U = standardised quality units

Frew AJ *et al. J Allergy Clin Immunol* 2006;117:319-25

ADDITIONAL BENEFIT OF A THIRD YEAR OF SPECIFIC GRASS POLLEN ALLERGOID IMMUNOTHERAPY IN PATIENTS WITH SEASONAL ALLERGIC RHINITIS

European Annals of Allergy and Clinical Immunology - volume 39 - n° 4 -

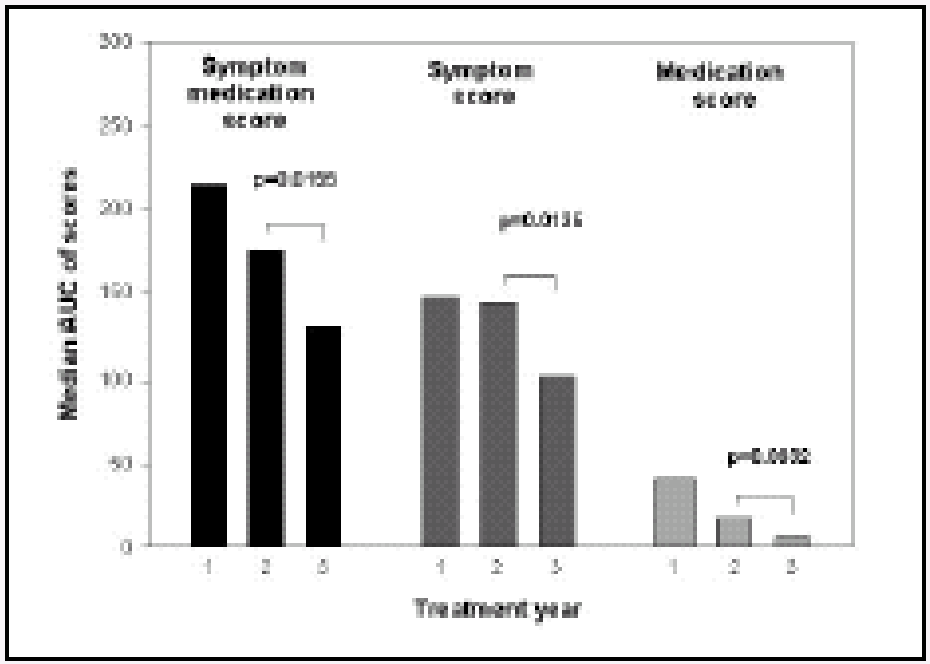
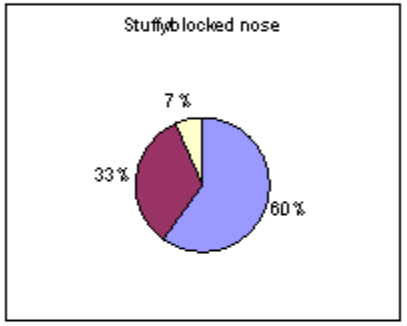


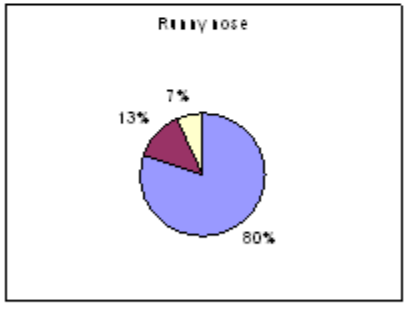
Figure 1: Symptom medication score (SMS), symptom score and medication score during treatment years 2002 to 2004 in patients treated preseasonally with the hypoallergenic preparation. Median values. Full analysis set (n=61).

Results of a pre and post Quality of Life questionnaire – Impact of treatment on severe seasonal allergic rhinitis
Homerton Adult Immunotherapy Clinic

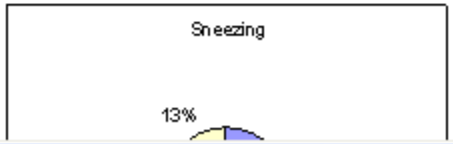
Nasal Symptoms



60% of patients were on average 54% less troubled by a stuffy or blocked nose.



80% of patients were on average 57% less troubled by a runny nose.



74% of patients were on average 62%

A cure for allergy

- “been able to sleep better, able to spend all day in the park….improved social life”.
- “Dramatic improvement in symptoms…”
- “Very happy with improvement”
- “Was able to be outside (and go), running which in previous years has not been possible”
- “Symptoms dropped by half and seemed (to last) a shorter time”.
- “Compared with two years ago my hay fever is now non existent”.

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Immunotherapy Preventive Effect

Multicentre, controlled & randomised. 205 infants (aged 6-14 years) with grass and/or birch allergic rhinoconjunctivitis. Three years SIT treatment. 3, 5 & 10 years evaluation.

Asthma, rhinitis, other respiratory diseases

Pollen immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis (the PAT-Study)

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Background: Children with allergic rhinitis are likely to develop asthma.
Objective: The purpose of this investigation was to determine whether specific immunotherapy can prevent the development of asthma and reduce bronchial hyperresponsiveness in children with seasonal allergic rhinoconjunctivitis.
Methods: From 6 pediatric allergy centers, 205 children aged 6 to 14 years (mean age, 10.7 years) with grass and/or birch pollen allergy but without any other clinically important allergy were randomized either to receive specific immunotherapy for 3 years or to an open control group. All subjects had moderate to severe hay fever symptoms, but at inclusion none reported asthma with need of daily treatment. Symptomatic treatment was limited to loratadine, levocabastine, sodium cromoglycate, and nasal budesonide. Asthma was evaluated clinically and by peak flow. Methacholine bronchial provocation tests were carried out during the season(s) and during the winter.
Results: Before the start of immunotherapy, 20% of the children had mild asthma symptoms during the pollen season(s). Among those without asthma, the actively treated children had significantly fewer asthma symptoms after 3 years as evaluated by clinical diagnosis (odds ratio, 2.52; $P < .05$). Methacholine bronchial provocation test results improved significant in the active group ($P < .05$).
Conclusion: Immunotherapy can reduce the development of asthma in children with seasonal rhinoconjunctivitis. (J Allergy Clin Immunol 2002;109:251-6.)

Key words: Prevention, specific immunotherapy, bronchial hyperresponsiveness, asthma, rhinitis

A link between hay fever and asthma is evident,[1,2] and more than 70% of asthma patients report nasal symptoms.[3] Approximately 20% of all hay fever patients develop asthma later in life.[4,5] It has been found that 11% to 73% of hay fever patients show bronchial hyperresponsiveness (BHR) outside the pollen season[6-9] and that up to approximately 50% of such patients show BHR during the season.[9,10] Rhinitis frequently precedes the onset of asthma,[11,12] and patients with allergic rhinitis who also have BHR are more likely to develop asthma.[6,10,13]

The clinical efficacy of specific immunotherapy (SIT) treatment for pollen allergy has been confirmed in several studies.[14-18] One investigation showed that none of the patients who initially had only hay fever developed asthma during the total study period of 8 years,[19] and in a study of oral immunotherapy in children with pollinosis, 31% of those in the placebo group, in comparison with none in the active group, developed asthma.[20] The only long-term investigation of the preventive potential of SIT showed a significant reduction in the number of children who developed asthma.[21]

In birch pollen–allergic patients with mild to moderate asthma, SIT can reduce BHR.[15] Although the process is not understood in detail, SIT has a profound influence on the immune system, and the clinical changes achieved appear to persist for many years.[22]

The primary aim of the present study was to investigate whether SIT with birch and/or timothy pollen allergen extracts in children with hay fever could reduce the risk of developing asthma and/or influence BHR.

METHODS

Patients

A total of 208 children aged 6 to 14 years from European 6 pediatric centers were included in the study; of these, 205 were randomized after a baseline season (season 0; Table I). Each of the chil-

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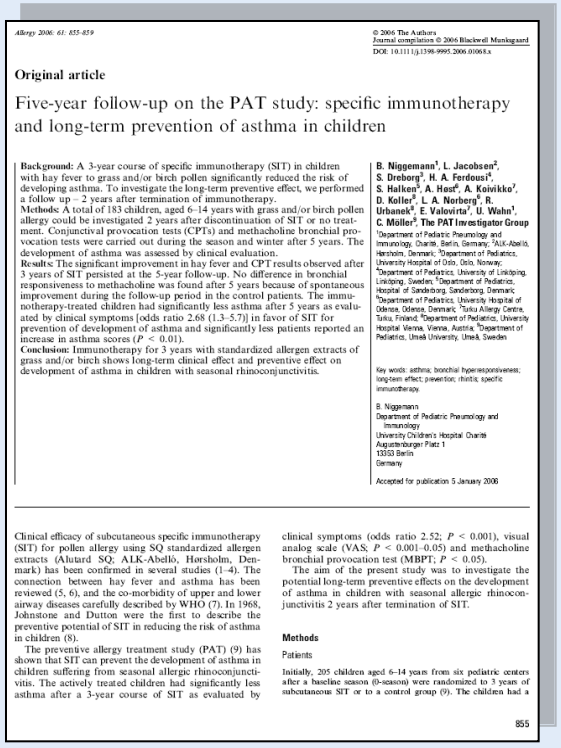

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Original article

Five-year follow-up on the PAT study: specific immunotherapy and long-term prevention of asthma in children

Background: A 3-year course of specific immunotherapy (SIT) in children with hay fever to grass and/or birch pollen significantly reduced the risk of developing asthma. To investigate the long-term preventive effect, we performed a follow up – 2 years after termination of immunotherapy.
Methods: A total of 183 children, aged 6–14 years with grass and/or birch pollen allergy could be investigated 2 years after discontinuation of SIT or no treatment. Conjunctival provocation tests (CPTs) and methacholine bronchial provocation tests were carried out during the season and winter after 5 years. The development of asthma was assessed by clinical evaluation.
Results: The significant improvement in hay fever and CPT results observed after 3 years of SIT persisted at the 5-year follow-up. No difference in bronchial responsiveness to methacholine was found after 5 years because of spontaneous improvement during the follow-up period in the control patients. The immunotherapy-treated children had significantly less asthma after 5 years as evaluated by clinical symptoms [odds ratio 2.68 (1.3–5.7)] in favor of SIT for prevention of development of asthma and significantly less patients reported an increase in asthma scores ($P < 0.01$).
Conclusion: Immunotherapy for 3 years with standardized allergen extracts of grass and/or birch shows long-term clinical effect and preventive effect on development of asthma in children with seasonal rhinoconjunctivitis.

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Key words: asthma; bronchial hyperresponsiveness; long-term effect; prevention; rhinitis; specific immunotherapy.

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Clinical efficacy of subcutaneous specific immunotherapy (SIT) for pollen allergy using SQ standardized allergen extracts (Alutard SQ; ALK-Abelló, Hørsholm, Denmark) has been confirmed in several studies (1–4). The connection between hay fever and asthma has been reviewed (5, 6), and the co-morbidity of upper and lower airway diseases carefully described by WHO (7). In 1968, Johnstone and Dutton were the first to describe the preventive potential of SIT in reducing the risk of asthma in children (8).

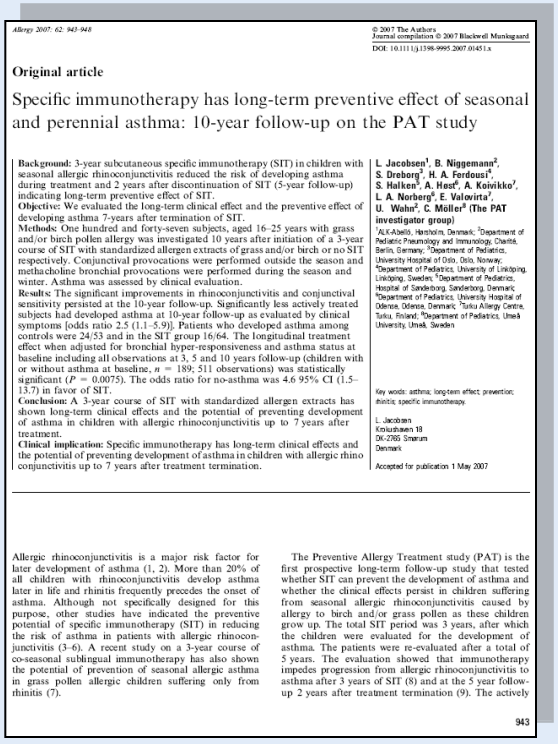
The preventive allergy treatment study (PAT) (9) has shown that SIT can prevent the development of asthma in children suffering from seasonal allergic rhinoconjunctivitis. The actively treated children had significantly less asthma after a 3-year course of SIT as evaluated by clinical symptoms (odds ratio 2.52; $P < 0.001$), visual analog scale (VAS; $P < 0.001–0.05$) and methacholine bronchial provocation test (MBPT; $P < 0.05$).

The aim of the present study was to investigate the potential long-term preventive effects on the development of asthma in children with seasonal allergic rhinoconjunctivitis 2 years after termination of SIT.

Methods

Patients

Initially, 205 children aged 6–14 years from six pediatric centers after a baseline season (0-season) were randomized to 3 years of subcutaneous SIT or to a control group (9). The children had a



Allergy 2007: 62: 943–948

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Original article

Specific immunotherapy has long-term preventive effect of seasonal and perennial asthma: 10-year follow-up on the PAT study

Background: 3-year subcutaneous specific immunotherapy (SIT) in children with seasonal allergic rhinoconjunctivitis reduced the risk of developing asthma during treatment and 2 years after discontinuation of SIT (5-year follow-up) indicating long-term preventive effect of SIT.
Objective: We evaluated the long-term clinical effect and the preventive effect of developing asthma 7-years after termination of SIT.
Methods: One hundred and forty-seven subjects, aged 16–25 years with grass and/or birch pollen allergy was investigated 10 years after initiation of a 3-year course of SIT with standardized allergen extracts of grass and/or birch or no SIT respectively. Conjunctival provocations were performed outside the season and methacholine bronchial provocations were performed during the season and winter. Asthma was assessed by clinical evaluation.
Results: The significant improvements in rhinoconjunctivitis and conjunctival sensitivity persisted at the 10-year follow-up. Significantly less actively treated subjects had developed asthma at 10-year follow-up as evaluated by clinical symptoms [odds ratio 2.5 (1.1–5.9)]. Patients who developed asthma among controls were 24/53 and in the SIT group 16/64. The longitudinal treatment effect when adjusted for bronchial hyper-responsiveness and asthma status at baseline including all observations at 3, 5 and 10 years follow-up (children with or without asthma at baseline, $n = 189$; 511 observations) was statistically significant ($P = 0.0075$). The odds ratio for no-asthma was 4.6 95% CI (1.5–13.7) in favor of SIT.
Conclusion: A 3-year course of SIT with standardized allergen extracts has shown long-clinical effects and the potential of preventing development of asthma in children with allergic rhinoconjunctivitis up to 7 years after treatment.
Clinical implication: Specific immunotherapy has long-term clinical effects and the potential of preventing development of asthma in children with allergic rhino conjunctivitis up to 7 years after treatment termination.

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Key words: asthma; long-term effect; prevention; rhinitis; specific immunotherapy.

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Allergic rhinoconjunctivitis is a major risk factor for later development of asthma (1, 2). More than 20% of all children with rhinoconjunctivitis develop asthma later in life and rhinitis frequently precedes the onset of asthma. Although not specifically designed for this purpose, other studies have indicated the preventive potential of specific immunotherapy (SIT) in reducing the risk of asthma in patients with allergic rhinoconjunctivitis (3–6). A recent study on a 3-year course of co-seasonal sublingual immunotherapy has also shown the potential of prevention of seasonal allergic asthma in grass pollen allergic children suffering only from rhinitis (7).

The Preventive Allergy Treatment study (PAT) is the first prospective long-term follow-up study that tested whether SIT can prevent the development of asthma and whether the clinical effects persist in children suffering from seasonal allergic rhinoconjunctivitis caused by allergy to birch and/or grass pollen as these children grow up. The total SIT period was 3 years, after which the children were evaluated for the development of asthma. The patients were re-evaluated after a total of 5 years. The evaluation showed that immunotherapy impedes progression from allergic rhinoconjunctivitis to asthma after 3 years of SIT (8) and at the 5 year follow-up 2 years after treatment termination (9). The actively

bsaci
improving allergy care
through education, training and research

Reason for current asthma prevention study

- **Injection immunotherapy** decreases asthma risk development **in children with seasonal rhinoconjunctivitis to grass and/or birch**
- **3-year course of SIT results in** long-term sustained clinically effect **up to 7 years after treatment discontinuation**

Is it safe?

In carefully selected patients the injection treatment is safe if administered in a clinic by appropriately trained personal

Tablet treatment is safe in carefully selected patients who have an initial dose in the specialist hospital clinic

Contraindications: Poorly controlled asthma (>BTS step 1), patients on beta blockers

Who is it for?

- 1. IgE-mediated seasonal pollen induced rhinitis, if symptoms have not responded adequately to optimal pharmacotherapy
- 2. Systemic reactions caused by bee or wasp venom allergy
- 3. Selected patients with animal dander or house dust mite (HDM) allergy in whom rigorous allergen avoidance and reasonable pharmacotherapy fail to control symptoms.

Referral

- Good adherence to combination therapy
- Significant symptoms
- Particularly if interfering with work & sleep or an early spring walk in Hylands Park
- Tree pollen Late Jan – mid May (peak April)
- Grass pollen mid May - August

Tree & Grass pollen and HDM injection immunotherapy

POLLINEX-R

modified ragweed tyrosine adsorbate

pre-seasonal allergy vaccine

bsaci

improving allergy care

through education, training and research

Sublingual immunotherapy

Licensed in UK

Awaiting UK license

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through education, training and research