

# Allergic Rhinitis – when all else fails!

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The Food Allergy  
Immunotherapy Centre

What are symptoms of  
Allergic Rhinitis?

# Allergic signs



Denny Morgan lines



Allergic shiner

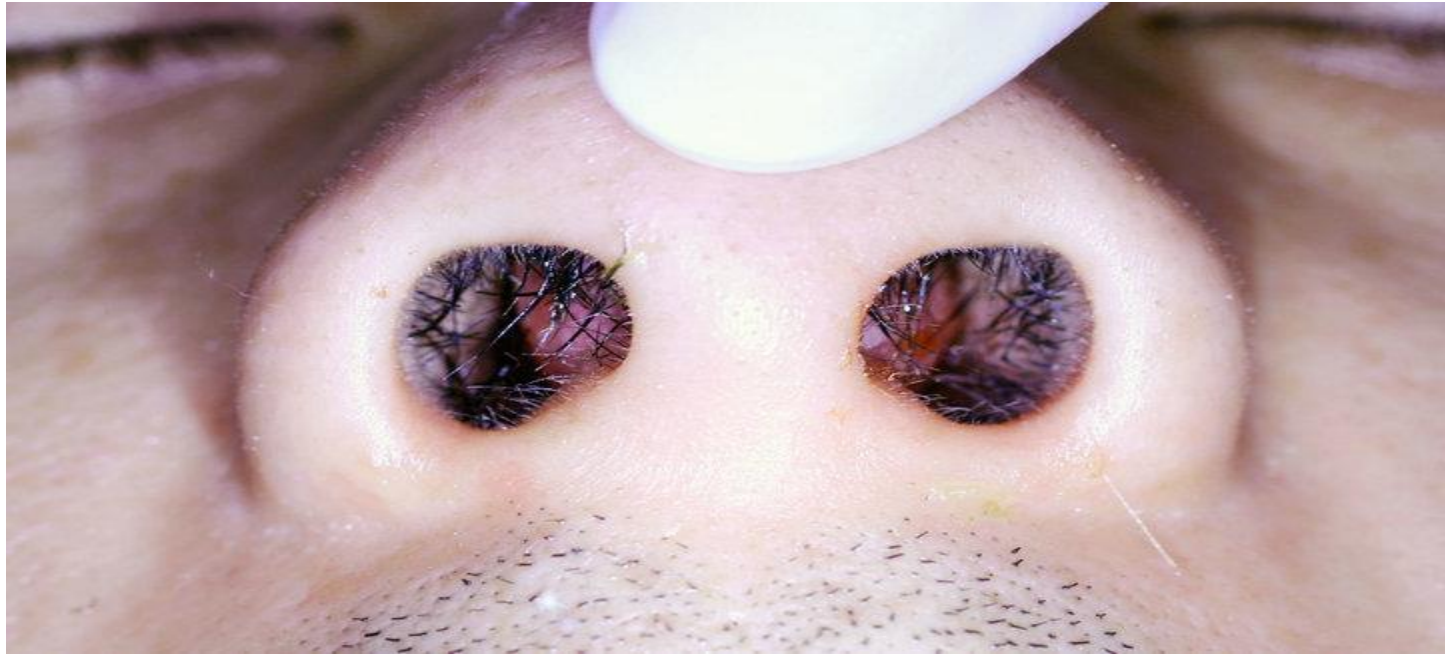


Allergic salute

Nasal crease



Allergic crease



# Is it Treatment-resistant Allergic Rhinitis?



## AR Treatment Satisfaction

*62% of patients receiving optimal standard symptomatic treatment experience poor symptoms control*

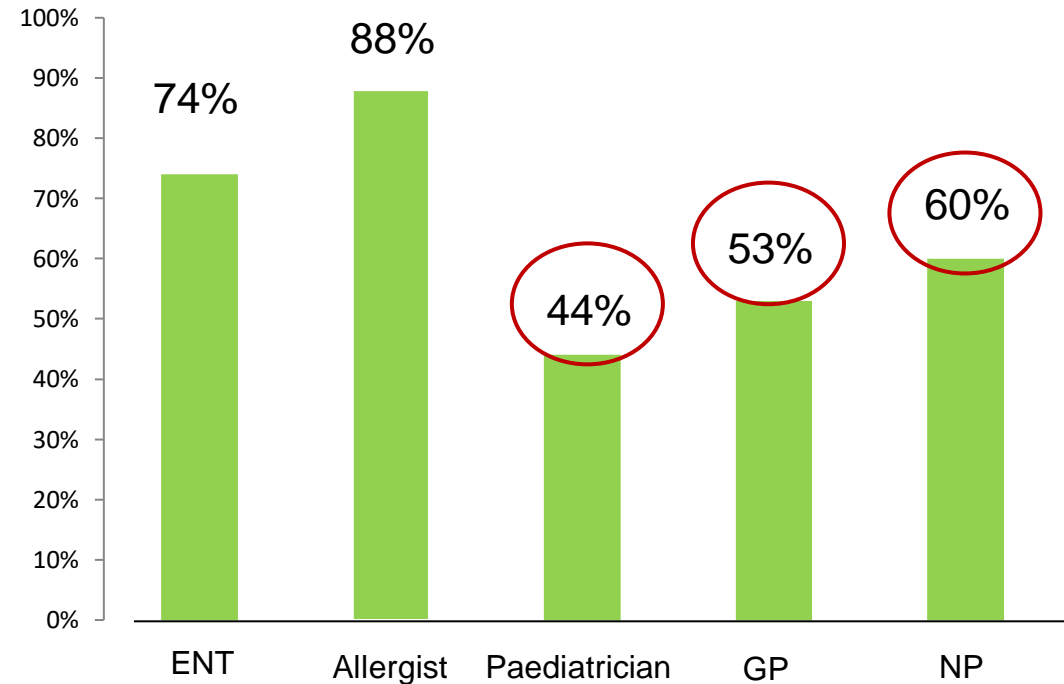
White P et al. *Clin Exp Allergy* 1998;28:266-70

# Compliance and Education

- Easy to use device
- Minimal Sensory Disturbance
- Once daily dosing
- Education
  - Device Technique
  - Safety of Drug
  - Warning of Possible Side Effect



# HCPs Awareness of Guidelines



HCPs awareness of professional guidelines for the management of AR

*Modified from Meltzer E et al: JACI 2009; 124:S43-70*



# Guidelines for Allergic Rhinitis



**bsaci**

Improving allergy care

- Scadding G et al *CEA*, 2008 38, 19–42



- Bousquet J et al *JACI* 2001 Nov;108(5 Suppl):S147-334.
- Bousquet J et al *Allergy* 2008; 63 (Suppl. 86): 8–160
- Brozek JL et al *JACI* 2010 Sep;126(3):466-76.

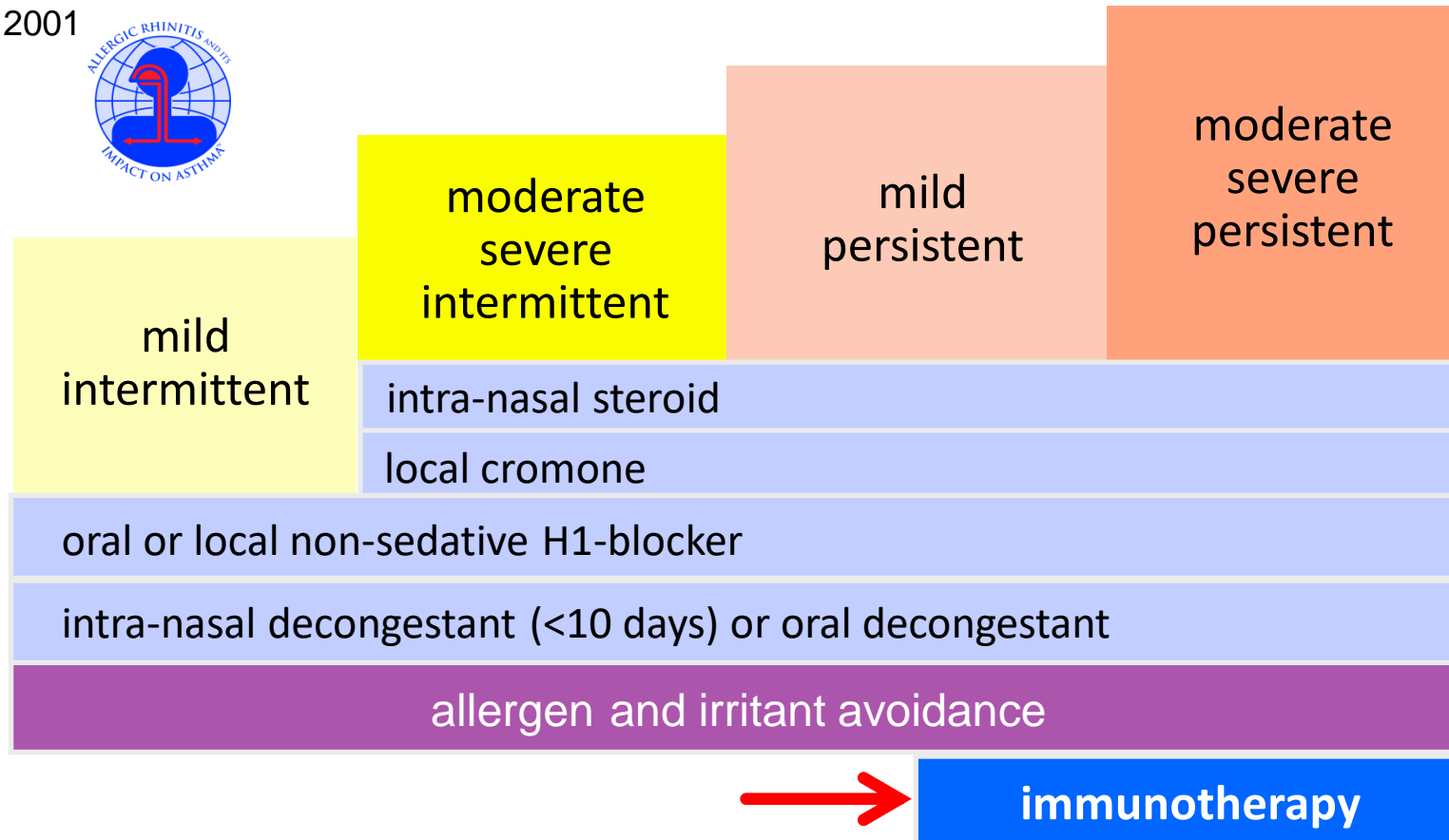


Roberts G et al  
*Allergy*. 2013 Sep;68(9):1102-16

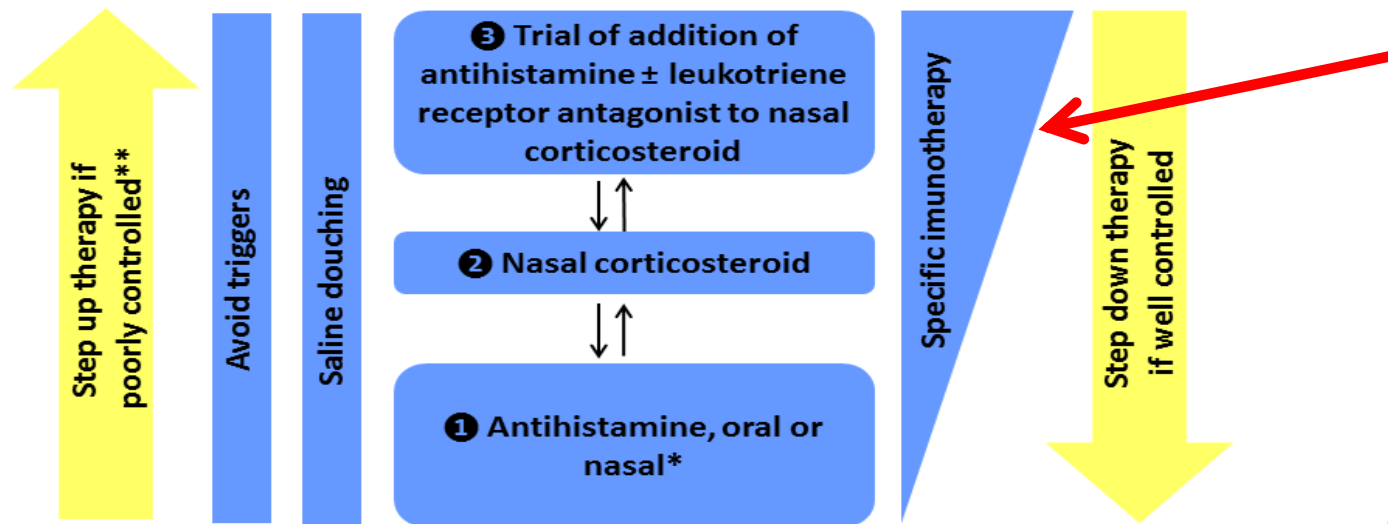
# Treatment of allergic rhinitis (ARIA)

## Allergic rhinitis and its impact on asthma

2001

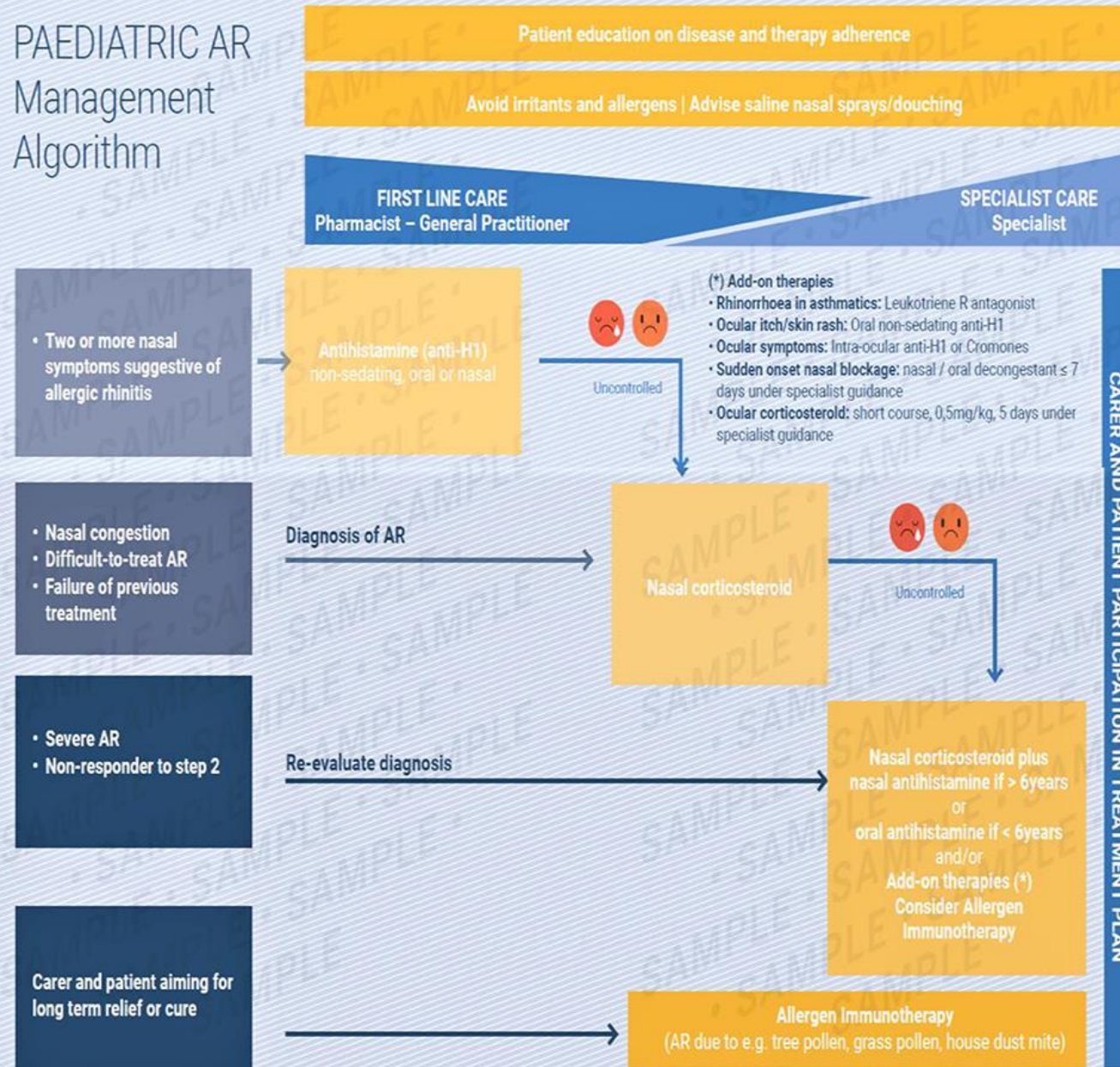


# Paediatric Rhinitis Proposed Therapeutic Approach



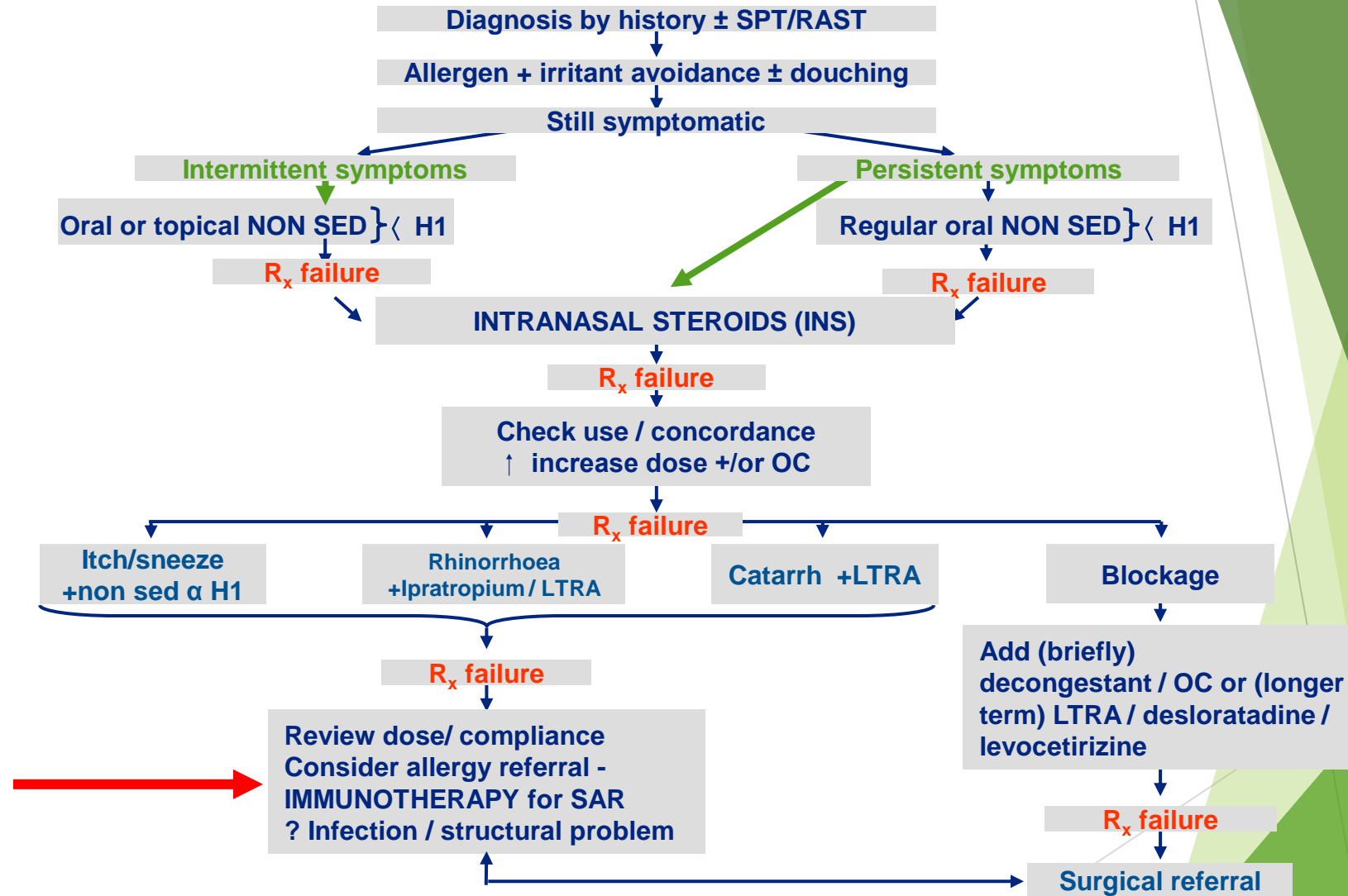
Roberts G et al  
*Allergy*. 2013 Sep;68(9):1102-16

# PAEDIATRIC AR Management Algorithm



# Treatment of Allergic Rhinitis

## BSACI Guidelines



# Apps for symptom monitoring

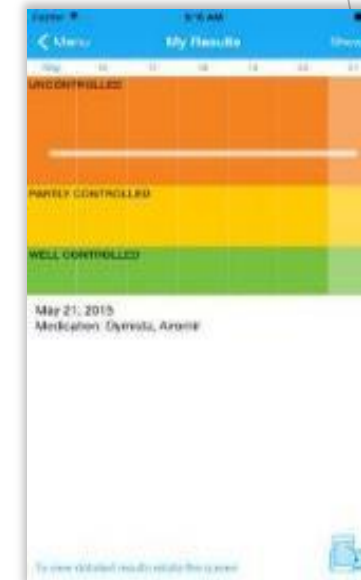
BRIEF COMMUNICATION

WILEY Allergy

The Allergic Rhinitis and its Impact on Asthma (ARIA) score of allergic rhinitis using mobile technology correlates with quality of life: The MASK study



**MASK AIR by  
ARIA**



Bousquet J, et al; Allergic Rhinitis and its Impact on Asthma (ARIA) Phase 4 (2018): Change management in allergic rhinitis and asthma multimorbidity using mobile technology. *J Allergy Clin Immunol.* 2019 Mar;143(3):864-879. doi: 10.1016/j.jaci.2018.08.049. Epub 2018 Sep 29. Erratum in: *J Allergy Clin Immunol.* 2019 Nov;144(5):1456.



### MASK-air

Monitoring of symptoms of allergic rhinitis, medication, and tracking the disease over months.  
 >10 000 downloads in Google Play



### AllergyMonitor

Recording of daily hay fever and asthma symptoms by patients with tracking capabilities over months.  
 >5000 downloads in Google Play



### Pollen

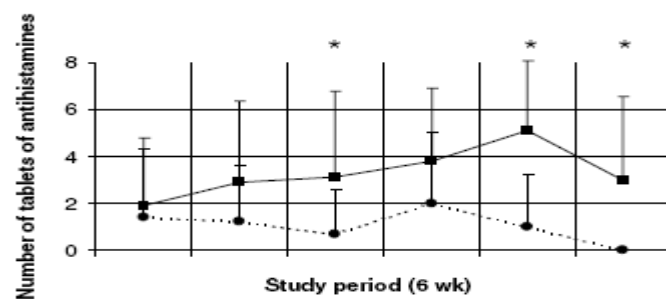
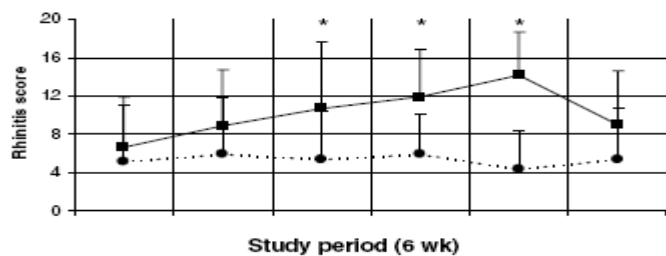
Recording of daily hay fever symptoms plus local pollen predictions for the following three days.  
 >100 000 downloads in Google Play

# Adjuvants

- ▶ Nasal irrigation
- ▶ Omalizumab
- ▶ Cellulose powder
- ▶ Probiotics



## Nasal Irrigation as adjuvant treatment in AR



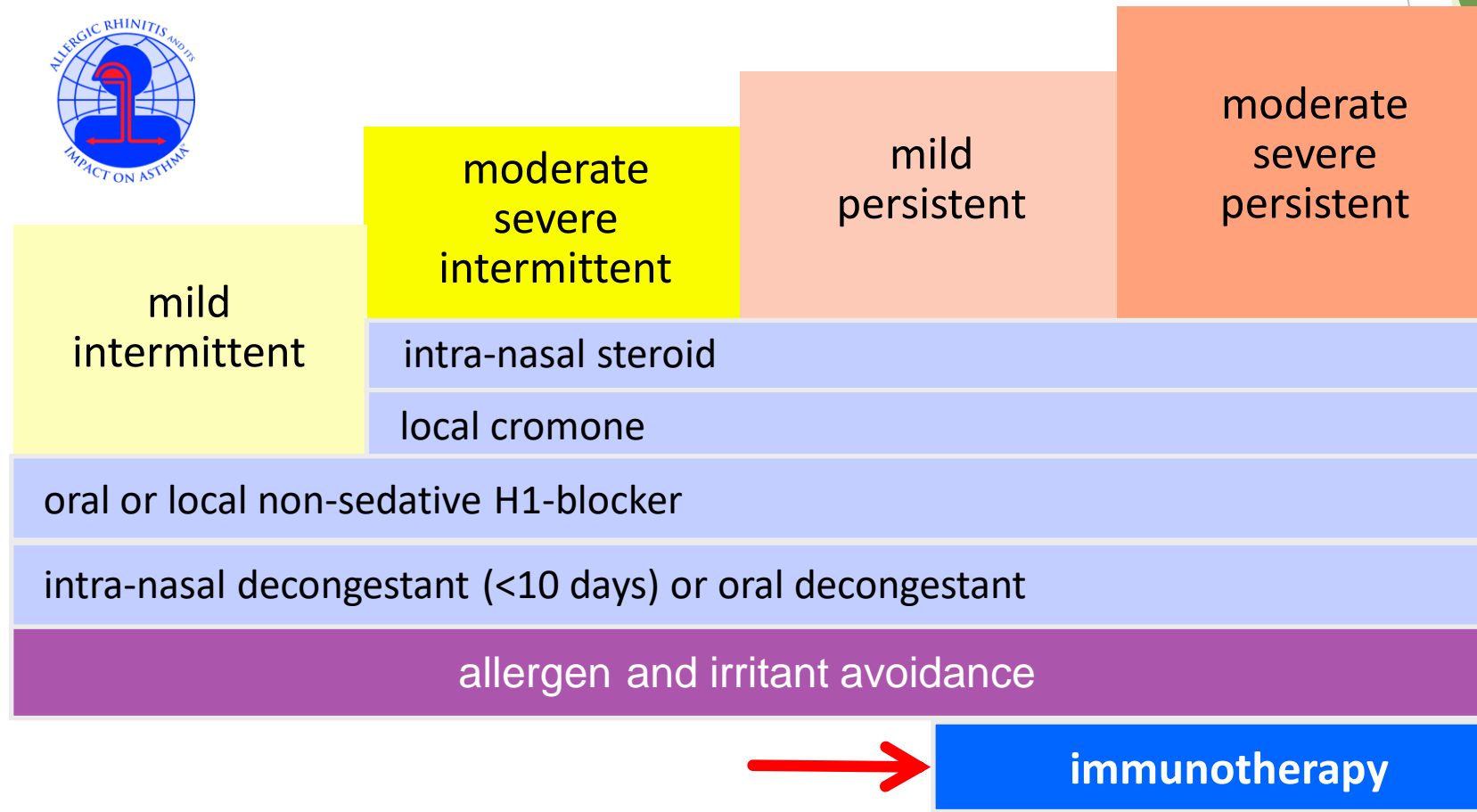
Three-times daily nasal irrigation with hypertonic saline in children (aged 6-12) with seasonal allergic rhinitis significantly reduces Total Rhinitis Symptoms Score and a reduction the amount of rescue anti-H1 in the treatment group.

Nasal Irrigation improves: Symptoms, RQLQ & MCT

Garavello W et al; *PAI* 2003:14  
Hermelingmeier K et al; *Am J Rhinol Allergy* 2012:26(5)

# Treatment of allergic rhinitis (ARIA)

## Allergic rhinitis and its impact on asthma



# Indication for Immunotherapy

- At least 1 year history of AR +/- Asthma
- Evidence of sensitisation
- Evidence for clinical relevance of disease related allergen
- Availability of standardised allergen extract

# Benefits of Immunotherapy

- ▶ Able to induced Immune-tolerance
- ▶ Sustained prevention of symptoms
- ▶ Able to modify disease progression
  - Prevention of new sensitization
  - Asthma prevention

# What's Available?

## Two Routes of Administration

### SCIT



- Used in 75% of children
- Potential Severe Side effects
- Administration by Specialist
- **\*\*Contraindicated in Asthmatic**

### SLIT



- Used in 25% of children
- Home Therapy  
(only 1<sup>st</sup> Dose Supervised)
- Can be used in asthmatic

Does it work?

## CME review article

This educational activity is supported by an educational grant from GlaxoSmithKline

# Comparison of allergen immunotherapy practice patterns in the United States and Europe

Linda Cox, MD,\* and Lars Jacobsen, MSc†

Table 1. Comparison of the Differences Between US and European Allergen Extracts and Specific Immunotherapy Practice Patterns

Variable	United States	Europe
Regulatory agency	FDA	EMA
Standardization		
Method	ID <sub>50</sub> EAL	Nordic
Test technique	Intradermal	Percutaneous
End point	Extract dilution that produces sum of erythema of 50 mm	Extract dilution that produces a wheal equal to the histamine control
Potency determination	Comparison with CBER reference control	Compared with in-house reference
Future focus	Overall allergenicity	Major allergen content
Potency units	BAU, wt/vol, PNU, milligrams of major allergen for ragweed and cat	Varies; each company essentially has its own potency units, some provide milligrams of major allergen
Extract formulation		
Location	Prepared in physicians offices	Prepared at extract manufacturer site
No. of allergens	Multiple	Generally 1
Allergen extract types	Aqueous and glycerinated unmodified extracts, alum-precipitated depot extracts	Approximately 100% depot extract, 20% allergoid, <5% adjuvants
SLIT	Approximately 5.9% of allergists, no FDA-approved formulation	Approximately 45% of prescribed SIT, solution and tablets available, some are registered
Reimbursement	Covered as a medical service by government and private insurers, prices can be negotiated but private insurers often use government schedule	Varies, extract companies negotiate coverage with each country

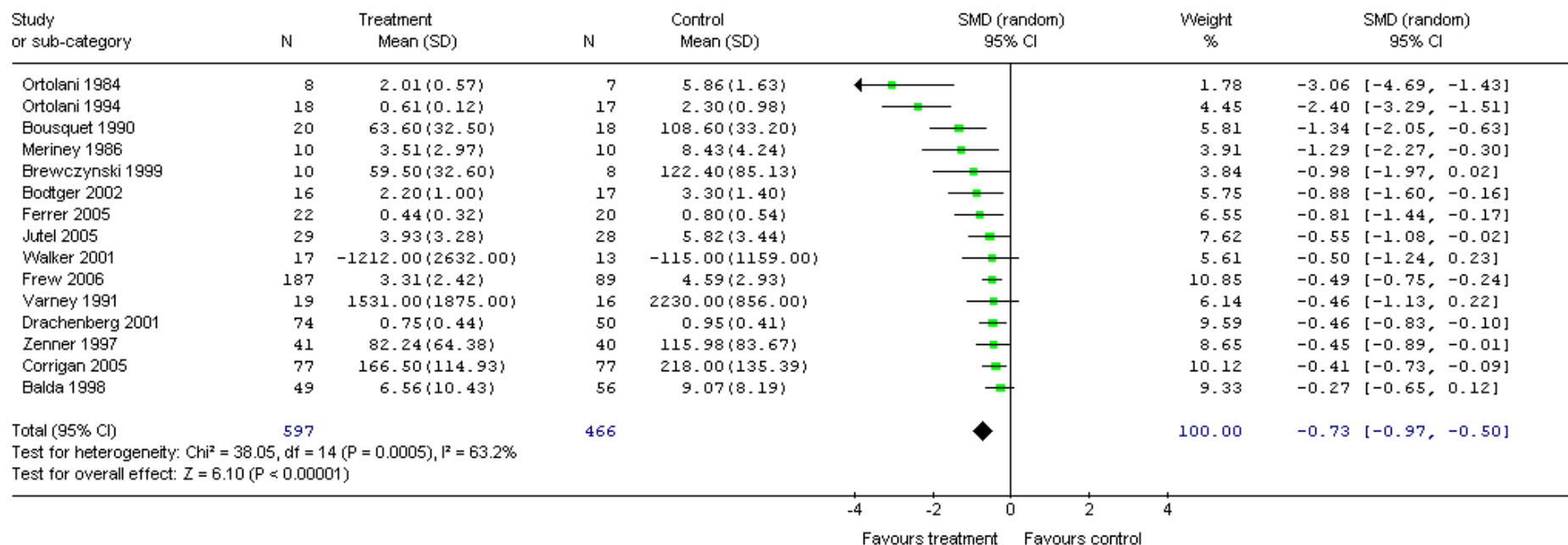
Abbreviations: BAU, bioequivalent allergy units; CBER, Center for Biologics Evaluation and Research; EMA, European Medicinal Agency; FDA, Food and Drug Administration; PNU, protein nitrogen units; SIT, specific immunotherapy; SLIT, sublingual immunotherapy.

# Allergen injection immunotherapy for seasonal allergic rhinitis (Review)

Calderon MA, Alves B, Jacobson M, Hurwitz B, Sheikh A, Durham S

## Symptom scores

Review: Allergen injection immunotherapy for seasonal allergic rhinitis  
 Comparison: 01 Active versus placebo  
 Outcome: 01 Symptom score



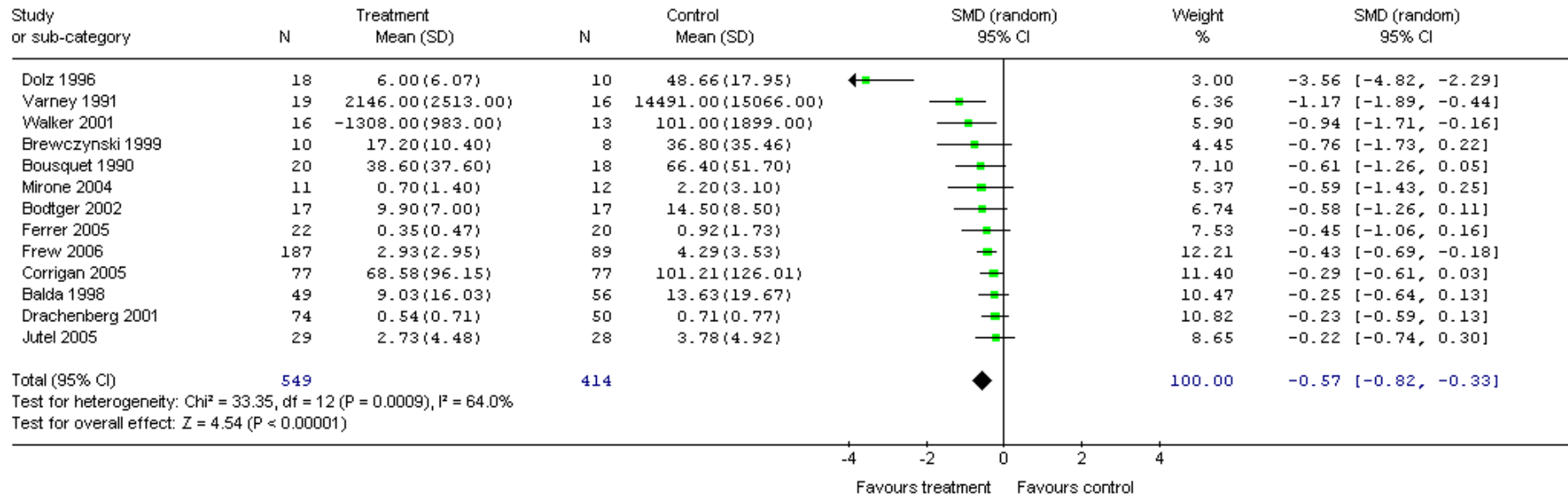


# Allergen injection immunotherapy for seasonal allergic rhinitis (Review)

Calderon MA, Alves B, Jacobson M, Hurwitz B, Sheikh A, Durham S

## Medication scores

Review: Allergen injection immunotherapy for seasonal allergic rhinitis  
 Comparison: 01 Active versus placebo  
 Outcome: 02 Medication score



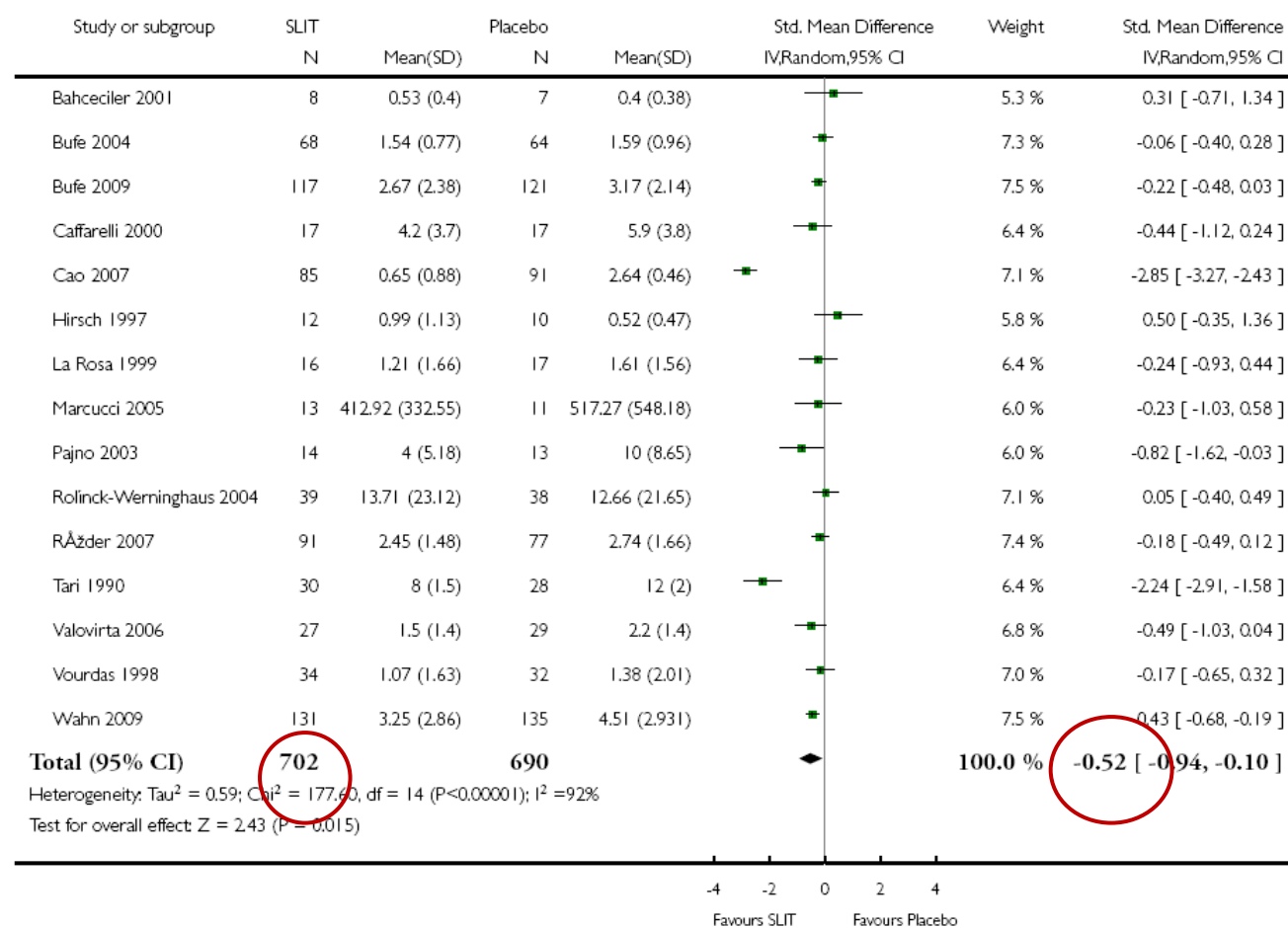


## Sublingual Immunotherapy for allergic rhinitis (Review)

Radulovic S,  
Calderon M, Wilson D,  
Durham S

### Comparison SLIT versus Placebo – Children: Outcome: Symptoms Score

#### 15 Studies



Author, yr (ref)	Allergen	Patients enrolled	St	Design of original trial	Duration St	Patients reevaluated	Outcomes at follow-up	Main results at follow-up
Mosbeck, 1988 (21)	Grass	39	SCIT	R-DB-C with 2 active arms. Open FU 6 yrs	2.5 yrs	32	Symptoms and drug intake in pollen season	The clinical benefit of SCIT was maintained at 6 yrs in both groups.
Grammer, 1984 (22)	Ragweed	63	SCIT	R-DB-PC, 2 arms + untreated group. Open FU 2 yrs	4 mo	63	Symptoms and drug intake in pollen season	Patients receiving placebo in the 2nd season maintained a clinical benefit similar to those receiving SCIT. Both groups better than untreated.
Hedlin, 1995 (23)	Cat/dog	32	SCIT	Open, prospective. Open FU 5 yrs	3 yrs	30	Specific and nonspecific bronchial challenge; subjective evaluation	Persisting clinical benefit reported 5 yrs after stopping SCIT. Bronchial responsiveness returned almost to baseline values.
Des Roches, 1996 (24)	Mite	40	SCIT	Prospective controlled. Open FU 3 yrs	1-6 yrs	40	Appearance of asthma symptoms	Most subjects remained asymptomatic after 3 yrs. The long-lasting effect is related to the duration of SCIT.
Durham 1999 (25)	Grass	40	SCIT	R-DB-C 3 or 4 yrs SCIT. One group continued for 3 years more	3-4 yrs	32	Symptoms and medication scores	After 3 years, symptoms and medication scores remained low in the group who discontinued and in the group who continued to receive maintenance SCIT.
Di Rienzo 2006 (26)	Mite	60	SLIT	Open, non R. control led. Open FU 5 yrs	5 yrs	60	Clinical evaluation of asthma symptoms	The effect of SLIT on asthma symptoms persisted up to 5 yrs after stopping.
Eng 2002 (27)	Grass	28	SCIT	R-DB-PC. Open FU 6 yrs	3 yrs	23	Symptom + drug score, individual symptoms, drug intake.	6 Years after discontinuation, the total score remained lower in the formerly SCIT group. No difference in drug intake between groups.
Tahamir 2007 (28)	Mite	137	SLIT	R-DB-C 2 or 3 years SLIT. Open FU 3 yrs	2-3 yrs	137	Symptom + drug score, individual symptoms, nasal resistance.	3 Years after discontinuation both groups maintained improvement in all parameters versus baseline, with better improvement in the 3-year SLIT group.
Durham 2010 (29)	Grass	308	SLIT	R-DB-PC. Open FU 1 yr	3 yrs	257	Rhinoconjunctivitis score; drug intake	1 Year after discontinuation, the difference remained in favour of the former SLIT group.
Marogna 2010 (27)	Mite	78	SLIT	Open, controlled, non R. Open FU up to 15 yrs	3 yrs 4 yrs 5 yrs	59	Symptoms, drug intake, nasal eosinophils, bronchial challenge	The 3 groups receiving SLIT improved significantly vs controls. Clinical benefit maintained for 7 years in groups treated for 4 or 5 years and for 5 years in group treated for 3 years
Musarra 2010 (28)	parietaria	57	SCIT	Open, controlled, nonrandomized. Open FU 5 yrs	3 yrs	57	Visual analog scale for symptoms. Severity of asthma/rhinitis	The clinical improvement persisted for 5 years after stopping SIT in the active group, according to VAS and severity of asthma/rhinitis

Abbreviations: R, randomised; DB, double blind; PC, placebo controlled; FU, follow-up.

## Ongoing Efficacy of Treatment

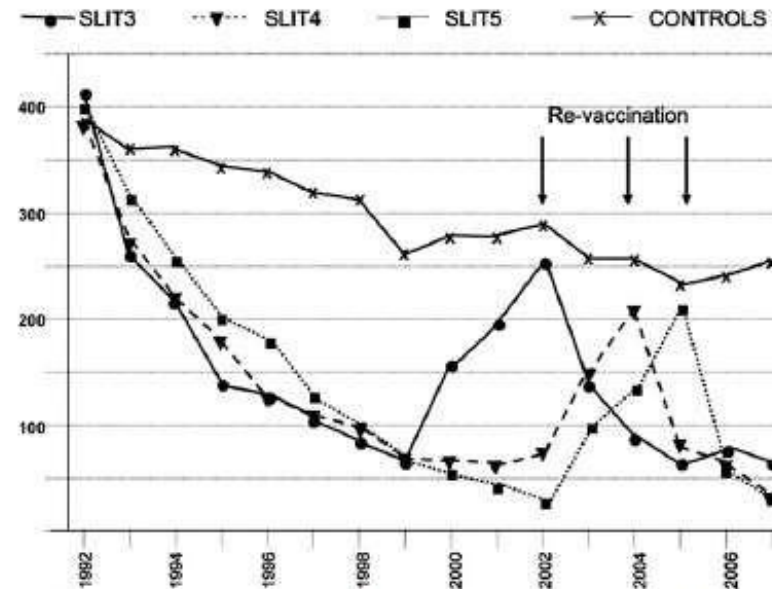


Figure 2. Symptom + medication scores year by year in 4 groups receiving mite SLIT for 3, 4, or 5 years or medications only. The arrows indicate the start of the new course of SLIT when the clinical benefit had vanished (from Marogna et al<sup>37</sup>).

Passalacqua G. *Ann Allergy Asthma Immunol.* 2011;107:401-406.

# Is it safe?



The Food Allergy  
Immunotherapy Centre

We have been doing it for some time...



Leonard Noon (1878-1913)

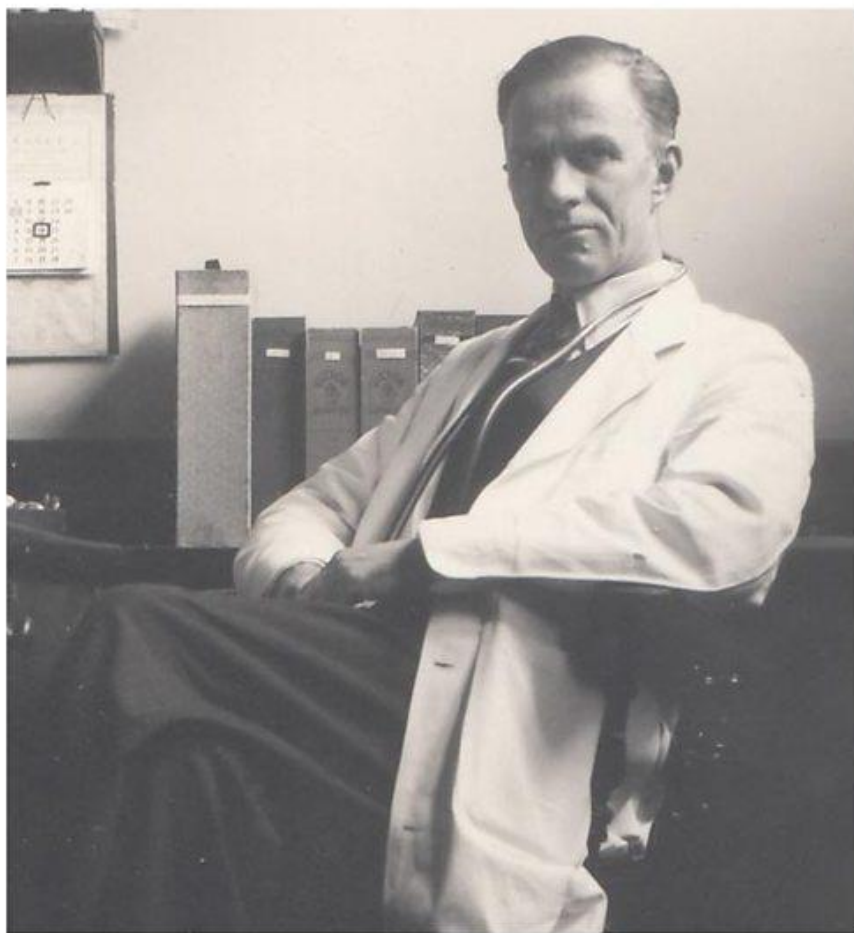


John Freeman (1877-1962)

**Prophylactic inoculation against hay fever.**

*The Lancet*, Volume 177, Issue 4580, 10 June 1911, Pages 1572-1573

L. Noon



# SAFETY:

- No fatal event have been reported over about 20 years
- Side effects are mostly local, transient and subsiding after the first doses
- The safety of SLIT is overall superior to that of SCIT
- A uniform grading system is required to describe and grade systemic and local side effects.

# Safety of Immunotherapy

- ▶ 528 SIT cycles (SCIT 31%) over 10 years.
- ▶ Fifty-five percent of all patients had asthma  
(SCIT programmes 24.5% patients had perennial ( $\pm$  seasonal) asthma)
- ▶ 75.6% of asthmatics undertaking SCIT had treatments at BTS/SIGN step 2 or above.
- ▶ AEs occurred frequently (50.4% of all SIT cycles) but were mild.
- ▶ SLIT- 44.9% local intraoral immediate reactions were most common
- ▶ SCIT - 28.3% delayed reactions around the injection site
- ▶ An asthma diagnosis had no impact on the number of cycles with AEs, or the severity reported. Few cycles (2.9%) were discontinued as a result of AE(s).



# SCIT - Fatalities

## U.K.

- ▶ Committee on Safety of Medicines
- ▶ 26 fatalities 1957-1986
- ▶ 16 / 17 in patients with asthma (poor control)

BMJ 1986; 293: 948-53

## U.S.A.

- ▶ AAAAI Survey
- ▶ 41 fatalities 1990-2001
- ▶ 1 per 2.5 million injections
- ▶ 15/17 had asthma (poor control)
- ▶ 59% occurred during maintenance

Bernstein DI et al. JACI 2004; 113: 1129-36

# Side Effects

- ▶ Cochrane review for SCIT 0.13% injections - adrenaline (0.01% placebo)
- ▶ RCT - 65/81 patients local reactions - no treatment req.
- ▶ Systemic reactions mainly rhino-conjunctivitis
- ▶ Paediatric Study - 25% local reactions
- ▶ 27% redness and swelling
- ▶ No anaphylaxis



# SLIT - Adverse Reactions

## Local

- Labial
- 

## Systemic

- Conjunctivitis

4 cases of anaphylactic reactions have been reported

- Headache
- No anaphylaxis

# Treatment-related adverse events

AEs are usually brief in duration and resolve soon after initiation

	Duration <sup>a</sup> (minutes) median  (P25%-P75%)	Resolution <sup>b</sup> (days) median  (P25%-P75%)
Oral pruritus	<b>8.5 min</b> (3.0 - 29.0)	<b>5.5 days</b> (2.0 - 16.0)
Mouth oedema	<b>46.0 min</b> (25.0 - 60.0)	<b>1.0 days</b> (0.0 - 7.0)
Ear pruritus	<b>8.5 min</b> (3.0 - 29.0)	<b>5.5 days</b> (2.0 - 16.0)
Throat irritation	<b>10.0 min</b> (5.0 - 20.5)	<b>13.5 days</b> (0.5 - 22.0)

*a. Duration of episode post administration*

*b. Resolution defined as days from first intake until AE no longer occurred*

# Changing the route of immunotherapy administration: An 18-year survey in pediatric patients with allergic rhinitis and asthma

Giovanni Pajno, M.D.,<sup>1</sup> Lucia Caminiti, M.D.,<sup>1</sup> and Giovanni Passalacqua, M.D.<sup>2</sup>

Table 2 Changing SLIT to SCIT and *vice versa*

	SCIT TO SLIT (n = 54/648)	SLIT TO SCIT (n = 340/4285)	$p\chi^2$
%	8.3	7.9	NS
Nonadherence	5 (9.25%)	48 (14.12%)	NS
Side effects	49 (90.75%)	0	<0.001
Inefficacy	0	292 (85.88%)	<0.001
<i>Parietaria</i>	29 (4.47%)*	184 (4.29%)*	NS
Grass	18 (2.77%)*	110 (2.56%)*	NS
Dust mite	5 (0.77%)	41 (0.95%)	NS
Olive	2 (0.30)	5 (0.11%)	NS

Numbers, percentages, and reasons for shifting the regimen.

\*SCIT for single allergen: *Parietaria*, 10.62%, and grass, 8.32%.

\*SLIT for single allergen: *Parietaria* 11.73%, and grass, 8.95%.

NS = not significant; SCIT = subcutaneous immunotherapy; SLIT = sublingual immunotherapy.

Allergy Asthma  
Proceedings  
2013

# Rahul



- ▶ 8yrs old
- ▶ Severe allergic rhinitis in summer
- ▶ Seen in local hospital, maximum treatment commenced
- ▶ GP concerned as not working, 2<sup>nd</sup> opinion

# Quality of Life

- ▶ 2 weeks of missed school at peak of pollen season
- ▶ Parents had to collect many times due to symptoms
- ▶ GP gave Kenalog injection
  
- ▶ RQLQ Score: 5.8 (0-6)



# When we met him....

## Skin Prick Test

Grass Pollen 18mm

- ▶ All other allergens tested negative (inc. HDM and Tree pollen)

## Specific IgE

Grass >100lu

## Medication List

- ▶ Fexofenadine
- ▶ Montelukast
- ▶ Avamys
- ▶ Cetirizine
  
- ▶ Seretide (no symptoms out of season)



Which immunotherapy to select?

# Sublingual Immunotherapy – Sublingual Tablets – Grass Pollen



Grazax-

One tablet daily sublingually  
for 3 years

Licensed

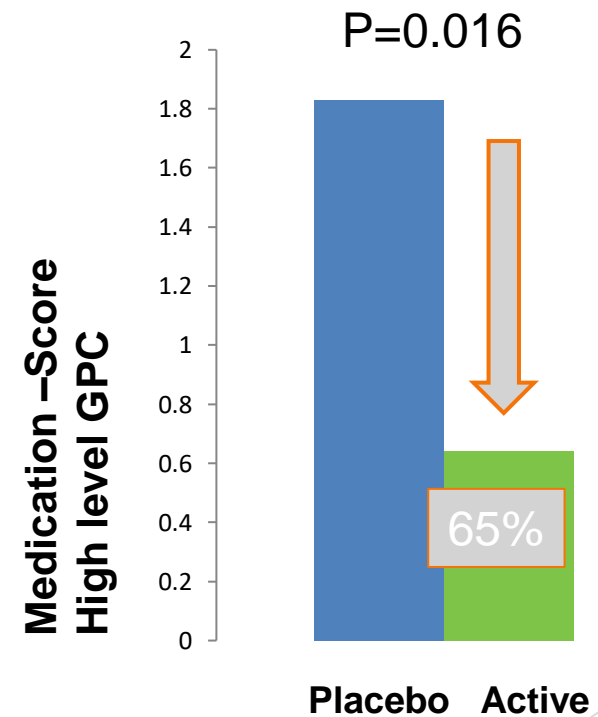
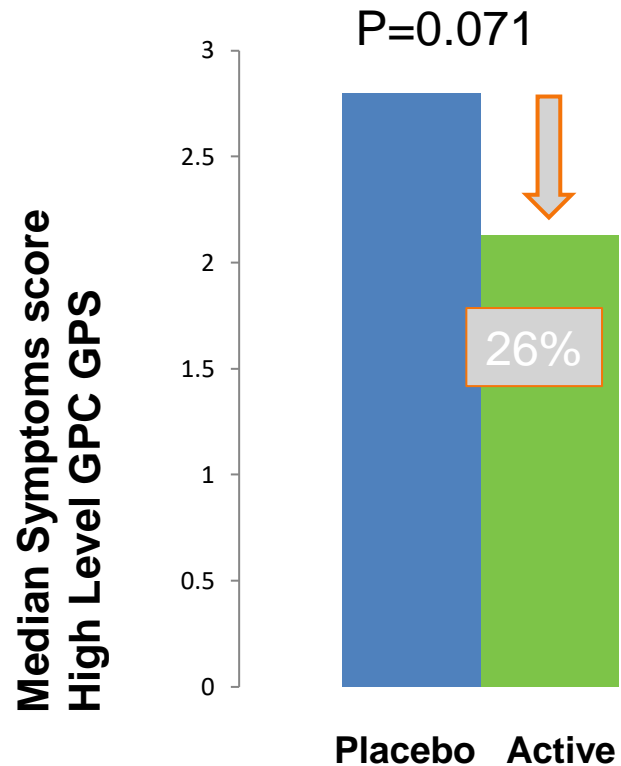


Oralair –  
1 tablet daily 4 months prior to  
season and throughout season

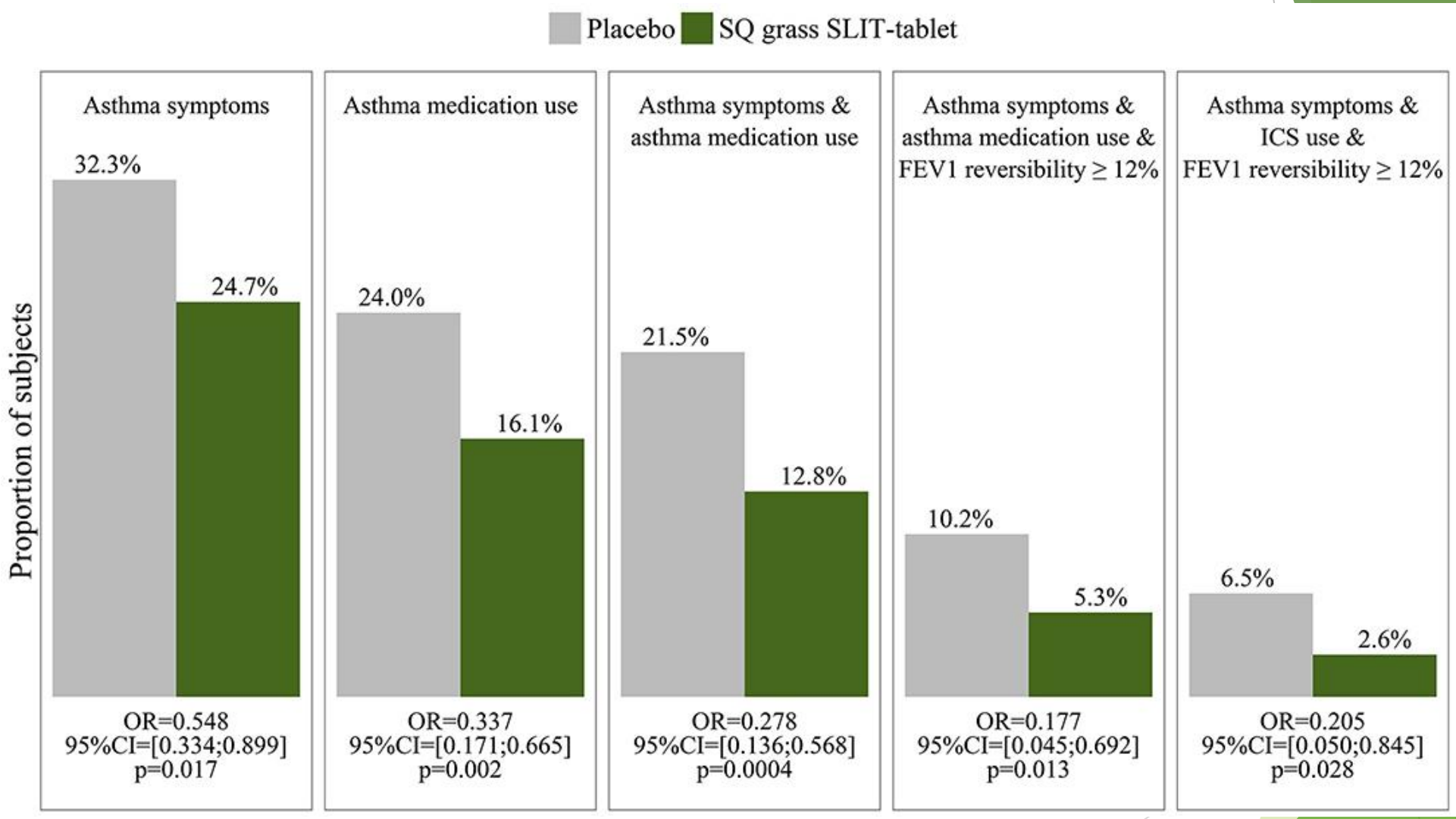
Paediatric up dosing over 3 days

# Safety and efficacy in children of an SQ-standardized grass allergen tablet for sublingual immunotherapy

Albrecht Bufe, PhD, MD,<sup>a</sup> Peter Eberle, MD,<sup>b</sup> Eivy Franke-Beckmann, MD,<sup>b</sup> Jürgen Funck, MD,<sup>b</sup> Martin Kimmig, MD,<sup>b</sup> Ludger Klimek, MD,<sup>c</sup> Roland Knecht, MD,<sup>b</sup> Volker Stephan, MD,<sup>d</sup> Bente Tholstrup, MSc,<sup>e</sup> Christian Weißhaar, MD,<sup>b</sup> and Friedrich Kaiser, MD<sup>b</sup> *Bochum, Hamburg, and Wiesbaden, Germany, and Hørsholm, Denmark*



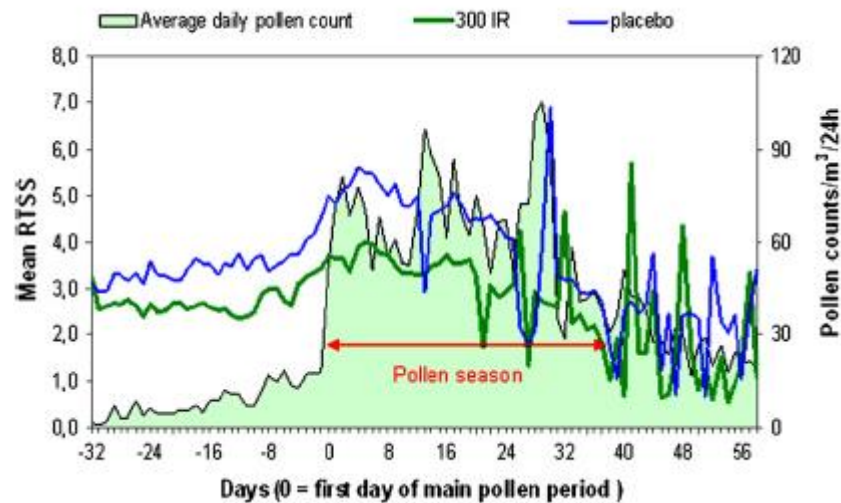
- RCT (1:1)
- 253 children (5-16)
- 75.000 SQU (15µg of Phl p 5)
- 8 weeks pre-seasonal and co-seasonal



Valovirta E, Petersen TH, Piotrowska T, Laursen MK, Andersen JS, Sørensen HF, et al. Results from the 5-year SQ grass sublingual immunotherapy tablet asthma prevention (GAP) trial in children with grass pollen allergy. *J Allergy Clin Immunol.* (2018) 141:529-38.e13

# Efficacy and safety of 5-grass-pollen sublingual immunotherapy tablets in pediatric allergic rhinoconjunctivitis

Ulrich Wahn, MD,<sup>a</sup> Ana Tabar, MD,<sup>b</sup> Piotr Kuna, MD,<sup>c</sup> Susanne Halken, MD, DMSc,<sup>d</sup> Armelle Montagut, PhD,<sup>e</sup> Olivier de Beaumont, MD,<sup>f</sup> Martine Le Gall,<sup>f</sup> on behalf of the SLIT Study Group Berlin, Germany, Pamplona, Spain, Lodz, Poland, Odense, Denmark, and Meylan and Antony, France



RTSS Median Improvement vs Placebo 39.3%

rescue medication score Median improvement 48.7%

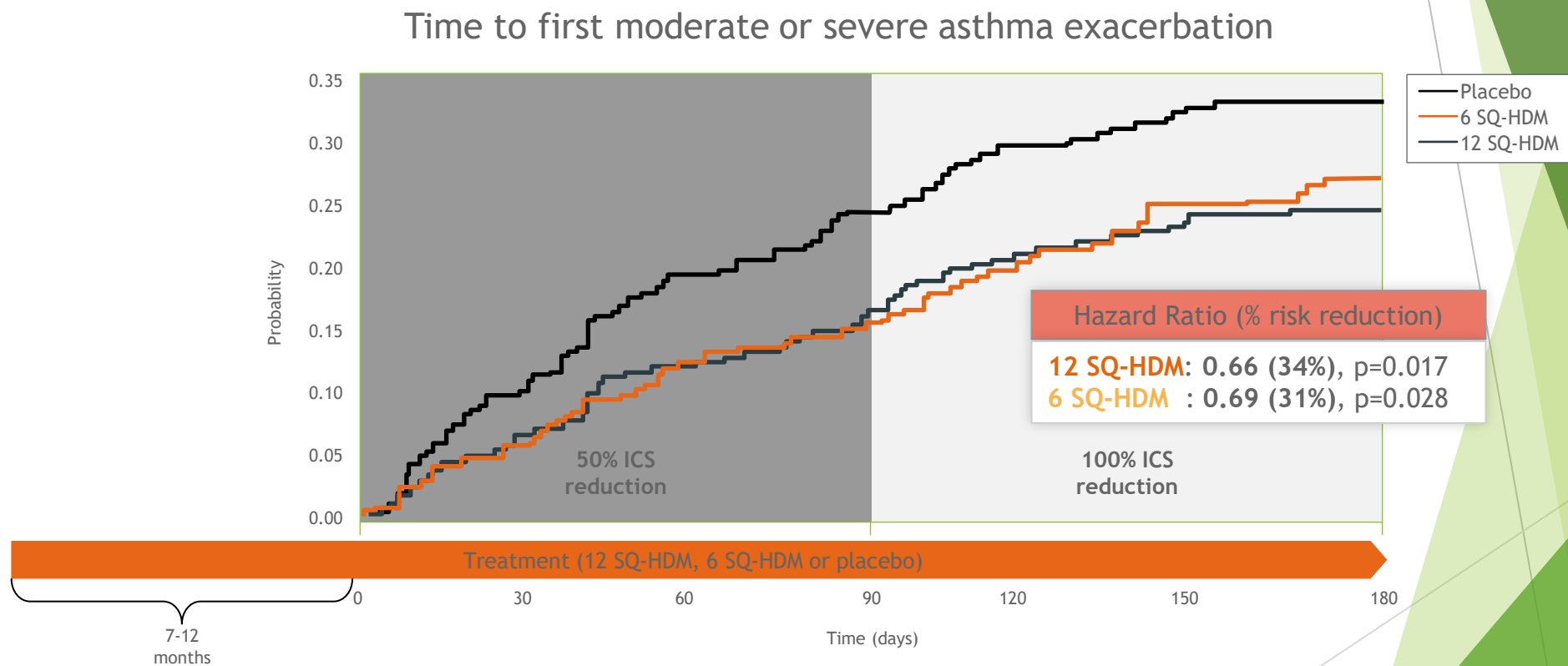
- RCT (1:1)
- 278 Children (5-17)
- 300 IR ( 20µg of Group 5 m. allergens)
- 4 months pre-seasonal and co-seasonal

# Sublingual Immunotherapy - House Dust Mite

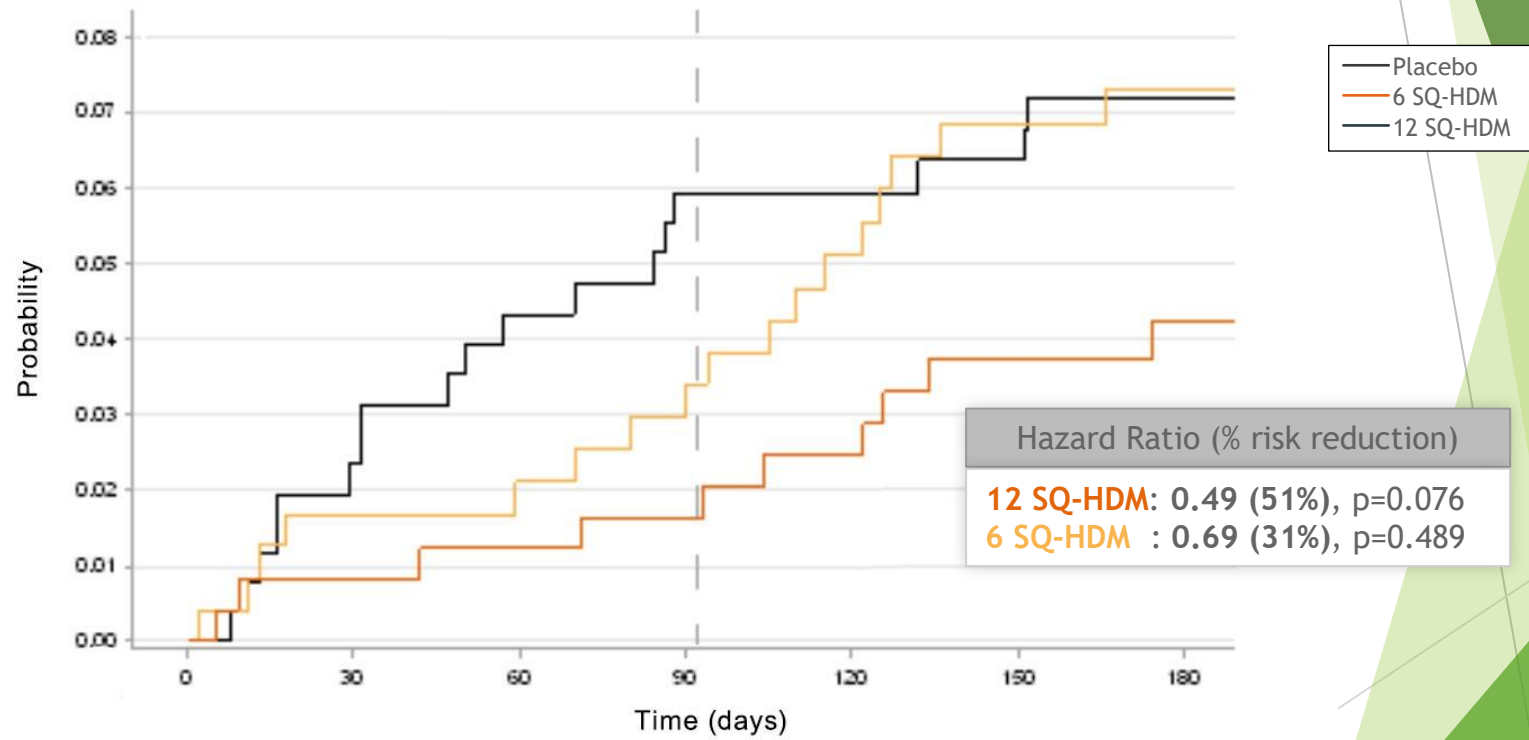
- ▶ Acarizax
- ▶ One tablet daily under the  
Tongue for 3 years



# MITRA (MT-04) - Reduced risk of exacerbations during ICS reduction

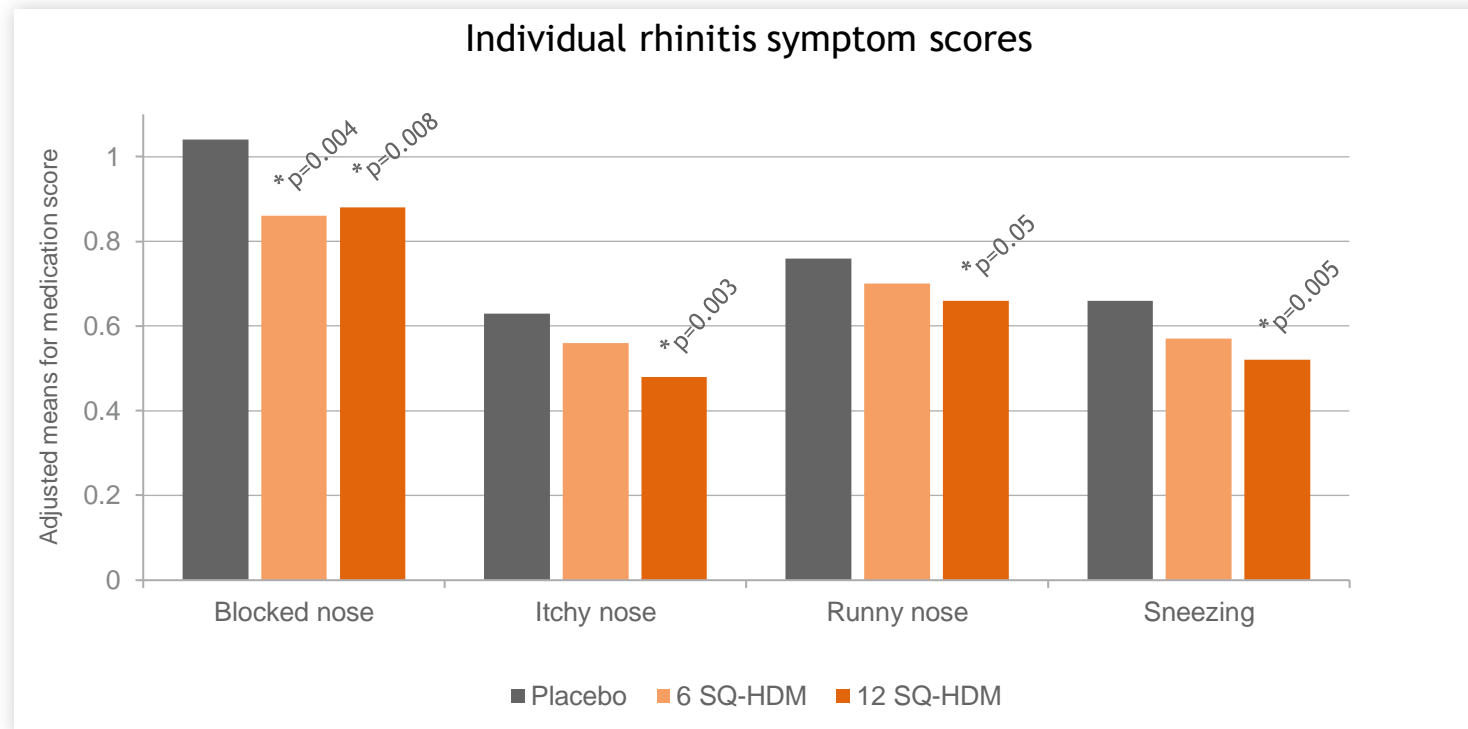


# Reduced risk of severe asthma exacerbation





# MERIT (MT-06) - All individual symptom scores significantly reduced for 12 SQ-HDM



Demoly P et al. J Allergy Clin Immunol. 2016;137(2):444-451

\* Statistically significantly different to Placebo

# Sublingual Immunotherapy – Oralvac



Time (min)	Bottle No. 3 (red)
0	1 pump
30	3 pumps
60	5 pumps
90	7 pumps
120	Observation ends

Pollen

Day	Bottle No. 1 (green)	Day	Bottle No. 2 (yellow)	Day	Bottle No. 3 (red)
1	1 pump	5	1 pump	9	1 pump
2	3 pumps	6	3 pumps	10	3 pumps
3	5 pumps	7	5 pumps		
4	7 pumps	8	7 pumps		

All Allergens

# Subcutaneous Immunotherapy

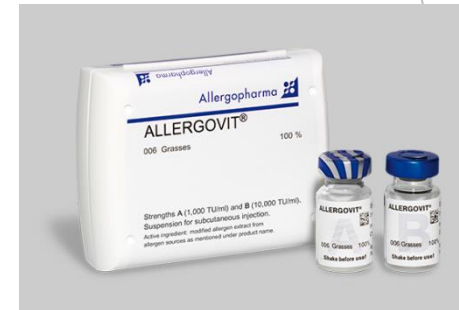
6-12 weeks regimes

Subcutaneous injection

Observation in hospital

Grass and Tree Pollen

Pollinex (Licensed)



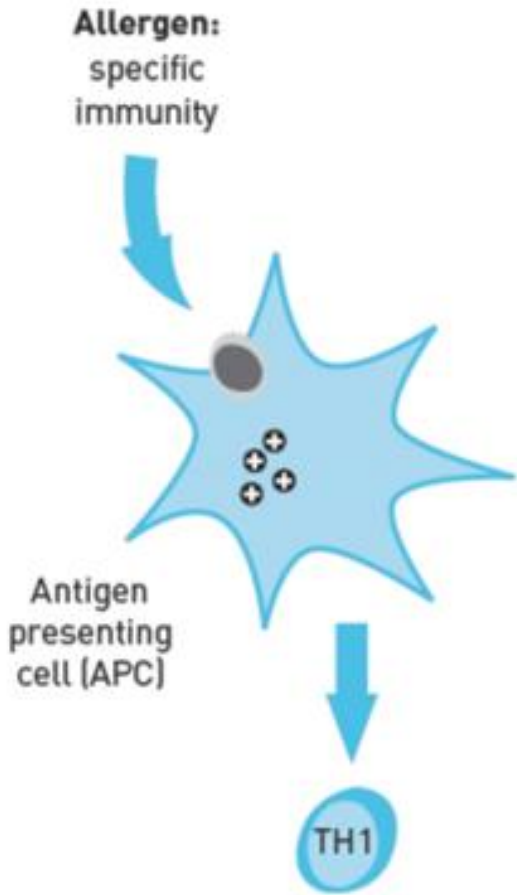
# Pollinex Quattro

- ▶ Short-course allergy vaccine
- ▶ Grass or Tree
- ▶ 4 pre-seasonal injections
- ▶ Been used in Germany since 1999
- ▶ Most common used product in children in UK (8 Centres)
- ▶ PQ (unlicensed)

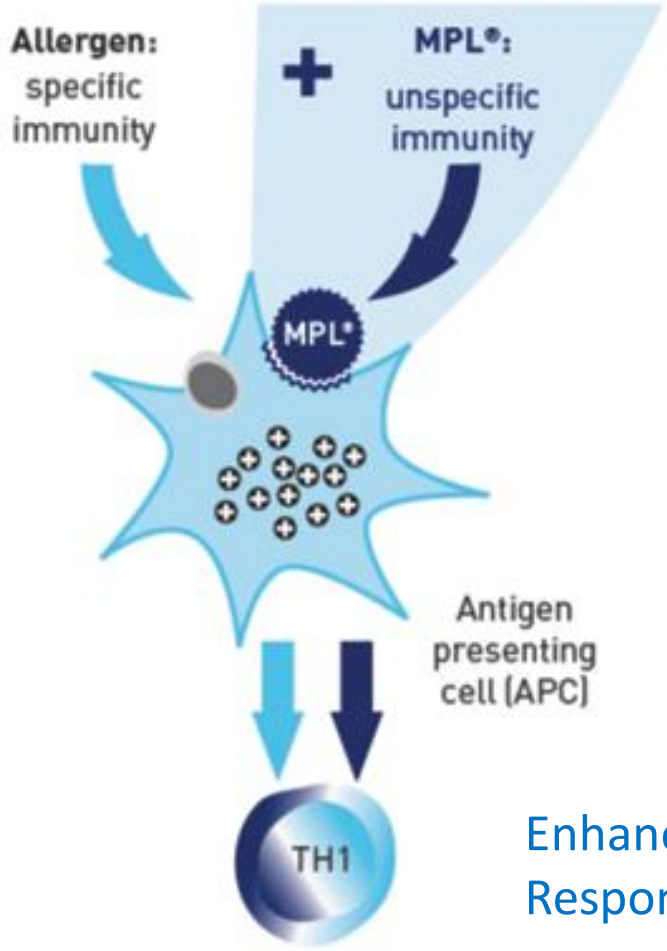


# Modified Allergen with MPL

## Conventional SIT



## Ultra-short-course SIT with MPL



Enhance Th1 Response

# Pollinex Quattro

- ▶ Pollinex Quattro is administered in increasing doses of allergen at weekly intervals. The dose steps are as follows:
- ▶ Step 1     300 SU
- ▶ Step 2     800 SU
- ▶ Step 3     2000 SU
- ▶ Step 4     2000 SU

## Original article

A well-tolerated grass pollen-specific allergy vaccine containing a novel adjuvant, monophosphoryl lipid A, reduces allergic symptoms after only four preseasonal injections

- ▶ Significant reduction in individual symptom scores for eyes and nose (P= 0.03, P= 0.04)
- ▶ Trend to reduced medicine use which did not reach significance due to the large variability in the placebo group

Significance level	Eyes <i>P</i> =0.003		Nose <i>P</i> =0.016		Medication <i>P</i> =0.28		Eyes, nose, and lungs <i>P</i> =0.003		Eyes, nose, lungs, and medication <i>P</i> =0.013	
	Placebo	Active	Placebo	Active	Placebo	Active	Placebo	Active	Placebo	Active
Mean	1.12	0.82	1.46	1.21	0.71	0.54	0.95	0.75	0.83	0.65
±SD	0.52	0.58	0.51	0.65	0.77	0.71	0.41	0.44	0.47	0.48
Median	1.13	0.71	1.43	1.09	0.34	0.23	0.9	0.65	0.71	0.54
Difference of medians							–28%		–24%	
Effect size							–0.46		–0.38	
95% Confidence limits of effect size							–0.10	–0.83	–0.01	–0.74

# Efficacy

Efficacy and tolerability of short-term specific immunotherapy with pollen allergoids adjuvanted by monophosphoryl lipid A (MPL<sup>®</sup>) for children and adolescents

K.J. Drachenberg<sup>a</sup>, M. Heinzkill<sup>a</sup>, E. Urban<sup>a</sup> and S.R. Woroniecki<sup>b</sup>

- ▶ Mean symptom scores reduced from 7 to 5 (grass pollen) and 9 to 5 (tree pollen) (both  $p < 0.01$ ).
- ▶ Medication scores reduced from 3 to 2 (grass pollen) and 3.4 to 2.1 (tree pollen) (both  $p < 0.01$ ).
- ▶ A significant increase in IgG was seen that persisted beyond the pollen season  $p < 0.001$ .



# Rahul - Which product?

- ▶ Asthma - seasonal
  - ▶ Allergen
  - ▶ Patient Choice
- 
- ▶ Opted for SCIT

# Pre-Injection

- ▶ Observations (BP, Pulse, RR)
- ▶ Lung function and PEFV
- ▶ Antihistamine - check they have taken a dose of cetirizine (0.5mg/kg maximum dose 10mg). At home or at least 30mins prior to injection
- ▶ Consent - Local reactions are common, 30%

## Our Experience - SCIT



Local Reactions in 30% and no systemic reactions



Reaction	Adjustment
Local reaction > 10 cm in diameter (swelling)	No increase in dose, the dose of the previous injection should be repeated, possibly reduce the dose
Mild to intense systemic reaction	Go back 1 stage in the posology regimen or start again from the beginning
Severe systemic reaction, anaphylactic shock	The doctor should review the treatment indication

# First Year of Treatment

- ▶ Remained on treatment
- ▶ No breakthrough symptoms
- ▶ No school/work days missed
  
- ▶ No asthma inhaler required.
  
- ▶ RQLQ Score = 2.9 (0-6)



# Carol

- ▶ 14yrs old
  - ▶ Severe Allergic Rhinitis
  - ▶ Severe Keratoconjunctivitis
- (under Eye Hospital)



# When we met her?

## Skin Prick Test

Birch Pollen 18mm

Tree Pollen 14mm

Grass 3mm

## Specific IgE

Birch >100iU

Tree 88.4

Grass 1.45

## Medication

Cetirizine

Avamys

Montelukast

Piriton (at night)

## Eye medication

Dexamethasone drops

Antihistamine drop

Intraocular injections



# Quality of Life

- ▶ Frequent absence from school (mainly embarrassment of eyes)
- ▶ Drop in examination results
- ▶ RQLQ Score = overall 4.0
- ▶ Ocular Symptoms = 6



# First Year of Treatment

- ▶ No school missed, grades comparable with winter exams
- ▶ Remained on medication - no need for steroid eye drops. (except 1 week when camping!)
- ▶ RQLQ Score = overall 2.5
- ▶ Ocular Symptom Score = 3.6

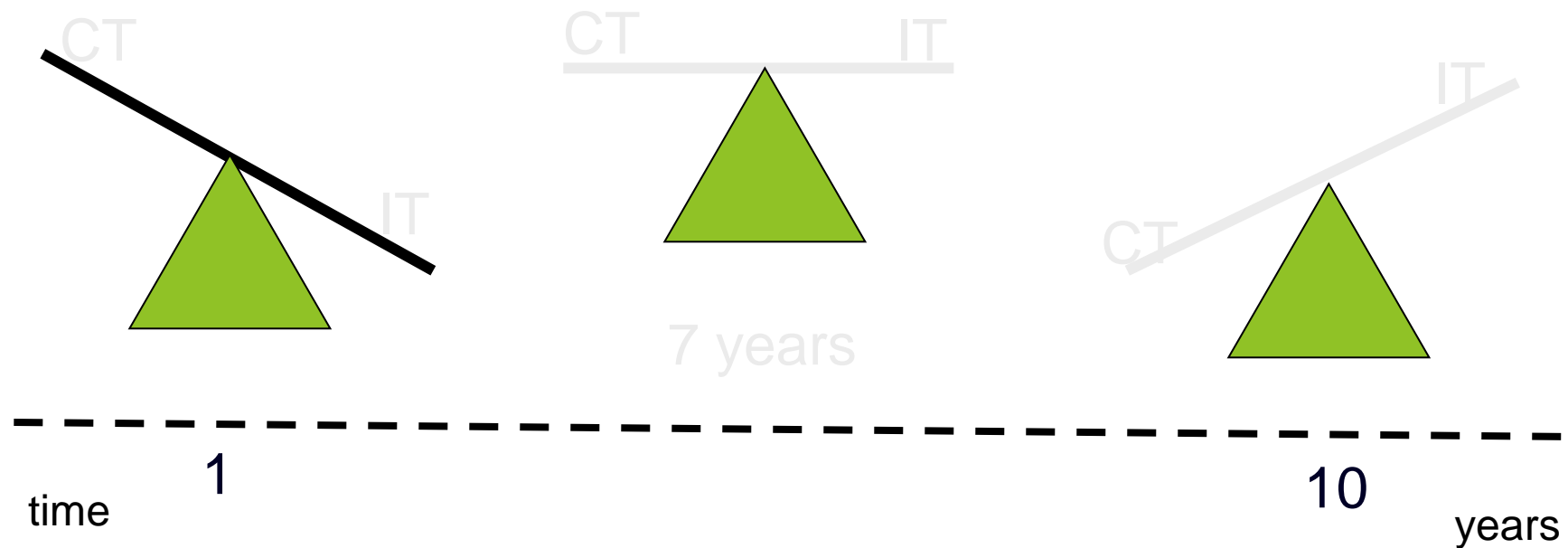




Let's talk  
money!

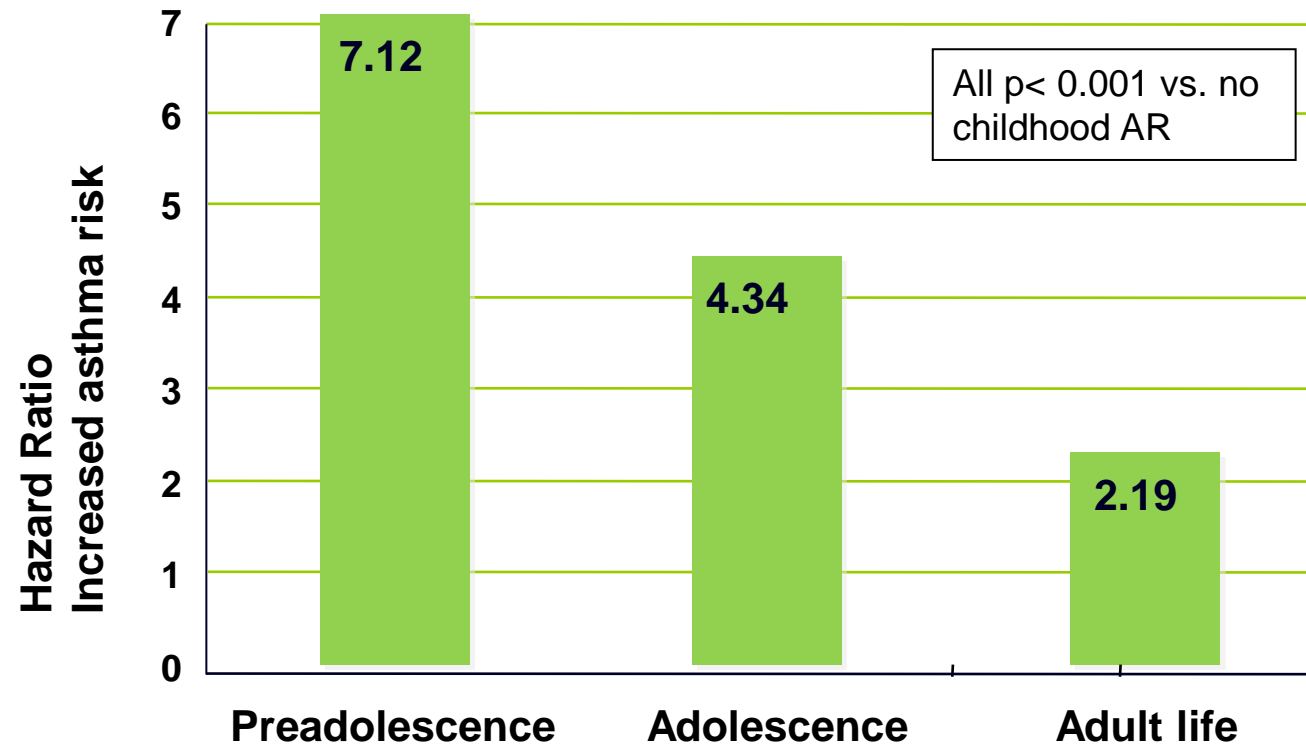
# IT cost effective in asthmatic patients with pollen & HDM allergy

- ▶ Cost of Immunotherapy (IT) vs Conventional Therapy (CT) at 1, 7 & 10 years



## Childhood allergic rhinitis increases the risk of developing asthma

Childhood allergic rhinitis has been associated with a significant 2-7 fold increase in the incidence of asthma in later life



*Burgess JA et al. J ACI 2007;120:863-9*

# Immunotherapy clinic

## **Original Article**

## **Standards for practical allergen-specific immunotherapy**

**E. Alvarez-Cuesta, J. Bousquet, G. W. Canonica, S. R. Durham, H.-J. Malling, E. Valovirta**

EAACI, Immunotherapy Task Force

*Allergy 2006; 61 (Suppl. 82): 1–20*

The future....

# Climate Change & Rhinitis



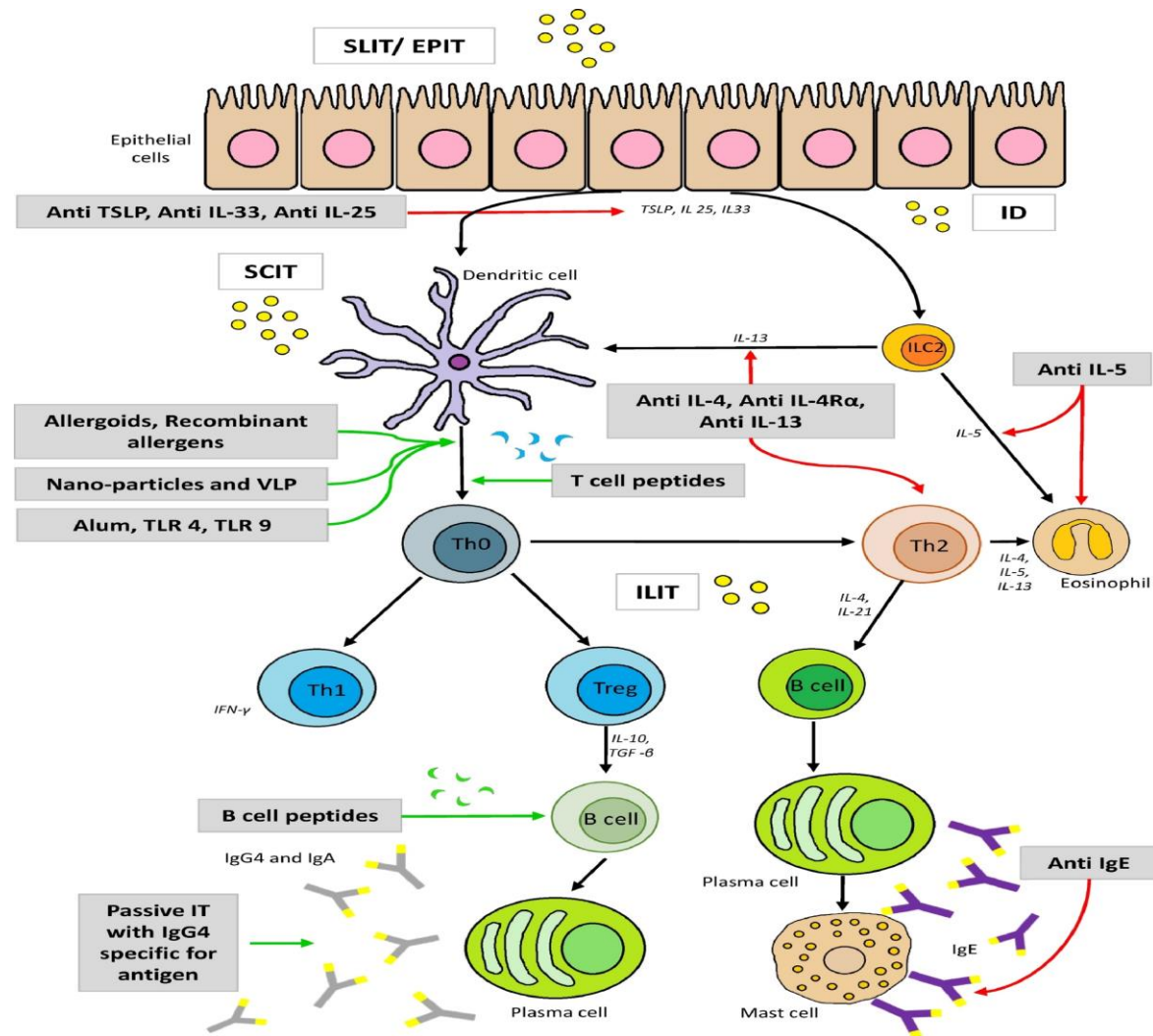
- Increases in temperature lead to:
  - ▶ Earlier onset of and longer pollination seasons
  - ▶ Migration of stinging and biting insects into new environments, and increased population of existing insect species
  - ▶ Changes to crop patterns, with the potential to introduce new allergenic pollens into the atmosphere
  - ▶ New food proteins in the local diet, and
- Increases in humidity associated with higher temperatures will lead to increased numbers of cockroaches, house dust mites, and molds, and, thus, “allergen load”.
- New pollen and mold sensitizations lead to increased prevalence and attacks of allergic rhinoconjunctivitis and asthma; longer pollen seasons lead to increased duration of symptoms.



**TABLE 1** New treatments under investigation/development for AR

Interventions	Tools/Drugs	Description	Administration route
Patients' education	MASK-allergy diary	-	Smartphone/Internet
Pharmacotherapy	ABH	Arginase inhibitor 2(S)-amino-6-boronohexanoic acid	Inhala
	MP29-02	Combination nasal spray of azelastine hydrochloride and fluticasone propionate	Intranasal
Allergen immunotherapy	Subcutaneous immunotherapy	<i>Lolium perenne</i> peptides/ recombinant B-cell epitopes	Subcutaneous
	Sublingual immunotherapy	Grass allergen peptide/house dust mite tablet	Sublingual
	Intra-lymphatic immunotherapy	Extracts of grass and birch pollen, house dust mites, dog or cat allergen	Intra-lymphatic
Biologics	Omalizumab	Anti-IgE	Subcutaneous
	Dupilumab	Anti-IL4R $\alpha$	Subcutaneous

# Mechanisms of immunotherapy and mechanistic effects on new



# Impact of IgE-sensitivity to profilins and other cross-reacting molecules on immunotherapy prescription

**Rhinitis, sinusitis, and upper airway disease**

## **The effect of component-resolved diagnosis on specific immunotherapy prescription in children with hay fever**

Giovanna Stringari, MD,<sup>a,b\*</sup> Salvatore Tripodi, MD,<sup>c\*</sup> Carlo Caffarelli, MD,<sup>b\*</sup> Arianna Dondi, MD,<sup>d,e</sup> Riccardo Asero, MD,<sup>f</sup> Andrea Di Rienzo Businco, MD,<sup>c</sup> Annamaria Bianchi, MD,<sup>g</sup> Paolo Candelotti, MD,<sup>g</sup> Giampaolo Ricci, MD,<sup>e</sup> Federica Bellini, MD,<sup>e</sup> Nunzia Maiello, MD,<sup>h</sup> Michele Miraglia del Giudice, MD,<sup>h</sup> Tullio Frediani, MD,<sup>i</sup> Simona Sodano, MD,<sup>i</sup> Iride Dello Iacono, MD,<sup>j</sup> Francesco Macrì, MD,<sup>i</sup> Ilaria Peparini, MD,<sup>i</sup> Carlotta Povesi Dascola, MD,<sup>b</sup> Maria Francesca Patria, MD,<sup>k</sup> Elena Varin, MD,<sup>l</sup> Diego Peroni, MD,<sup>m</sup> Pasquale Comberiati, MD,<sup>m</sup> Loredana Chini, MD,<sup>n</sup> Viviana Moschese, MD,<sup>n</sup> Sandra Lucarelli, MD,<sup>i</sup> Roberto Bernardini, MD,<sup>o</sup> Giuseppe Pingitore, MD,<sup>p</sup> Umberto Pelosi, MD, PhD,<sup>q</sup> Mariangela Tosca, MD,<sup>r</sup> Anastasia Cirisano, MD,<sup>s</sup> Diego Faggian, Biol Sci,<sup>t</sup> Alessandro Travaglini, MSc,<sup>u</sup> Mario Plebani, MD,<sup>†</sup> and Paolo Maria Matricardi, MD<sup>a\*</sup>: The Italian Pediatric Allergy Network (I-PAN) *Berlin, Germany, and Parma, Carpi, Rome, Bologna, Milan, Ascoli Piceno, Naples, Benevento, Verona, Empoli, Iglesias, Genoa, Crotone, and Padua, Italy*

J Allergy Clin Immunol 2014;134: 78-



## Allergen Components - cross reactivity

Pollens	Primary sensitization	Cross-reactivity
Ragweed	Amb a 1	
Mugwort	Art v 1, Art v 3	Art v 3
Parietaria	Par j 2	Par j 2
Plantain or Ribwort	Pla l 1	Pla l 1
Timothy	Phl p 1, Phl p 5, Phl p 6	Phl p 4, Phl p 7, Phl p 11, Phl p 12
Bermuda grass	Cyn d 1	Cyn d 1
Birch	Bet v 1, Bet v 6	Bet v 1, Bet v 2, Bet v 4
Bee	Api m 1, Api m 4	CCDs
Wasp	Pol d 5, Ves v 1, 5	Ves v 2, CCDs
House dust mite	Der p 1, Der p 2, Der f 1, Der f 2, Der p 23	Der p 10



## 3 patients with symptoms in UK in April-May and a positive SPT/IgE to whole grass and birch pollen extracts

### Patient 1:

- ▶ Specific-IgE
  - Phl p 1
  - Phl p 5
  - Phl p 12

### Patient 2:

- ▶ Specific-IgE
  - Phl p 1
  - Phl p 5
  - Bet v 1

### Patient 3:

- Specific-IgE
  - Bet v 1
  - Bet v 2

## 3 patients with symptoms in UK in April-May and a positive SPT/IgE to whole grass and birch pollen extracts

Patient 1:

Grass pollen SAR

► Specific-IgE

- Phl p 1
- Phl p 5
- Phl p 12 (Bet v 2)

Patient 2:

Grass and birch SAR

► Specific-IgE

- Phl p 1
- Phl p 5
- Bet v 1

Patient 3:

Birch pollen SAR

• Specific-IgE

- Bet v 1
- Bet v 2 (Phl p 12)

# Patterns of HDM sensitization and implications for AIT



**Allergy** EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY

EAACI

Allergy

ORIGINAL ARTICLE EXPERIMENTAL ALLERGY AND IMMUNOLOGY

**Patterns of IgE sensitization in house dust mite-allergic patients: implications for allergen immunotherapy**

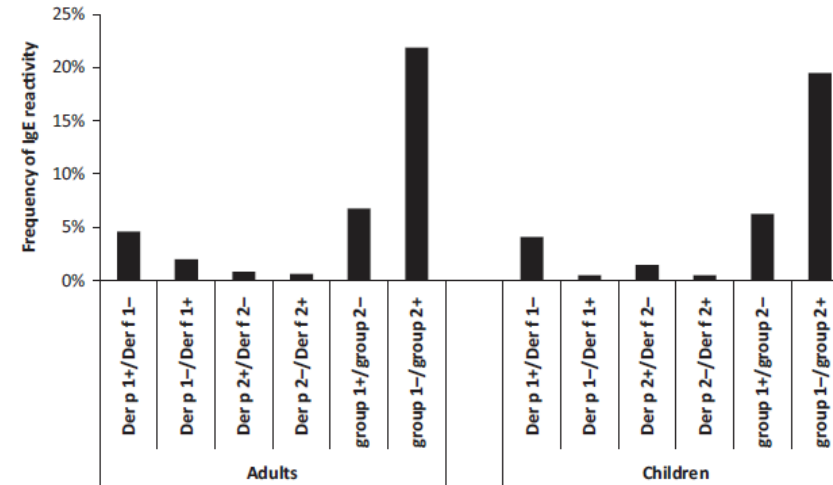
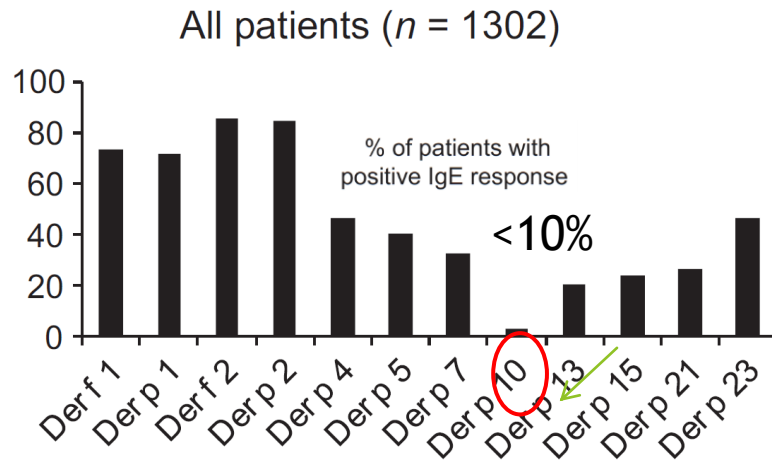
T. Batard<sup>1</sup>, V. Baron-Bodo<sup>1</sup>, A. Martelet<sup>1</sup>, M. Le Mignon<sup>1</sup>, P. Lemoine<sup>1</sup>, K. Jain<sup>1</sup>, S. Mariano<sup>1</sup>,

Batard et al; Allergy 2015

- 1300 HDM allergic patients were assessed for 12 purified allergens from Der p or Der f across Europe, Japan and North America



# Patterns of HDM sensitization and implications for AIT



## Patterns of Der p/f sIgE sensitization

Der p/f 1-2 >80% - Major allergens

Der p 4, 5, 7, 13, 15 21 23 > 20%

Der p 10 <10 %- Minor allergen

# 6–7% of patients have IgEs to group 1 only

#19–22% of patients have IgEs to group 2 only

**\*Mite-specific AIT should rely upon a mixture of *D. pteronyssinus* and *D. farinae***

**extracts with both major allergens**



## EAACI Guidelines on Allergen Immunotherapy: House dust mite-driven allergic asthma

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Juan José Yepes-Nuñez<sup>31</sup>  | Marek Jutel<sup>5,6</sup>

# Any Questions?

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