McMaster University
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TRUE or FALSE?

1. Intranasal steroids are the first line for the treatment of rhinitis when moderate nasal congestion is present
2. Sublingual house dust mite immunotherapy reduces allergic rhinitis and asthma symptoms

18 year old girl

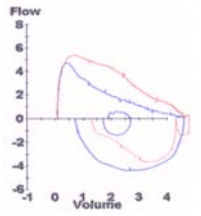
- Severe ear itching and nasal congestion in May and June but can occur anytime of year
- Peaches give her a very itchy throat if raw but not cooked
- Chest tightness with exertion and wakes with cough at least one night per week
- Tried allergy shots in past with some benefit but still has symptoms this year

18 year old girl

- Tried oral antihistamines but got drowsiness
- Tried nasal steroids but got bleeding
- Uses inhaled steroid when cough severe
- Uses salbutamol 2 puffs before exercises and every morning

Blood eosinophils 0.4 (0-0.4 X 109/L)

Spirometry

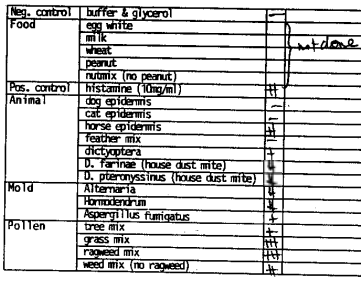


		Measured		
	Reference Values	PRE	% Predicted	POST
FEV_1 (Liters)	3.6	2.8	78	3.5
FVC (Liters)	3.8	4.5	118	4.7
VC (Liters)	4.4			
FEV_1/FVC%	85	62		76

25% reversible

Allergy skin prick testing

18 year old girl



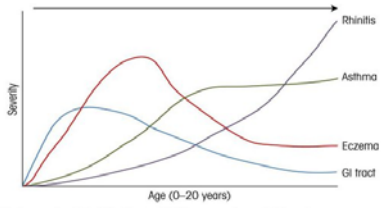
Skin Test Size:
+ = 1-2mm
++ = 3-5mm
+++ = 6-9 mm
++++ = >9mm

Birch pollen ++
Mugwort pollen ++
Mouse -

What do you think is causing her symptoms?

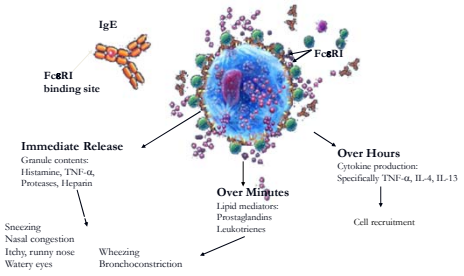
What are your next steps?

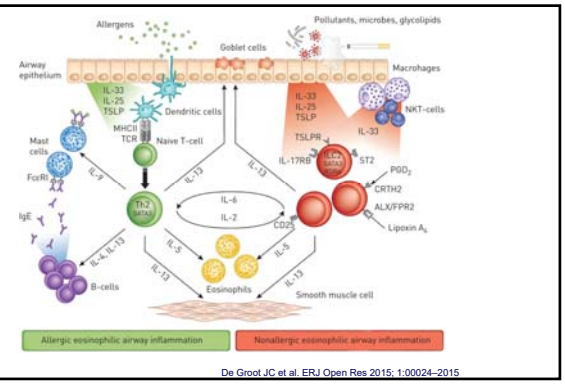
The atopic march



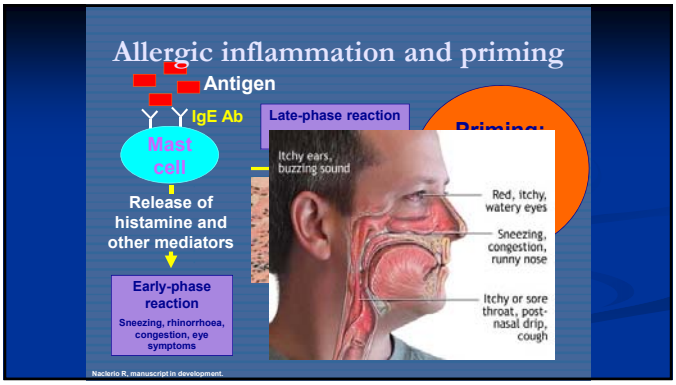
Delves *et al. Roitt's Essential Immunology, 12th ed.*
© 2011 Delves *et al.* Published 2011 by Blackwell Publishing Ltd.

IgE-dependent Release of Inflammatory Mediators

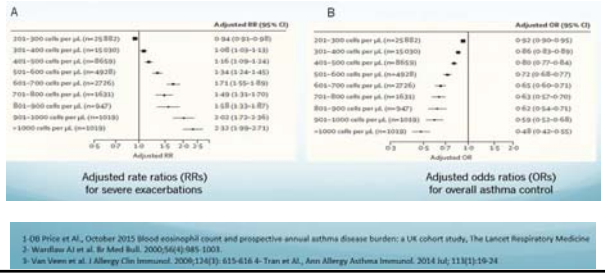




De Groot JC et al. ERJ Open Res 2015; 1:00024–2015

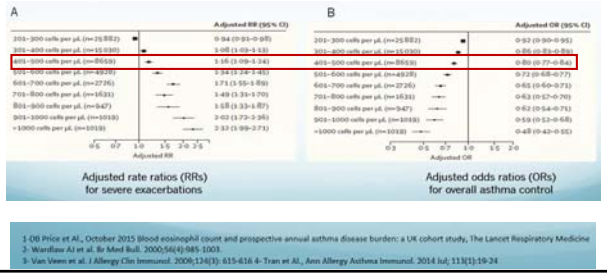


Blood eosinophils in asthma: relationship to exacerbations and control



1-08 Price et al., October 2015 Blood eosinophil count and prospective annual asthma disease burden: a UK cohort study, The Lancet Respiratory Medicine
2- Wardlaw AJ et al. Br Med Bull. 2000;56(4):985-1003.
3- Van Veen et al. J Allergy Clin Immunol. 2006;134(3): 615-616 4- Tran et Al., Ann Allergy Asthma Immunol. 2014 Jul; 113(1):19-24

Blood eosinophils in asthma: relationship to exacerbations and control



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3- Van Veen et al. J Allergy Clin Immunol. 2006;134(3): 615-616 4- Tran et Al., Ann Allergy Asthma Immunol. 2014 Jul; 113(1):19-24

The effect of reducing levels of cat allergen (Fel d 1) on clinical symptoms in patients with cat allergy:

Only 31 of 219 initial volunteers completed the study once it was explained

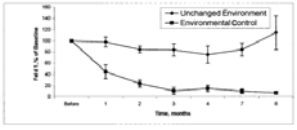
Environmental Control Measures:

Wash all wall and floors at study entry.
Remove carpeting from bedrooms.
Remove upholstered furniture from bedrooms.
Close closets at all times when not in use.
Vacuum floors, carpets, and furniture weekly.
Apply tannic acid (3%) to carpeting and upholstered furniture every 2 months.
Wash bedding at 60° C (130° F) weekly.
Replace old duvets and pillows with polyester-filled duvets and pillows for both patient and spouse.
Cover mattresses and pillows with impermeable covers, mop floor, and wet-wipe surfaces weekly.
Wash cat every 2 weeks.
Keep cat out of bedroom.
Sleep with bedroom windows open.

Bjornsdottir US et al. Ann Allergy Asthma Immunol. 2003;91:189–194

The effect of reducing levels of cat allergen (Fel d 1) on clinical symptoms in patients with cat allergy

Mean Fel d 1 concentrations in dust from environmental control vs unchanged environment homes



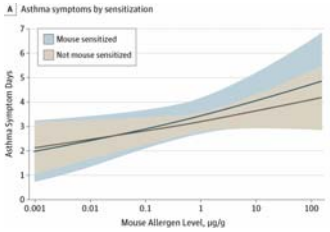
Results are presented as mean ± SEM percentage decrease from baseline Fel d 1 values.
Baseline Fel d 1 equals 100%.
After 2, 3, and 8 months, there was a significant difference between EC and UE groups

Nasal Scores for the Environmental Control (EC) and Unchanged Environment (UE) Groups*

Symptom		Mean (SEM) nasal score 0 mo	8 mo	P value†	
Nasal flow					
	EC	154.9 (10.5)	216.7 (10.8)	0.01	↑40%
	UE	177.6 (11.2)	168.8 (12.8)		
Congestion					
	EC	3.4 (0.5)	0.9 (0.2)	0.05	↓74%
	UE	2.7 (0.4)	2.9 (0.4)		
Rhinorrhea					
	EC	3.6 (0.6)	1.1 (0.2)	0.005	
	UE	2.6 (0.3)	2.4 (0.4)		
Itching					
	EC	1.1 (0.4)	0.1 (0.09)	<0.001	
	UE	0.9 (0.4)	1.7 (0.6)		

Bjornsdottir US et al. Ann Allergy Asthma Immunol. 2003;91:189–194

Mouse allergen exposure in schools



Sheehan WJ et al. JAMA Pediatr. 2017;171(1):31-38.

House dust mite

ORIGINAL ARTICLE

Preventing Severe Asthma Exacerbations in Children
A Randomized Trial of Mite-Impermeable Bedcovers

Clare S. Murray[1,2,3], Philip Foden[1,2], Helen Sumner[1], Elizabeth Shepley[1,2,4], Adnan Custovic[5], and Angela Simpson[1,2]

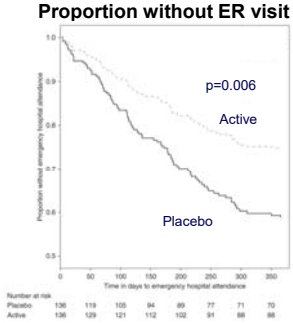
[1]Division of Infection, Immunity and Respiratory Medicine, Manchester Academic Health Sciences Centre, University of Manchester, Manchester, United Kingdom; [2]University Hospital of South Manchester, Manchester, United Kingdom; [3]Royal Manchester Children's Hospital, Central Manchester University Hospitals National Health Service Foundation Trust, Manchester, United Kingdom; [4]National Institute for Health Research South Manchester Respiratory and Allergy Clinical Research Facility, University Hospital of South Manchester, United Kingdom; and [5]Department of Paediatrics, Imperial College London, London, United Kingdom

ORCID ID: 0000-0003-2733-6666 (A.S.).

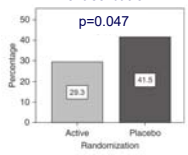
- randomized, double-blind, placebo-controlled, parallel-group study of the effect of mite-impermeable bedcovers on the risk of severe asthma exacerbations in mite-sensitized children with asthma
- Children 3 to 17 without dust mite covers, excluded premature
- required admission to hospital with asthma

American Journal of Respiratory and Critical Care Medicine Volume 196 Number 2|July 15 2017

Proportion without ER visit



Hospital attendance with asthma exacerbation



Murray CS et al. AJRCCM 2017;196:150-158.

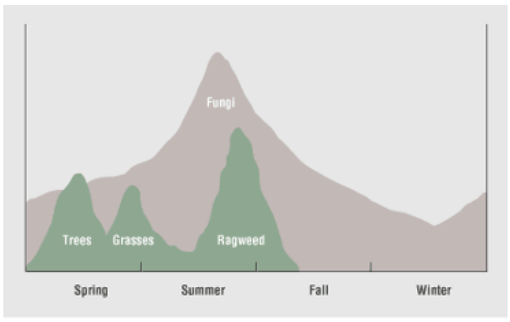


Figure 1. Seasonal aeroallergens in the Midwest.

Oral allergy syndrome

Alder pollen: almonds, apples, celery, cherries, hazel nuts, peaches, pears, parsley, raspberry, strawberry

Birch pollen: almonds, apples, apricots, avocados, bananas,carrots, celery, cherries, chicory, coriander, fennel, fig, hazel nuts, kiwifruit, nectarines, parsley, parsnips, peaches, pears, peppers, plums, potatoes, prunes, soy, strawberries, wheat; Potential: walnuts

Grass pollen: fig, melons, tomatoes, oranges, celery, peach

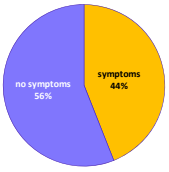
Mugwort pollen : carrots, celery, coriander, fennel, parsley, peppers, sunflower

Ragweed pollen : banana, cantaloupe, cucumber, green pepper, paprika, sunflower seeds/oil, honeydew, watermelon, zucchini, echinacea, artichoke, dandelions, honey (if bees pollinate with pollen from wild flowers), hibiscus or chamomile tea

Possible cross-reactions (to any of the above): berries (blueberries, raspberries, etc.), citrus (oranges, lemons, etc.), grapes, mango, figs, peanut, pineapple, pomegranates, watermelon

https://en.wikipedia.org/wiki/Oral_allergy_syndrome

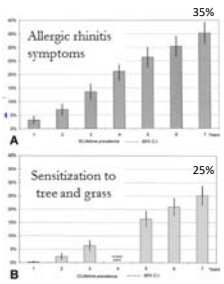
Do you have nasal congestion or nasal symptoms?



N =3671

- 44% of eligible respondents reported either nasal congestion or nasal symptoms
- 20% had been diagnosed with AR by a physician

Keith PK *et al*, Allergy Asthma & Clin Immunology 2012, 8:7



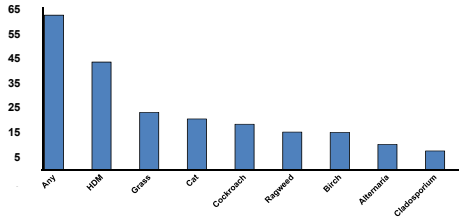
Prevalence at 7 years in a prospective birth cohort of 939 children of rhinitis

Risk factors were:
male sex (odds ratio [OR] = 2.4),
atopic mothers (OR = 2.6),
fathers have AR (OR = 3.6),
first-born child (OR = 2.0),
early sensitization to food (OR =3.3),
and atopic dermatitis (OR = 2.5),
whereas early wheezing was not associated with SAR.

Kulig M et al. JACI 2000;105:832

Prevalence of positive skin test responses among the Canadian population aged 20 to 44 years

- Skin testing was conducted on 2873 patients



Chan-Yeung et al. *Allergy* 2010; 65:1404-13

Rhinitis Differential Diagnosis

Structural/Mechanical Abnormalities	Systemic Disease
Septal deviation	Primary ciliary dyskinesia (PCD)
Turbinate hypertrophy	Cystic fibrosis
Nasal tumours	Churg–Strauss syndrome
Adenoidal hypertrophy	Granulomatosis with polyangiitis
Pharyngonasal reflux	Sarcoidosis
Nasal polyps	Amyloidosis
Choanal atresia	Relapsing polychondritis
Nasal trauma/foreign object	
Cerebrospinal fluid rhinorrhea	
Nasal valve problems	

Papadopoulos et al.; Allergy 2015; 70: 474-94

42

Table 6. Diagnostic Tests for Allergic Rhinitis

Prick or puncture skin tests	Most sensitive test for presense of skin test allergen-specific IgE; cost-effective
Serum specific IgE (e.g. RAST)	Reasonable alternative when skin testing cannot be performed; drugs and skin disease do not affect results
Sweat chloride	Rule out polyps caused by cystic fibrosis
Antineutrophil cytoplasmic antibodies (cANCA,ANCA)	Useful if considering vasculitis
Routine sinus radiograph	May reveal anatomic abnormalities but can misleading
CT/MRI	Useful in assessing anatomy, particularly for sinus disease

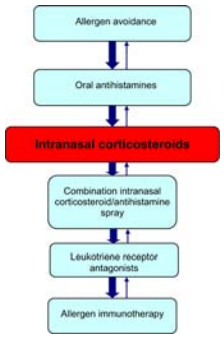
CT = computed tomography; Ig = immunoglobulin; MRI = magnetic resonance imaging; RAST = radioallergosorbent test

For allergy skin prick tests:
- Use appropriate positive and negative controls
- Repeat if indicated (results can change over time)
- Size of wheal does not correlate with symptoms

Rhinitis: a practical & comprehensive approach to assessment and treatment. J Otolaryngol 2007;36(1):51-S28

Simplified AR Treatment Algorithm

Treatments can be used individually or in any combination

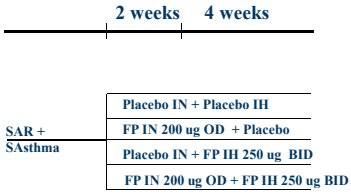


Small P, Keith PK, Kim H. AACI 2018;14:51

Intranasal and inhaled fluticasone propionate for pollen-induced rhinitis and asthma

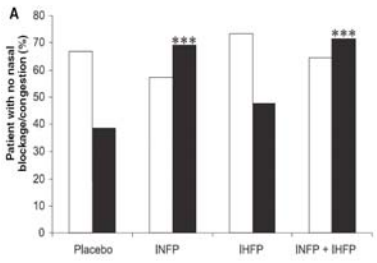
Dahl R et al. Allergy 2005; 60: 875-81

Study Design



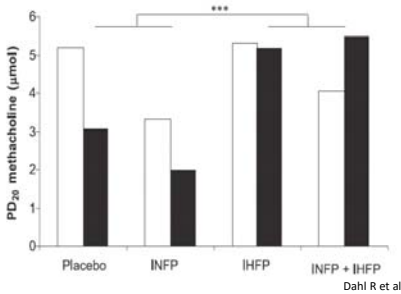
Dahl R et al. Allergy 2005; 60: 875-81

Nasal symptoms: nasal blockage



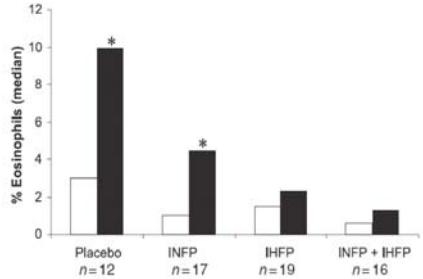
Dahl R et al. Allergy 2005; 60: 875-81

Lower airway hyperresponsiveness

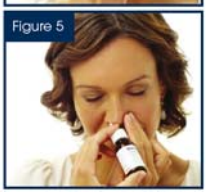


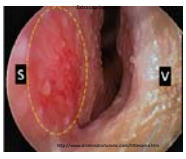
Dahl R et al. Allergy 2005; 60: 875-81

Sputum eosinophils

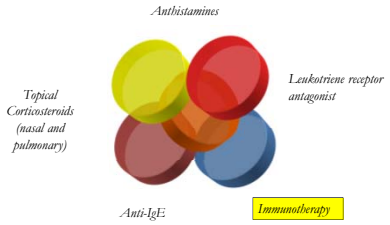


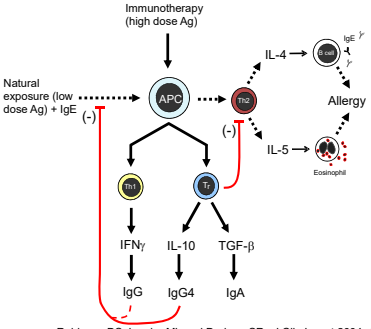
Dahl R et al. Allergy 2005; 60: 875-81





First and Second Line Therapies for Patients with Allergic Rhinitis and Asthma

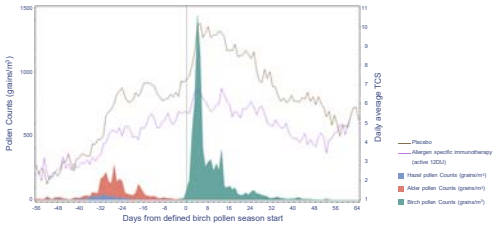




Robinson DS, Larche ML and Durham SR. J Clin Invest 2004; 114: 1389-97

Sublingual Immunotherapy (SLIT) Products

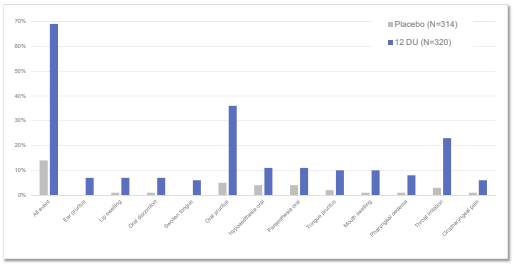
Birch tree pollen SLIT: Primary endpoint during the pollen season (TCS; max. 38)



Biedermann T et al. J Allergy Clin Immunol. 2019 Mar;143:1058

Most frequently reported AEs

Proportion of subjects reporting treatment related AEs (safety analysis set)

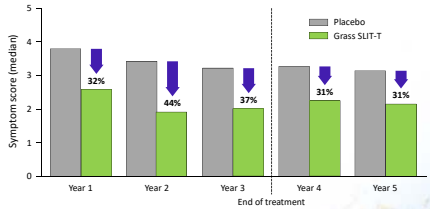


Biedermann T., J Allergy Clin Immunol 2019;143:1058-66

Grass Pollen Tablet Long-term Efficacy

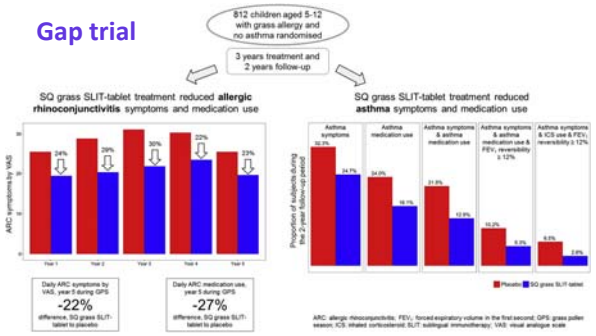
Effect sustained 2 years after treatment

Total daily rhinoconjunctivitis symptom score (median values)



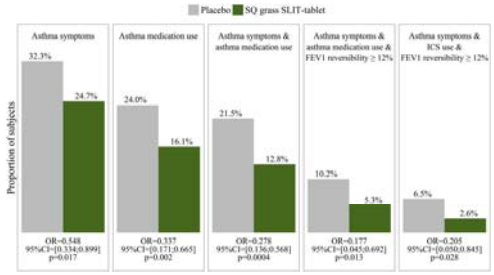
SLIT-T = sublingual immunotherapy tablet treatment
Durham SR, et al. J Allergy Clin Immunol 2010; 125:131-8.

Gap trial



Valovirta E et al. JACI 2018;141:529

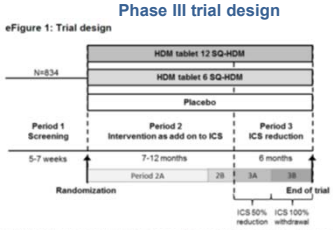
Gap trial: 2 year followup period



Valovirta E et al. JACI 2018;141:529

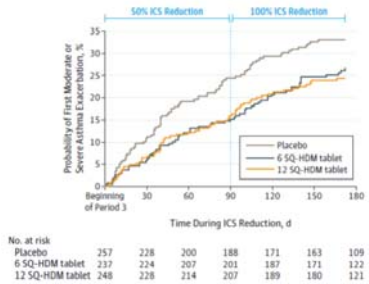
SLIT-tablet in House dust mite allergic Asthma

Phase III trial design

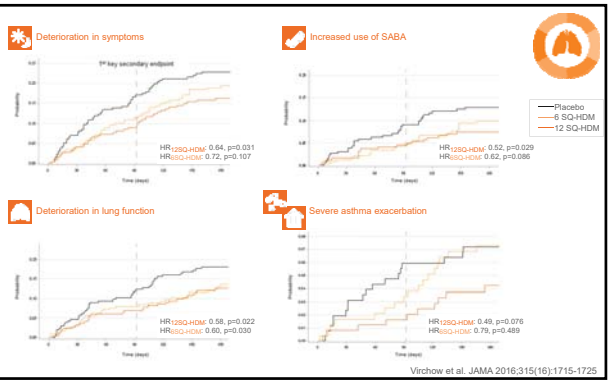


Period 2 (where participants received intervention as add-on to ICS) lasted 7-12 months; period 2B was the last 4 weeks of the period where subjects stated filling in a daily electronic diary. Period 3 (ICS reduction/withdrawal) lasted 6 months; both period 3A and 3B lasted approximately 3 months.

SLIT-tablet in HDM Allergic Asthma: probability of having first moderate or severe asthma exacerbation

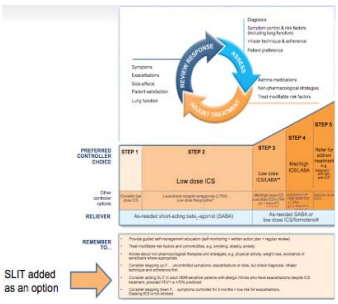


Virchow et al. JAMA 2016;315(16):1715-1725



Virchow et al. JAMA 2016;315(16):1715-1725

Allergic asthma: HDM SLIT included in the **GINA 2017** recommendations



- Although the phase 3 study was designed as a step-down approach *(artificial model to induce exacerbations)* it was interpreted as a step-up option by the GINA 2017 recommendations

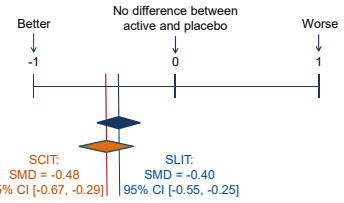
" Consider adding SLIT in adult HDM-sensitive patients with asthma who have exacerbations despite ICS treatment, provided FEV1 is >70% predicted " - GINA 2017

SLIT Is Comparable to SCIT

(Systematic Review of Double-Blind Randomized Clinical Trials of SCIT and SLIT With Inhalant Allergens)

Symptom-Medication Scores

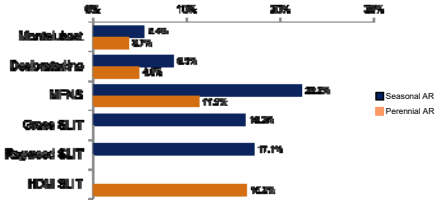
Standardized Mean Difference (SMD)



Modified from Dretzke, et al. Allergy Clin Immunology. 2013;131:1361-6.
SLIT=sublingual immunotherapy; SCIT=subcutaneous immunotherapy.

SLIT vs. Pharmacotherapy Alone For Seasonal and Perennial AR: Pooled Analysis

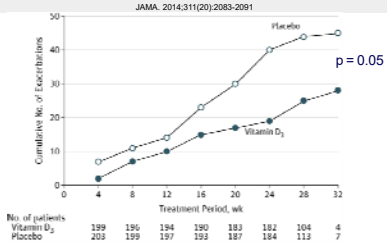
Summary of Relative TNSS Improvements vs. Placebo



Durham S, et al. EAACI 2016. Presentation #54.

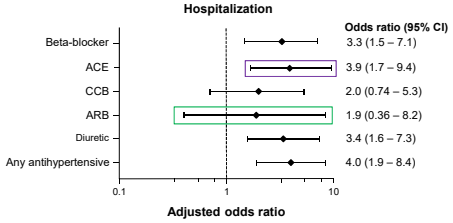
Effect of Vitamin D_3 on Asthma Treatment Failures in Adults With Symptomatic Asthma and Lower Vitamin D Levels: The VIDA Randomized Clinical Trial

JAMA. 2014;311(20):2083-2091



Secondary Exacerbation Outcome: The first data point corresponds to the number of exacerbations that occurred during the first 4 weeks of treatment. The adjusted hazard ratio for cumulative number of exacerbations that occurred over the course of the trial was 0.63 (95% CI, 0.39-1.01; P = .05).

Antihypertensive Medication Use is Associated with *Increased Hospitalization* in Emergency Department Patients with Anaphylaxis



Lee S, et al. J Allergy Clin Immunol 2013; 131(4):1103-8.

18 year old girl

- Severe ear itching and nasal congestion in May and June but can occur anytime of year
- Peaches give her a very itchy throat if raw but not cooked
- Chest tightness with exertion and wakes with cough at least one night per week
- Tried allergy shots in past with some benefit but still has symptoms this year

18 year old girl

- Allergen avoidance – particularly dust mite covers for pillow and mattress, window filter for bedroom
- Intranasal and inhaled steroid regularly
- Vitamin D3 2000 IU daily
- Nonsedating antihistamine prn
- Consider leukotriene receptor antagonist
- Consider intranasal corticosteroid/antihistamine combination
- Consider immunotherapy, particularly sublingual immunotherapy to house dust mite, which would reduce her asthma and rhinitis symptoms and need for treatment

Summary:

- Allergic rhinitis and asthma are common conditions which often co-exist
- Effective therapy can reduce symptoms and improve outcomes
- Immunotherapy can reduce symptoms and medication use if given appropriately for sufficient duration

Summary

- Sublingual immunotherapy products available:
  - Grass (5 years of age and over) – Oralair and Grastek
  - Ragweed (Ragwitek)
  - House dust mite (Acarizax)
  - Birch tree (Itulatek)
- Asthma benefits emerging as an important treatment benefit
- Safety profile for sublingual immunotherapy continues to be robust

TRUE or FALSE?

1. Intranasal steroids are the first line for the treatment of rhinitis when moderate nasal congestion is present TRUE
2. Sublingual house dust mite immunotherapy reduces allergic rhinitis and asthma symptoms TRUE