

# Allergy Immunotherapy: A New Role for the Family Physician

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## ***Incredible 4-year scientific study proves:***

By BEATRICE DEXTER

Chrome domes may have less hair than other men — but they've got more brains, a surprising new study reveals!

According to endocrinologist Paul Rantala of Tampere, Finland, hormones that deprive a male of his crowning glory also beef up his IQ.

"To date, we have no explanation for our findings, but they are clear," Rantala wrote in a report on his four-year research

study. "Bald males score higher in 24 key tests of intellectual ability, including conceptualization, abstract reasoning and recall.

"Our hypothesis is that hairless men metabolize the male hormone testosterone differently than men with a full head of hair. But how they do this, or why, we simply don't know."

Dr. Rantala and three colleagues at the University of Tampere studied 432 men be-

conference of endocrinologists in Reykjavik, Iceland.

"Bald men had more receptors for the hormone testosterone, for example.

"But we were astonished to find that hairless men were

overall on IQ tests," Rantala said.

He's begun follow-up research on testosterone.

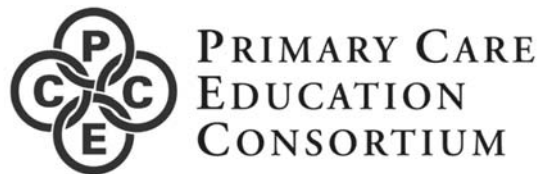
He hopes to find a correlation between that hormone and the development of cer-

# **BALD MEN ARE SMARTER!**

***There's a definite link between lack of hair and IQ, say docs***

tain areas of the brain. He is also planning psychological profiles of bald men to see if their attitudes or life-styles lead to greater intellectual development. "It is possible that bald men spend a greater amount of time reading or studying," the scientist said.

This program is sponsored by



and supported by an educational grant from Stallergenes Greer



The Primary Care Respiratory Group (PCRG) is a national educational initiative providing comprehensive respiratory disease education. Free Membership at PCRG offers free CME and a host of educational resources.

Join at <http://www.pcr-g-us.org>

# Disclosures

- **Stephen Brunton MD has no real or apparent conflicts of interest to report**

# CME

- **This Live activity, Allergy Immunotherapy: A New Role for the Family Physician, from 07/23/2017 - 07/22/2018, has been reviewed and is acceptable for up to 1.00 Prescribed credit(s) by the American Academy of Family Physicians. Physicians should claim only the credit commensurate with the extent of their participation in the activity.**

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## Sublingual Immunotherapy: A Guide for Primary Care

Eli O. Meltzer, MD

## Learning Objectives

After attending this program, the family physician should be able to:

- Compare the mechanisms of sublingual and subcutaneous immunotherapy
- Describe the efficacy and impact on the natural history of allergy of sublingual immunotherapy
- Compare the safety profiles of sublingual and subcutaneous immunotherapy
- Safely initiate sublingual immunotherapy in appropriate patients in family medicine

# Case Study



- **Donna is a 44-year-old woman being seen because hay fever is causing her much discomfort**
- **Symptoms are worse this spring than last spring**
  - Symptoms include rhinitis with watery discharge; itchy, watery eyes; frequent sneezing episodes
- **As in past years, her symptoms began shortly after the snow disappeared and are much worse when her husband mows the lawn**
- **Last year, an intranasal steroid provided adequate relief**
  - She restarted the intranasal steroid once-daily a month ago

?

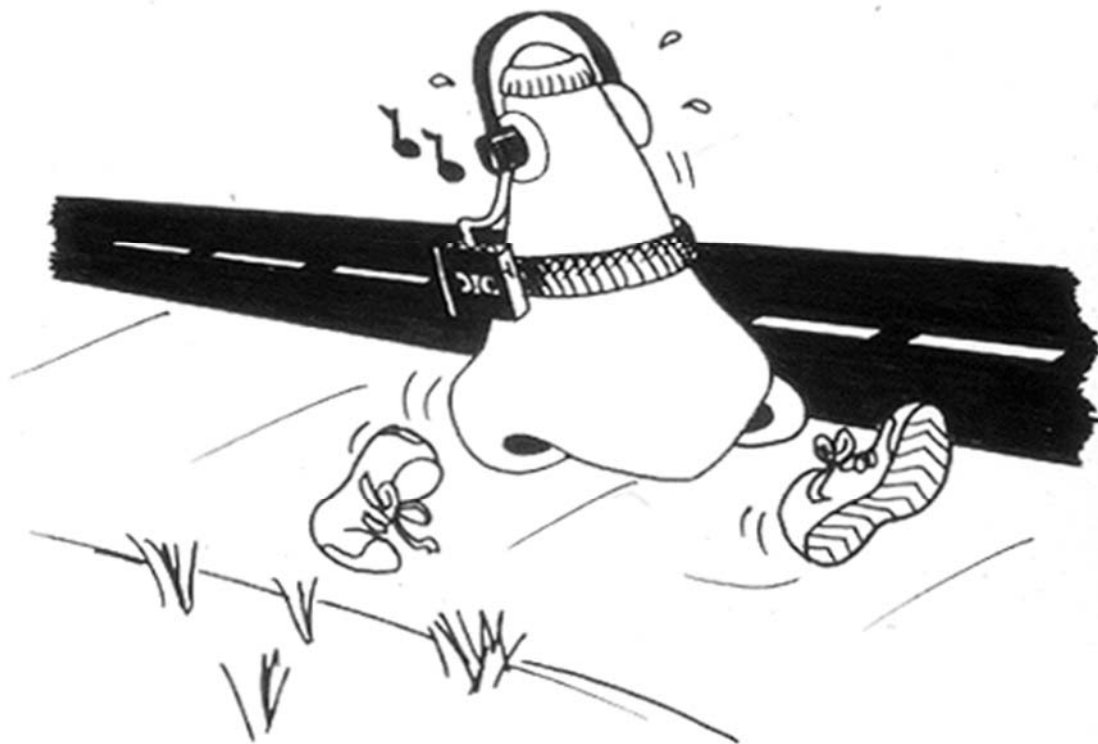
## What would you do?

1. **Refer to an allergist**
2. **Verify sensitivity to allergen by positive skin test or in vitro pollen-specific IgE antibodies**
3. **Discuss with her initiating sublingual immunotherapy**
4. **Verify inhaler technique and discuss allergen avoidance**

# Sample Panel of Respiratory Allergens/Region 4

Level		Level		Level	
	Immunoglobulin E				
	House dust mites/D. pteronyssinus		Penicillium chrysogenum		Elm
	House dust mites/D. farina		Cladosporium		Walnut tree
	Cat epithelium		Aspergillus fumigatus		Cottonwood
	Dog dander		Alternaria tenuis		Mulberry
	Bermuda grass		Olive tree		Short ragweed
	Timothy grass		Grey alder		Mugwort
	Johnson grass		Mountain cedar		Russian thistle
	Cockroach		Oak		Rough pigweed

Profile includes allergens commonly observed in geographic region. Each allergen is tested individually and reported.



# Allergic Rhinitis/Rhinoconjunctivitis

## ■ Allergic rhinitis (AR)

- Affects about 20% of the general population in North America

## ■ Seasonal allergens

- Tree, grass, and weed pollens

## ■ Perennial allergens

- cat dander, cockroach, or dust mite

Lin SY, et al. AHRQ Comparative Effectiveness Review No. 111. Available at [https://www.ncbi.nlm.nih.gov/books/NBK133240/pdf/Bookshelf\\_NBK133240.pdf](https://www.ncbi.nlm.nih.gov/books/NBK133240/pdf/Bookshelf_NBK133240.pdf).  
Min YG. *Allergy Asthma Immunol Res.* 2010;2(2):65-76.

# Management of Allergy Symptoms

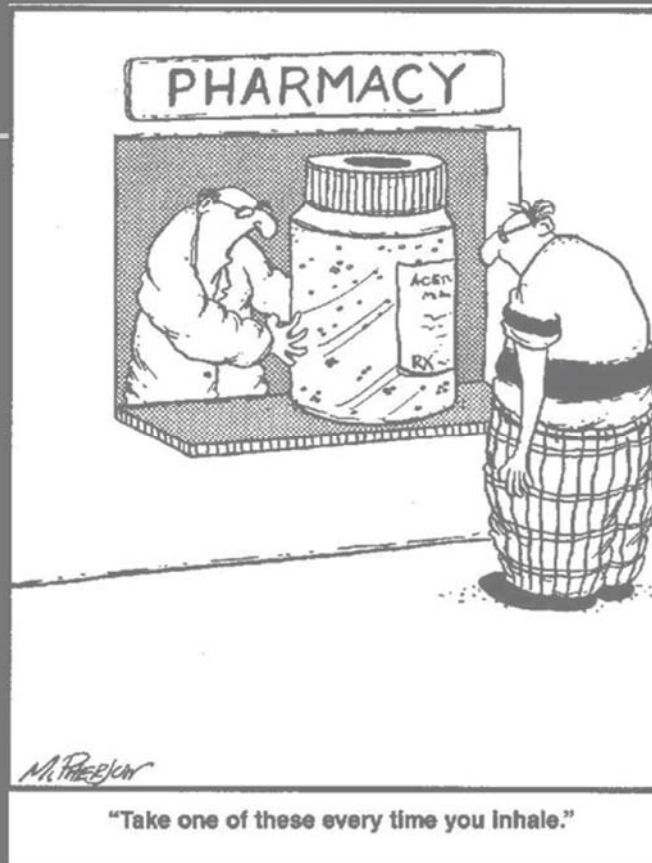
## ■ Medical management of patients with AR includes:

- Allergen avoidance
- Pharmacotherapy
- Immunotherapy

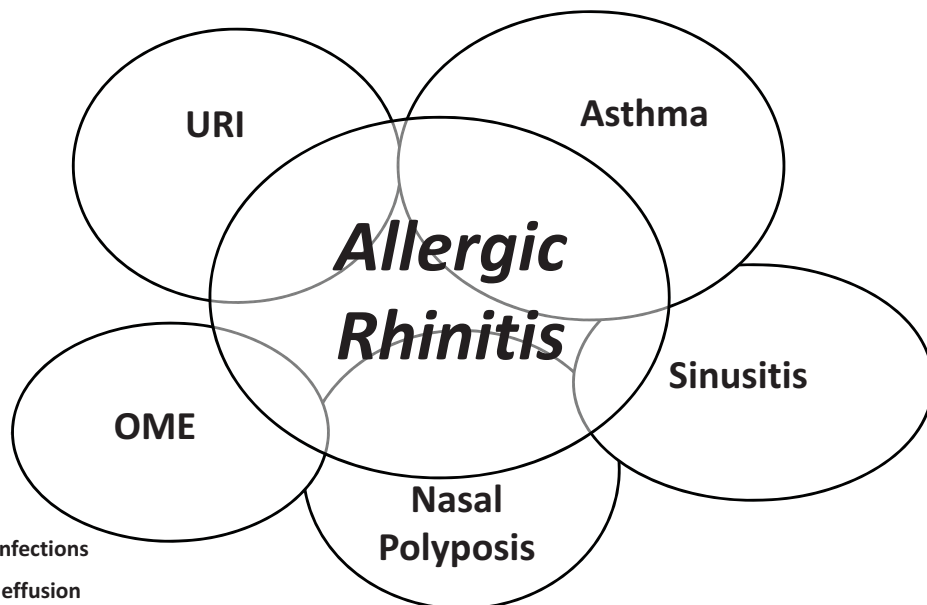
## ■ Daily use of medications for AR symptoms raises issues related to adherence, safety, and cost.

## ■ Long-term use of inhaled nasal steroids can have adverse effects.

Lin SY, et al. AHRQ Comparative Effectiveness Review No. 111. Available at [https://www.ncbi.nlm.nih.gov/books/NBK133240/pdf/Bookshelf\\_NBK133240.pdf](https://www.ncbi.nlm.nih.gov/books/NBK133240/pdf/Bookshelf_NBK133240.pdf).



# Respiratory Comorbidities of AR



URI=upper respiratory infections

OME=otitis media with effusion

Spector SL. *J Allergy Clin Immunol.* 1997;99:5773-5780.



The nose is that part of the lung that you can reach with your finger

## A Link Between AR and Asthma?

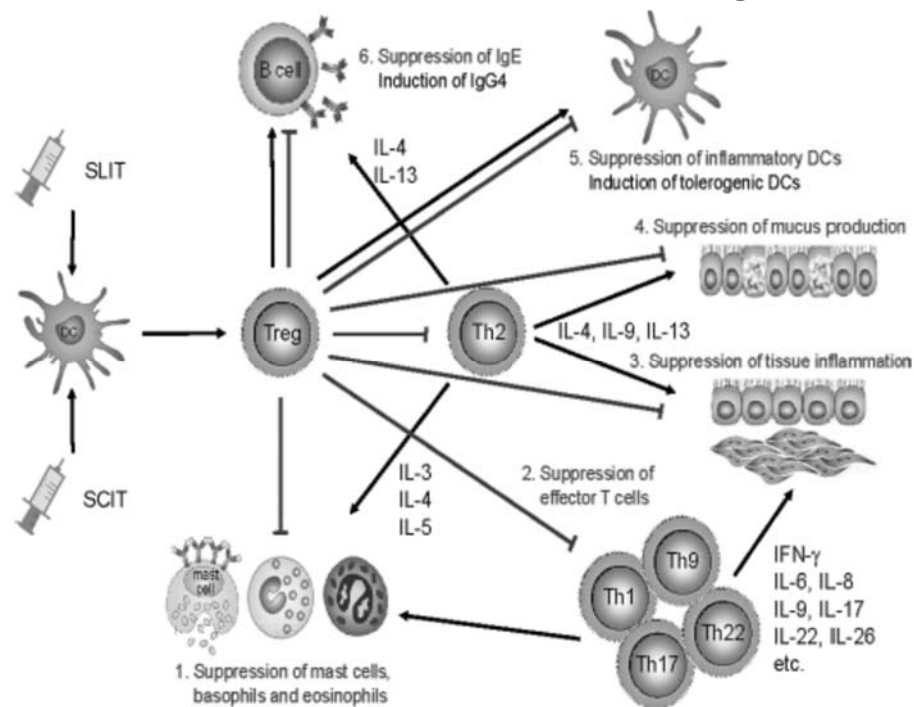
- **AR affects ~78% of patients with allergic asthma**
- **Asthma affects up to 38% of patients with AR**
- **Patients who have AR without asthma often have bronchial hyperresponsiveness**
- **Onsets of AR and asthma often coincide**

# Subcutaneous Immunotherapy for Allergies

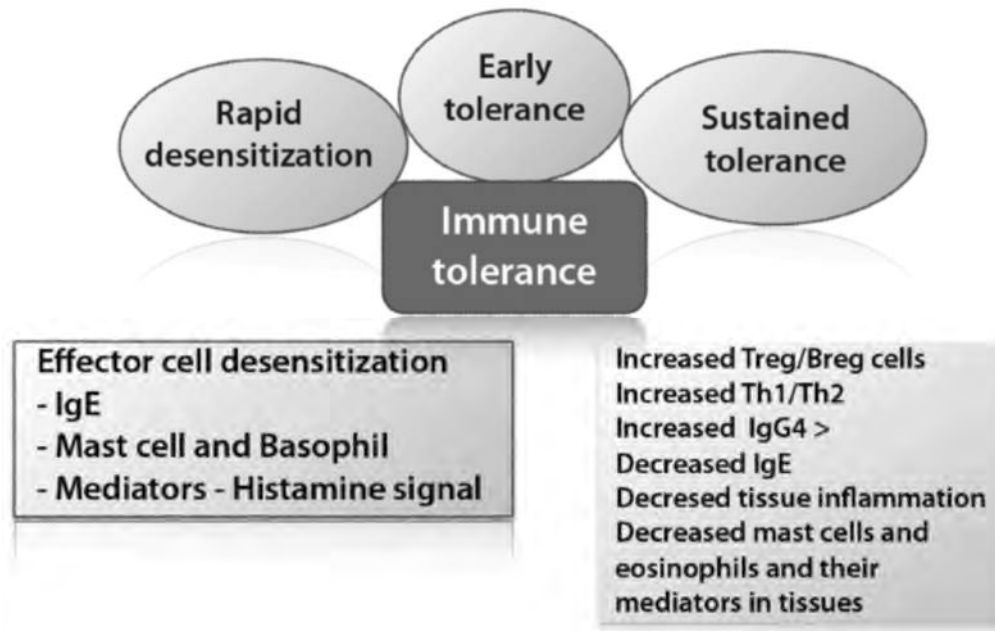
- Allergen-specific immunotherapy is typically used for patients:
  - Whose allergic rhinoconjunctivitis (ARC) symptoms cannot be controlled by medication and environmental measures
  - Who cannot tolerate their medications
  - Who do not adhere to chronic medications
- Historically, a patient with allergies underwent subcutaneous immunotherapy (SCIT) with an extract of the relevant allergen(s) in an attempt to suppress or eliminate allergy-related symptoms.

Lin SY, et al. AHRQ Comparative Effectiveness Review No. 111. Available at [https://www.ncbi.nlm.nih.gov/books/NBK133240/pdf/Bookshelf\\_NBK133240.pdf](https://www.ncbi.nlm.nih.gov/books/NBK133240/pdf/Bookshelf_NBK133240.pdf).

## Mechanisms of Allergen-Specific Immunotherapy



# Mechanisms of Allergen-Specific Immunotherapy (cont)



Jutel M, et al. *J Allergy Clin Immunol.* 2016;137(2):358-368.

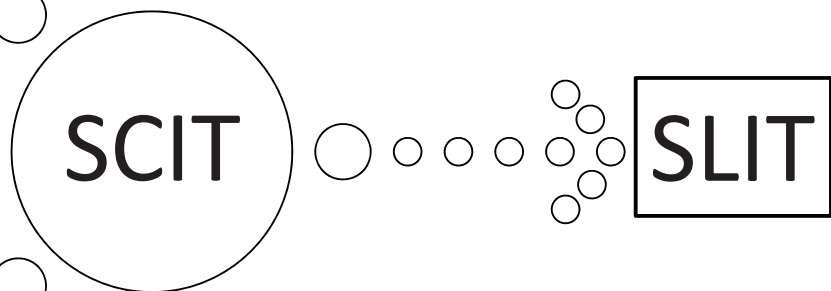
# The Dawn of Sublingual Immunotherapy

## Benefits

○ ○ ○ ○ ○ ○ ○ ○ ○ ○  
(↓ incidence/severity of symptoms; addresses natural history of allergy)

## Limitations

○ ○ ○ ○ ○ ○ ○ ○ ○ ○  
(injections, frequent office visits, rare anaphylaxis)



Lin SY, et al. AHRQ Comparative Effectiveness Review No. 111. Available at [https://www.ncbi.nlm.nih.gov/books/NBK133240/pdf/Bookshelf\\_NBK133240.pdf](https://www.ncbi.nlm.nih.gov/books/NBK133240/pdf/Bookshelf_NBK133240.pdf).  
Jutel M, et al. *J Allergy Clin Immunol.* 2015;136(3):556-568.

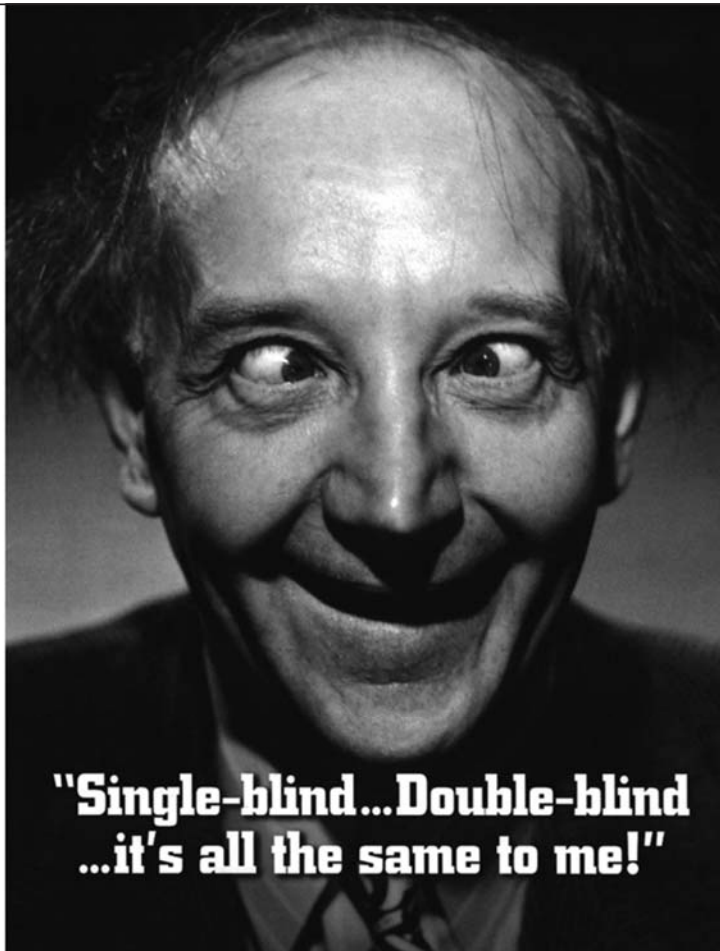
# AHRQ Comparative Effectiveness Review

- 142 randomized, controlled studies
- Subjects
  - Adults only 52%
  - Children only 24%
  - Adults and children 22%
- SLIT studies mainly included patients with allergic rhinitis and/or mild asthma

Allergen	Number of Studies		
	SCIT	SLIT	SCIT vs. SLIT
Dust mite	21	14	6
Grass	11	15	–
Weeds	9	7	–
Cat	5	2	–
Dog	1	–	–
Mold	6	2	–
Tree	6	13	2
Multiple allergens	15	7	–

SCIT, subcutaneous immunotherapy;  
SLIT, sublingual immunotherapy

Lin SY, et al. AHRQ Comparative Effectiveness Review No. 111. Available at [https://www.ncbi.nlm.nih.gov/books/NBK133240/pdf/Bookshelf\\_NBK133240.pdf](https://www.ncbi.nlm.nih.gov/books/NBK133240/pdf/Bookshelf_NBK133240.pdf).



**"Single-blind...Double-blind  
...it's all the same to me!"**

## AHRQ CER: SCIT Versus SLIT\*: All Outcomes

Primary Outcome	Results	No. of RCTs No. of Patients (n)	Strength of Evidence
Improves asthma symptom score	SCIT may improve asthma symptoms more effectively than SLIT	4 RCTs (n = 171)	Low
Improves rhinitis/ rhinoconjunctivitis symptoms	SCIT is superior to SLIT for improving allergic nasal and/or eye symptoms	6 RCTs (n = 412)	Moderate
Decreases use of asthma plus rhinoconjunctivitis medications	There are no consistent differences between SCIT and SLIT	5 RCTs (n = 219)	Low
Improves asthma plus rhinitis/rhinoconjunctivitis symptom and medication score	SCIT is favored in 1 of 2 studies	2 RCTs (n = 65)	Low

RCT, randomized controlled trial; SCIT, subcutaneous immunotherapy; SLIT, sublingual immunotherapy

\*SLIT using drops or tablets of an allergen extract placed under the tongue

Lin SY, et al. AHRQ Comparative Effectiveness Review No. 111. Available at [https://www.ncbi.nlm.nih.gov/books/NBK133240/pdf/Bookshelf\\_NBK133240.pdf](https://www.ncbi.nlm.nih.gov/books/NBK133240/pdf/Bookshelf_NBK133240.pdf).

## AHRQ CER: SLIT\* Versus Placebo or Standard Therapy: Rhinitis/Rhinoconjunctivitis Outcomes

Primary Outcome	Results	No. of RCTs No. of Patients (n)	Strength of Evidence
Rhinitis/ rhinoconjunctivitis symptoms	Significant improvement in 56% of studies vs. controls	36 RCTs (n = 2,658)	Moderate
Conjunctivitis symptoms	Significant improvement in 46% of studies vs. placebo	13 RCTs (n = 1,074)	Moderate
Disease-specific quality of life in patients with rhinitis/ rhinoconjunctivitis	Significant improvement by RQLQ in 75% of studies vs. controls	8 RCTs (n = 819)	Moderate

RCT, randomized controlled trial; RQLQ, Rhinoconjunctivitis Quality of Life Questionnaire

\*SLIT using drops or tablets of an allergen extract placed under the tongue

Lin SY, et al. AHRQ Comparative Effectiveness Review No. 111. Available at [https://www.ncbi.nlm.nih.gov/books/NBK133240/pdf/Bookshelf\\_NBK133240.pdf](https://www.ncbi.nlm.nih.gov/books/NBK133240/pdf/Bookshelf_NBK133240.pdf).



## AHRQ CER: Pediatric Patients—SLIT\* Versus Placebo or Standard Therapy: Rhinitis/Rhinoconjunctivitis Outcomes

Primary Outcome	Results	No. of RCTs No. of Patients (n)	Strength of Evidence
Rhinitis/ rhinoconjunctivitis symptoms	Significant improvement in 42% of studies vs. controls	12 RCTs (n = 1,065)	Moderate
Conjunctivitis symptoms	Significant improvement in 40% of studies vs. placebo	5 RCTs (n = 513)	Moderate

RCT, randomized controlled trial; SLIT, sublingual immunotherapy

\*SLIT using drops or tablets of an allergen extract placed under the tongue

## AHRQ CER: Overview of Conclusions

- **There is sufficient evidence to support the overall effectiveness and safety of both SCIT and SLIT\* for treating ARC.**
- **However, there is not enough evidence to determine if either SCIT or SLIT is superior.**
- **SCIT and SLIT are usually safe, although local reactions are commonly reported regardless of the mode of delivery.**

\*Aqueous allergen extract placed under the tongue as drops or on a tablet

Lin SY, et al. AHRQ Comparative Effectiveness Review No. 111. Available at [https://www.ncbi.nlm.nih.gov/books/NBK133240/pdf/Bookshelf\\_NBK133240.pdf](https://www.ncbi.nlm.nih.gov/books/NBK133240/pdf/Bookshelf_NBK133240.pdf).

## Case Study






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  - She restarted the intranasal steroid once-daily a month ago
- **Testing confirms sensitivity to grass pollen**



# What would you do?

1. Refer to an allergist
2. Discuss initiating sublingual immunotherapy
3. Verify inhaler technique and discuss allergen avoidance

## SLIT Products Available in the United States

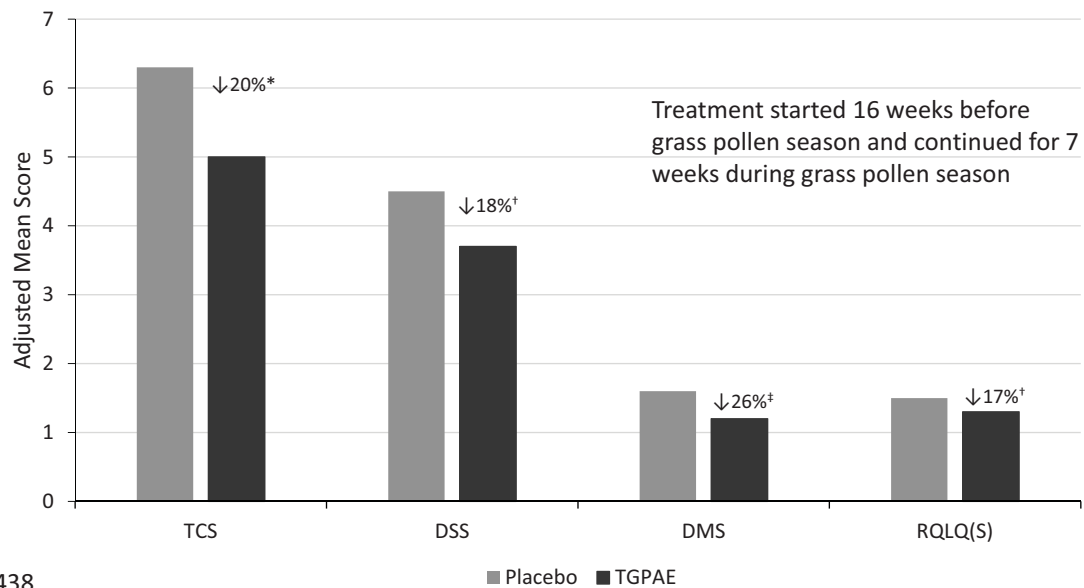
	<b>TGPAE</b> <b>(Grastek)</b> 	<b>5-GPAE</b> <b>(Oralair)</b> 	<b>SRPAE</b> <b>(Ragwitek)</b> 	<b>HDMAE</b> <b>(Odactra)</b>
Extract(s)	Timothy grass	Sweet Vernal, Orchard, Perennial Rye, Timothy, Kentucky Blue grasses	Short ragweed	House dust mite
Indication(s)	Grass pollen-induced AR/ARC confirmed by positive skin test/in vitro test for pollen-specific IgE antibodies for Timothy grass or cross-reactive grass pollens	Grass pollen-induced AR/ARC confirmed by positive skin test/in vitro test for any of the 5 grass pollens	Short ragweed pollen-induced AR/ARC confirmed by positive skin test/in vitro test for pollen-specific IgE antibodies for short ragweed pollen	House dust mite-induced AR/ARC confirmed by in vitro testing for IgE antibodies to <i>D. farinae</i> or <i>D. pteronyssinus</i> house dust mites or skin testing to licensed house dust mite allergen extracts
Patient ages	5-65 years	10-65 years	18-65 years	18-65 years

5-GPAE, 5-grass pollen allergen extract; AR, allergic rhinitis; ARC, allergic rhinitis with conjunctivitis; HDMAE, house dust mite allergen extract; SRPAE, short ragweed pollen allergen extract; TGPAE, Timothy grass pollen allergen extract

Grastek [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; September 2016. Oralair [package insert]. Lenoir, NC: Greer Laboratories, Inc.; December 2016. Ragwitek [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; March 2017. Odactra [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; March 2017.



# Once-daily TGPAE for Grass Pollen-Induced Allergic Rhinoconjunctivitis: Efficacy



N=438

\* $P=0.005$ ; † $P=0.02$ ; †† $P=0.08$

DMS, daily medication score; DSS, daily symptom score; RQLS(S), Rhinoconjunctivitis Quality of Life Questionnaire with standardized activities; TCS, total combined score; TGPAE, Timothy grass pollen allergen extract (Grastek)

Nelson HS, et al. J Allergy Clin Immunol. 2011;127:72-80.

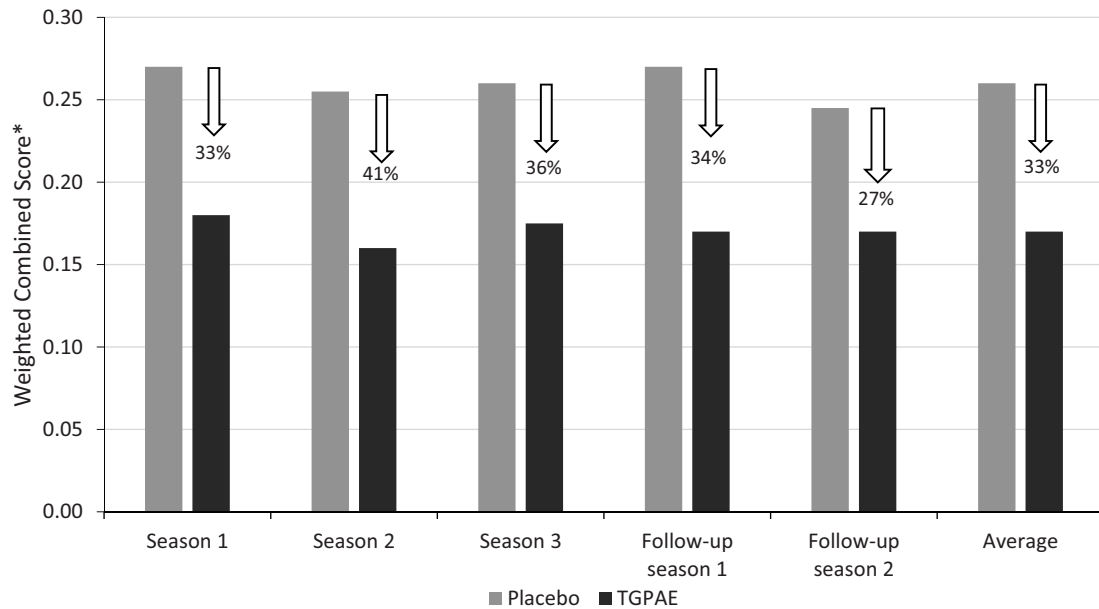
## Sustained Use of Once-daily TGPAE for Grass Pollen-Induced Allergic Rhinoconjunctivitis: Study Design

- **Adults (age 18-65 y) with  $\geq 2$ -y history of grass pollen-induced ARC despite treatment**
- **Beginning 4-8 months prior to anticipated start of grass pollen season, patients were randomized to**
  - TGPAE or placebo once daily
  - Continued for 3 seasons until end of grass pollen season
  - Followed for 2 additional years without treatment

TGPAE, Timothy grass pollen allergen extract (Grastek)

Durham SR, et al. J Allergy Clin Immunol. 2012;129:717-725.

# Sustained Use of Once-daily TGPAE for Grass Pollen-Induced Allergic Rhinoconjunctivitis: Efficacy



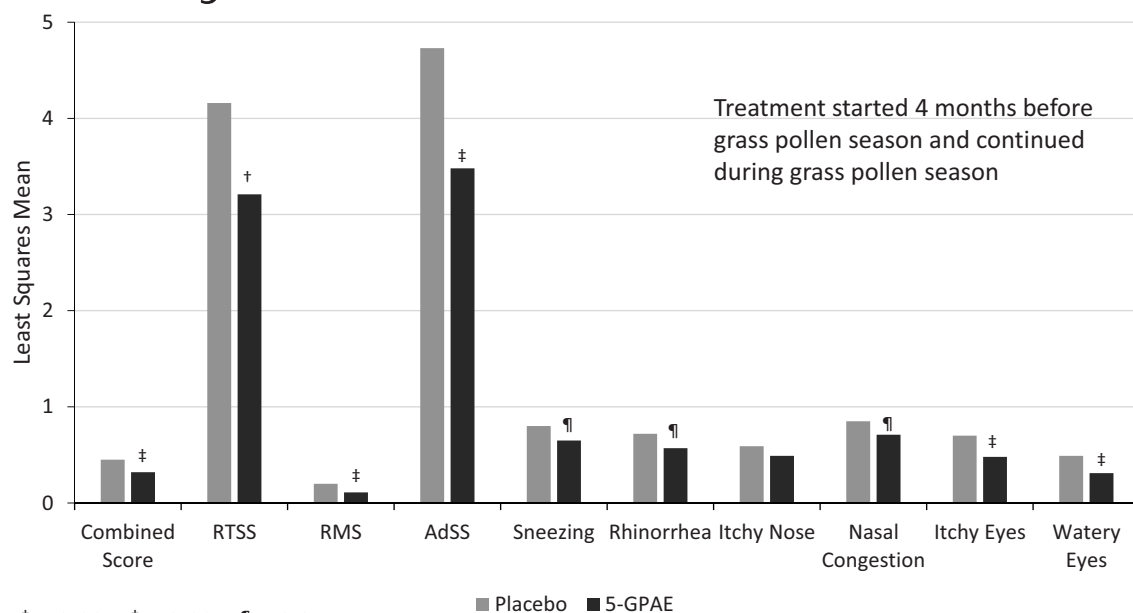
N=473

\*Weighted rhinoconjunctivitis combined symptom and medication score

TGPAE, Timothy grass pollen allergen extract (Grastek)

Durham SR, et al. *J Allergy Clin Immunol.* 2012;129:717-725.

# Once-daily 5-GPAE for Grass Pollen-Induced Allergic Rhinoconjunctivitis: Efficacy



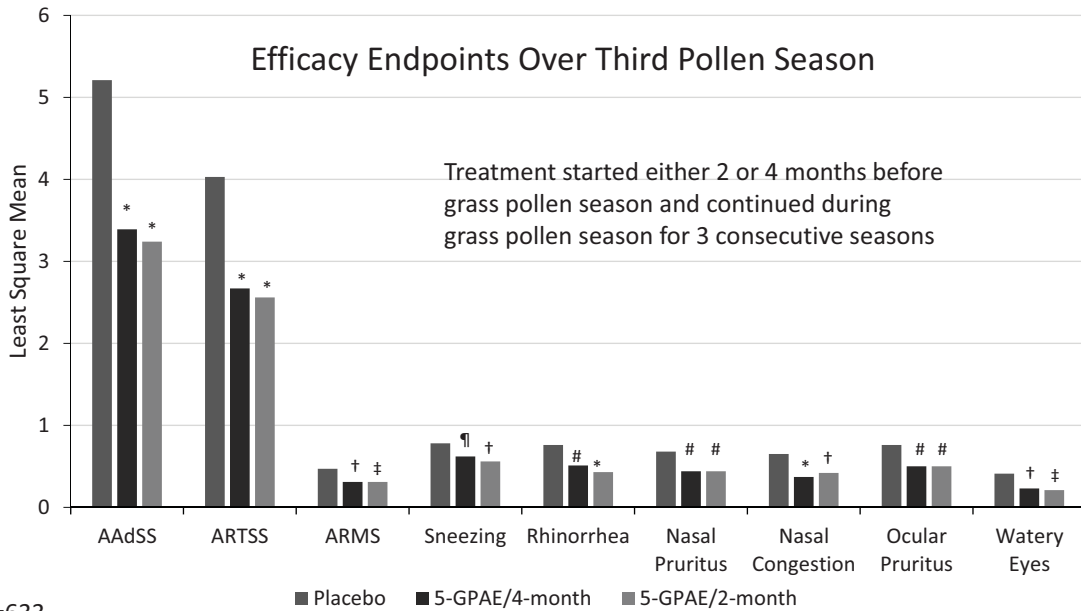
Treatment started 4 months before grass pollen season and continued during grass pollen season

<sup>†</sup> $P \leq 0.005$ ; <sup>‡</sup> $P \leq 0.001$ ; <sup>¶</sup> $P \leq 0.05$

5-GPAE, 5-grass pollen allergen extract (Oralair); AdSS, Adjusted Symptom Score; RMS, Rescue Medication Score; RTSS, Rhinoconjunctivitis Total Symptom Score

Cox LS, et al. *J Allergy Clin Immunol.* 2012;130(6):1327-1334.

# Sustained Use of Once-daily 5-GPAE for Grass Pollen-Induced Allergic Rhinoconjunctivitis: Efficacy



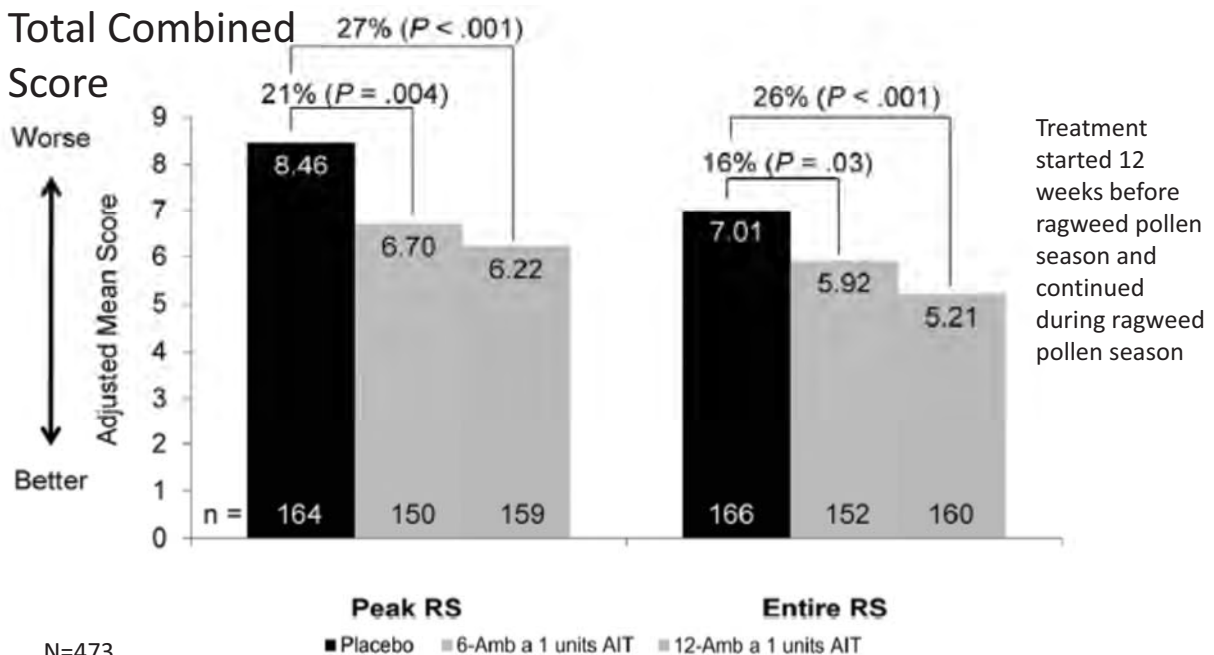
N=633

\* $P \leq 0.0001$ ; † $P \leq 0.005$ ; ‡ $P \leq 0.001$ ; ¶ $P \leq 0.05$ ; # $P \leq 0.0005$

5-GPAE, 5-grass pollen allergen extract (Oralair); AAdSS, Average adjusted symptom score; ARMS, average rescue medication score; ARTSS, average rhinoconjunctivitis total symptom score

Didier A, et al. *J Allergy Clin Immunol.* 2011;128(3):559-566.

# Once-daily SRPAE for Grass Pollen-Induced Allergic Rhinitis/ Rhinoconjunctivitis: Efficacy



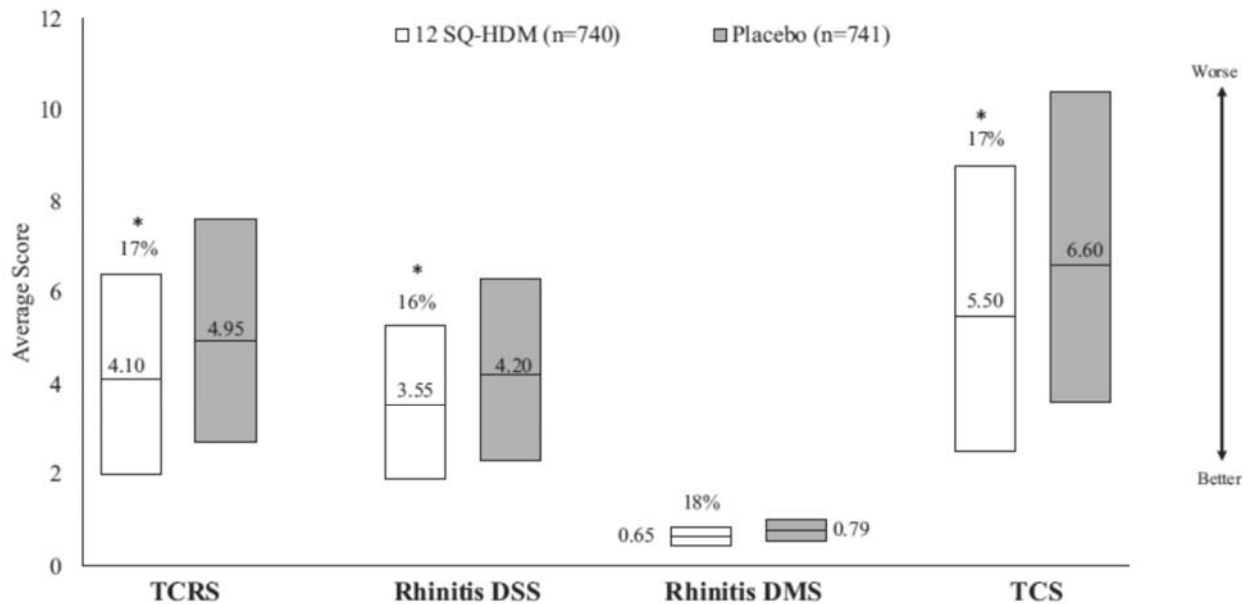
N=473

RS, ragweed season; SRPAE, short ragweed pollen allergen extract (Ragwitek)

Note: 6-Amb a 1 units AIT not available in the United States

Nolte H, et al. *Ann Allergy Asthma Immunol.* 2013;110:450-456.

# Once-daily HDMAE for Dust Mite-Induced Allergic Rhinitis/Rhinoconjunctivitis: Efficacy Over 52 weeks






\*P<0.001

HDMAE, house dust mite allergen extract (Odactra); Rhinitis DMS, rhinitis daily medication score; Rhinitis DSS, rhinitis daily symptom score; TCRS, total combined rhinitis score; TCS, total combined score

Nolte H, et al. *J Allergy Clin Immunol.* 2016;138(6):1631-1638.

## Safety of SLIT Products Available in the United States

	<b>5-GPAE (Oralair)</b> 	<b>TGPAE (Grastek)</b> 	<b>SRPAE (Ragwitek)</b> 	<b>HDMAE (Odactra)</b>
Common adverse events	AEs in ≥5%: Oral pruritus, throat irritation, ear pruritus, mouth edema, tongue pruritus, cough, oropharyngeal pain	AEs in ≥5%: Ear pruritus; oral pruritus; tongue pruritus; mouth edema; throat irritation	AEs in ≥5%: Throat irritation; oral pruritus; ear pruritus; oral paraesthesia; mouth edema; tongue pruritus	AEs in ≥10%: Throat irritation/tickle; mouth pruritus; ear pruritus; swelling of uvula/back of mouth; swelling of lips; swelling of tongue; nausea; tongue pain; throat swelling; tongue ulcer/sore; stomach pain; mouth ulcer/sore; taste alteration
Contraindications	Severe, unstable or uncontrolled asthma; history of severe systemic allergic reaction; history of severe local reaction to SLIT; history of eosinophilic esophagitis; hypersensitivity to any ingredient of product			

5-GPAE, 5-grass pollen allergen extract; AEs, adverse events; HDMAE, house dust mite allergen extract; SLIT, sublingual immunotherapy; SRPAE, short ragweed pollen allergen extract; TGPAE, Timothy grass pollen allergen extract

Oralair [package insert]. Lenoir, NC: Greer Laboratories, Inc.; December 2016. Grastek [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; September 2016. Ragwitek [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; March 2017. Odactra [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; March 2017.

## Limitations of SLIT

- **Small number of allergens**
  - Grass(es), ragweed, dust mite
- **Limited experience vs SCIT**
- **Cost**
  - 5-GPAE: \$14/day
  - TGPAE: \$10/day
  - SRPAE: \$10/day
  - HDMAE: not yet available
  - However, avoids cost of office visit(s) for SCIT

## What advice would you provide to the patient?

?

1. **Wear latex gloves when handling medication**
2. **Suck on hard candy after medication has dissolved**
3. **Report worsening dysphagia and/or heartburn**
4. **Discontinue treatment if nausea occurs**

## Key Points for Family Physicians

- **Verify patient sensitivity to allergen by positive skin test or in vitro pollen-specific IgE antibodies<sup>1-4</sup>**
- **Transitioning from SCIT to SLIT should be guided by allergist**
- **Efficacy and safety of SLIT are similar in children as adults**
- **Initiate therapy**
  - 5-GPAE: ≥16 weeks before expect seasonal onset<sup>1</sup>
  - TGPAE: ≥12 weeks before expect seasonal onset<sup>2</sup>
  - SRPAE: ≥12 weeks before expect seasonal onset<sup>3</sup>
  - HDMAE: at diagnosis<sup>4</sup>

1. Oralair [package insert]. Lenoir, NC: Greer Laboratories, Inc.; December 2016. 2. Grastek [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; September 2016. 3. Ragwitek [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; March 2017. 4. Odactra [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; March 2017.

## Key Points for Family Physicians (cont)

- **It is not clear if grass/ragweed products can be initiated during the pollen season → potential risk for systemic allergic reactions<sup>1</sup>**
- **Dosing once daily with no increase in dose *except*<sup>2-5</sup>**
  - 5-GPAE: children 10-17 y → increase dose over 3 days<sup>2</sup>
- **Administer first dose with close medical supervision for at least 30 minutes<sup>2-5</sup>**
- **Prescribe epinephrine auto-injector for home use; educate patients about symptom(s) of allergic reaction and management**

1. Creticos PS, et al. *J Allergy Clin Immunol Pract.* 2016;4(6):1194-1204. 2. Oralair [package insert]. Lenoir, NC: Greer Laboratories, Inc.; December 2016. 3. Grastek [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; September 2016. 4. Ragwitek [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; March 2017. 5. Odactra [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; March 2017.

## Key Points for Family Physicians (cont)

- **Advise patient to remove tablet with dry hands and immediately place under tongue; let dissolve<sup>1-4</sup>**
  - Do not swallow for  $\geq 1$  minute; no food/beverage for  $\geq 5$  minutes
  - Wash hands after administration
- **H1 and H2 blockers useful for**
  - mild/moderate oral AEs
  - mild abdominal pain and nausea<sup>5</sup>
- **Counsel patients to report worsening dysphagia and/or heartburn<sup>1-4</sup>**
- **Currently no CPT code for billing for SLIT administration**

1. Oralair [package insert]. Lenoir, NC: Greer Laboratories, Inc.; December 2016. 2. Grastek [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; September 2016. 3. Ragwitek [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; March 2017. 4. Odactra [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; March 2017. 5. Epstein TG, et al. *J Allergy Clin Immunol Pract*. 2017;5(1):34-40.

## Case Study



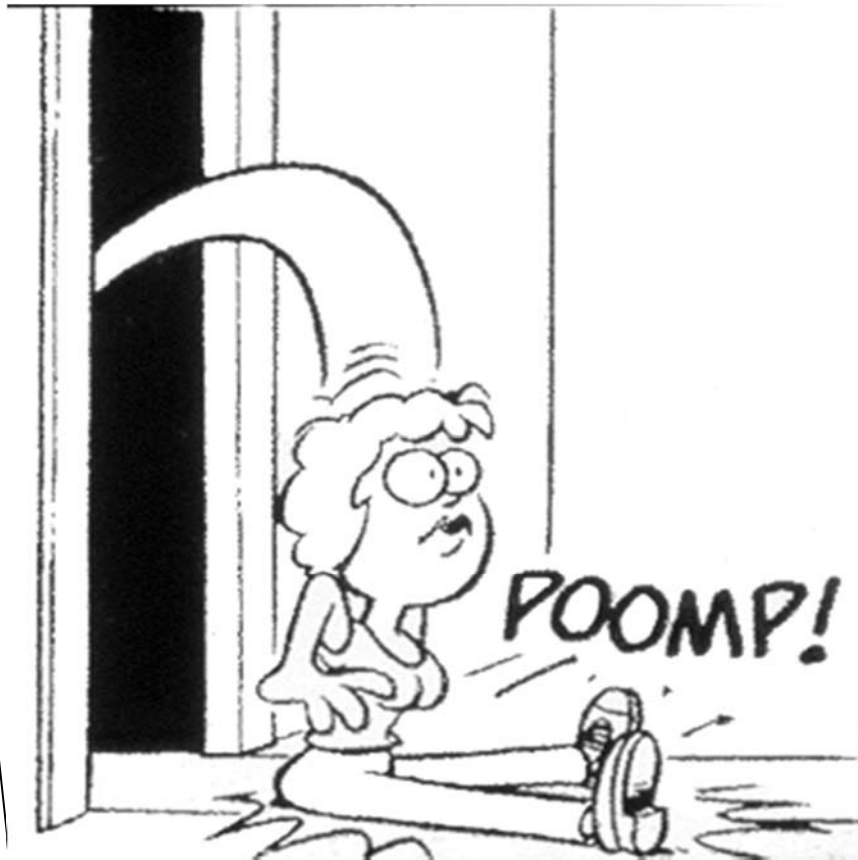
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*Allergy Immunotherapy:  
A New Role for the  
Family Physician*

Thank you!

# *Back-up Slides*

## AHRQ CER: SCIT Versus Placebo or Standard Therapy: Rhinitis/Rhinoconjunctivitis Outcomes

Primary Outcome	Results	No. of RCTs No. of Patients (n)	Strength of Evidence
Rhinitis/ rhinoconjunctivitis symptoms	Significant improvement in 73% of studies vs. controls	25 RCTs (n = 1,734)	High
Use of rhinitis/ rhinoconjunctivitis medications	Significantly decreased in 70% of studies vs. controls	10 RCTs (n = 564)	Moderate
Combined rhinitis/ rhinoconjunctivitis symptom and medication score	Significant improvement in 83% of studies vs. controls	6 RCTs (n = 400)	Low

RCT, randomized controlled trial; SCIT, subcutaneous immunotherapy

# AHRQ CER: SCIT Versus Placebo or Standard Therapy: Rhinitis/Rhinoconjunctivitis Outcomes (cont)

Primary Outcome	Results	No. of RCTs No. of Patients (n)	Strength of Evidence
Conjunctivitis symptoms	Significant improvement in 43% of studies vs. placebo	14 RCTs (n = 1,104)	High
Combined symptoms (nasal, ocular, and bronchial)	Significant improvement in 67% of studies vs. placebo	6 RCTs (n = 591)	High
Disease-specific quality of life in patients with rhinitis/rhinoconjunctivitis	Significant improvement by RQLQ in 67% of studies vs. placebo	6 RCTs (n = 889)	High

RCT, randomized controlled trial; RQLQ, Rhinoconjunctivitis Quality of Life Questionnaire; SCIT, subcutaneous immunotherapy