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Oral Tablet Immunotherapy for Allergic Rhinitis: Advancing Management in the Pediatric Setting

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Advisory Boards: Abionics, ALK-Abello Inc., Allergy Therapeutics, AstraZeneca, GlaxoSmithKline, Regeneron, Sanofi

Speakers' Bureaus: ALK-Abello Inc., AstraZeneca, GlaxoSmithKline, Novartis, Regeneron, Sanofi

Research: Abionics, AstraZeneca, Regeneron

Learning Objectives

- Discuss the burden of symptoms of AR/C and the associated impacts on QOL in children and adolescents
- Implement strategies for the early diagnosis and optimal assessment of AR/C in the pediatric setting
- Describe the role of allergy immunotherapy in the management of patients with AR/C
- Utilize available therapies to achieve optimal management of pediatric patients with AR/C

AR/C, allergic rhinitis and rhinoconjunctivitis; QOL, quality of life.

Introduction

The Burden of AR/C

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Pediatric AR/C in US

- Prevalence estimated to be as high as **40%**[1]
- Reported to affect **5.2 million** (**7.2%**) US children in the past 12m[2]
- More common in boys[3]
- Increases steadily from **4 YOA (3.4%)** to **18 YOA (27.3%)**[3]
- Symptoms develop **before 20 YOA in 80%** of patients[4]

m, months; YOA, years of age.

1. Nathan RA, et al. *Allergy Asthma Proc*. 2008;29:600-608. **2**. National Center for Health Statistics: Allergies and Hay Fever. Available at: https://www.cdc.gov/nchs/fastats/allergies.htm **3**. Meltzer EO, et al. *J Allergy Clin Immunol.* 2009;124:S43-S70. **4**. Kurukulaaratchy RJ, et al. *Clin Exp Allergy.* 2011;41:851-859.

Consequences of Poorly Controlled AR/C

Direct Impact of Symptoms

- Sleep loss leading to daytime fatigue
- Learning impairment
- Decreased overall cognitive functioning
- Decreased long-term productivity
- Decreased QOL

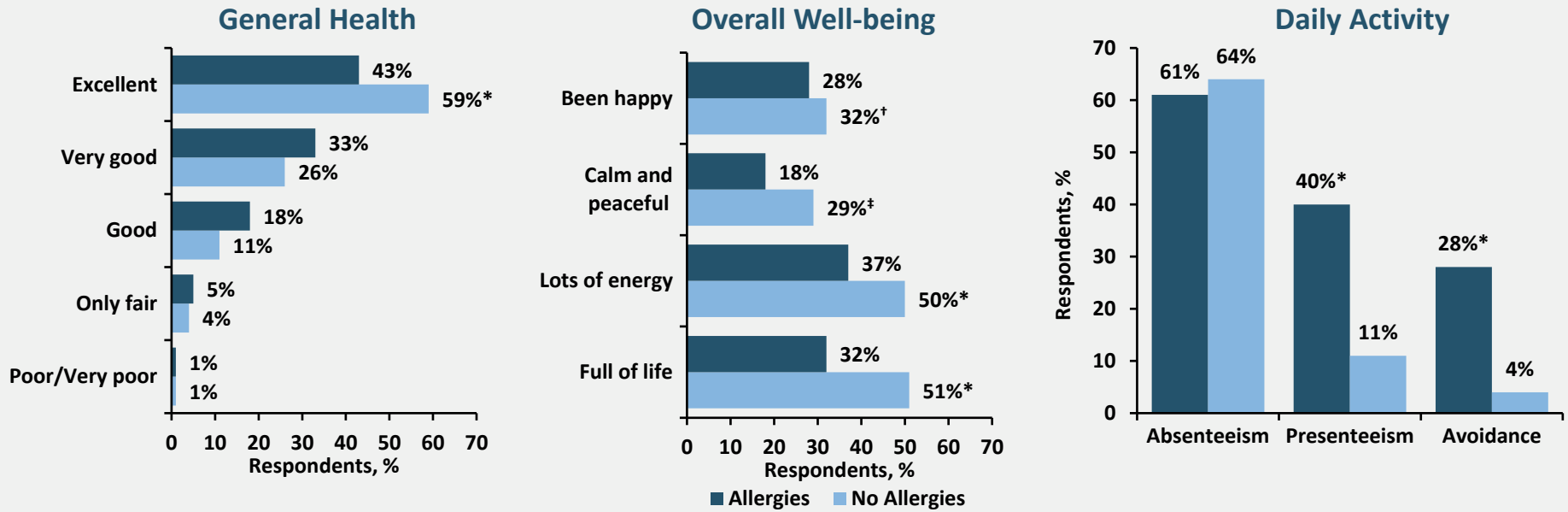
Potential Contribution to Related Disease Processes

- Acute and chronic sinusitis
- Recurrence of nasal polyps
- Otitis media/otitis media with effusion
- Hearing impairment
- Abnormal craniofacial development
- Sleep apnea and related complications
- Aggravation of underlying asthma
- Increased propensity to develop asthma

Settipane RA. *Allergy Asthma Proc.* 1999;20:209-213.

Effects of AR on Physical and Mental Health in Children

Pediatric Allergies in America Survey



Note: Reported outcomes based on parent perceptions

*P < .001; †P < .05; ‡P < .01.

AR, allergic rhinitis.

Meltzer EO, et al. *J Allergy Clin Immunol.* 2009;124:S43-S70.

Panel Discussion

- What do you view as being the most important unmet needs in the care of patients with AR/C?
  - Earlier diagnosis
  - Better symptom control
  - Reduced medication use (particularly INS)

Diagnosis of AR/C

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Allergic vs Nonallergic Rhinitis

Allergic	Nonallergic
• Early onset of symptoms (80% before age 20) • Family history of allergy • Symptoms: – Seasonal – Associated with animal exposure – Worse outdoors and/or near fresh-cut grass – Improve in air-conditioned environments • Severity ranges from mild and intermittent to seriously debilitating	• Later onset of symptoms (70% after age 20) • No family history of allergy • Weather changes provoke symptoms • No seasonal aspect to symptoms

Wallace DV, et al. *J Allergy Clin Immunol*. 2008;122:S1-S84.

Seasonal vs Perennial AR/C Symptoms

Seasonal AR/C

- Caused by an IgE-mediated reaction to seasonal aeroallergens
- Usually seen in spring or fall
- Typical pattern of sensitivity:
  - Trees in spring
  - Grasses in summer
  - Weeds in fall
- Timing varies by geographic location and climatic conditions

Perennial AR/C

- Caused by an IgE-mediated reaction to perennial environmental aeroallergens
- Occur throughout the year
- Most often due to sensitivity to dust, dust mites, animal dander, or mold spores

IgE, immunoglobulin E.

Crown WH, et al. *Value Health.* 2003;6:448-456; Wallace DV, et al. *J Allergy Clin Immunol*. 2008;122:S1-S84.

Case Patient: Presentation

David is a 9-year-old patient brought to you by his parents for a several week history of repetitive sneezing, nasal itching, and runny nose. He also complains of his eyes watering and itching. This has been occurring each spring for the last three years, but this is the worst it has ever been. It usually gets better with OTC oral antihistamines and intranasal steroids but these have not been working this season. What should be the first steps in his evaluation?

OTC, over the counter.

Initial Evaluation for AR: History

- Effective evaluation determines:
  - Pattern, chronicity, and seasonality
  - Response to medications
  - Presence of comorbid conditions
  - Detailed environmental history and identification of precipitating factors
  - Include QOL assessment for nasal and nonnasal AR severity

Wallace DV. *J Allergy Clin Immunol*. 2008;122:S1-S84.

Physical Examination

EYES
Possible conjunctivitis, clear watery discharge, “allergic shiners”

EARS (pneumatic otoscopy)
Possible otitis media

NOSE
External appearance: possible nasal crease

NASAL PASSAGES (with anterior rhinoscopy)
Possible pale blue, boggy, enlarged nasal turbinates, mucus production

SINUSES
Possible tenderness to palpation

MOUTH & THROAT
Possible posterior pharyngeal cobblestoning, clear posterior nasal discharge, lymphadenopathy

LUNGS
Wheezing, asthma

SKIN
Atopic dermatitis

Case Patient: History

- Symptoms: Trouble sleeping and snoring; trouble staying awake in school
- Past medical history: History of mild atopic dermatitis
- Family history: Mother with allergic rhinitis and asthma
- Environmental history: No pets; no smokers in house

Case Patient: Physical Examination

- Eyes: Conjunctiva injected bilaterally
- Ears: Tympanic membranes WNL
- Nose: Turbinates swollen, bluish pale bilaterally with profuse serous drainage
- Throat: Mild cobblestoning with slight serous drip
- Chest: Clear
- Skin: Small patches of eczema in popliteal fossae bilaterally

WNL, within normal limits.

Case Discussion

- Based on his history and physical examination, it appears David has seasonal allergic rhinitis. Would you do specific allergy blood testing as part of his evaluation?

Case Patient: Lab Findings

- David's specific IgE tests showed positive results to:
  - Timothy grass
  - Ragweed
  - House dust mites

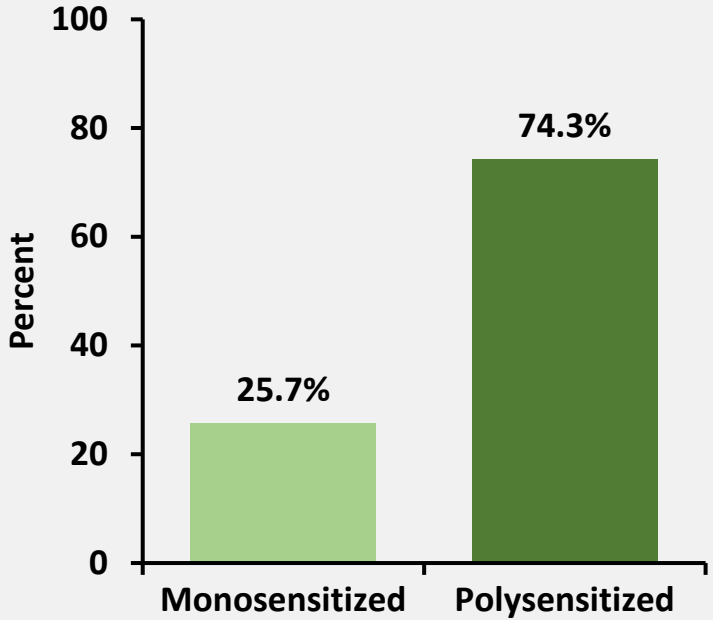
  - SLIT Panel blood test Code 607706 Thermo Fisher Scientific- Lab Corp – (4 allergens- timothy grass/ short ragweed/ D. Farinae- Dust Mite/ and D. Pteronyssinus- Dust Mite plus Total IgE)

Case Discussion

- How would you interpret the results of David's testing?
  - Polysensitized vs monosensitized patients (*next slides included to support discussion*)
  - Importance of assessing the seasonal timing of symptoms
- Is he a candidate for treatment in the pediatric setting?

Monosensitized vs Polysensitized Patients

Cross-sectional Study of a Large Cohort of AR Patients (N=2445)



Key Points

- Most patients demonstrate ≥1 positive test
- A positive test *does not* necessarily translate into clinical relevance (a patient may test positive for dust mite allergy, but it may not underlie their symptoms)
- The patient history *together* with the testing results should guide the diagnosis and treatment

Ciprandi G, Cirillo I. *Eur J Int Med.* 2011;22:e75-e79.

Case Patient: AR/C Diagnosis

Based on David's test results **AND** the timing of his symptoms, it's determined that his symptoms are due to his grass sensitivity. What are the options for treatment?

The Current Landscape for Symptom-Relieving Treatment of AR/C

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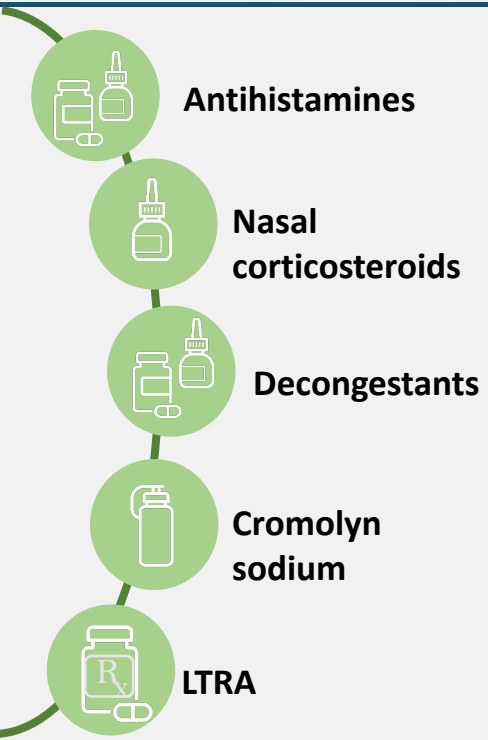
Symptom-Relieving Interventions

Nonpharmacologic Management	Pharmacotherapy	Allergen Immunotherapy
• Allergen avoidance • Nasal saline (nasal irrigation)	• INSs • INAs • Combined INSs + INAs • Intranasal cromolyn • Intranasal anticholinergics • Oral antihistamines • Oral LTRAs • Decongestants (oral and topical) • OCS	• SCIT • SLIT (tablets & drops)

INA, intranasal antihistamine; INS, intranasal corticosteroid; LTRA, leukotriene antagonist; OCS, oral corticosteroid; SCIT, subcutaneous immunotherapy; SLIT, sublingual immunotherapy.

Caregivers and Children May Be Unsatisfied With Symptomatic Medications



Caregivers expressed their dissatisfaction with current pharmacotherapy options in the Pediatric Allergies in America Survey*

- Inability to address all symptoms
- Incomplete relief of symptoms
- Lack of rapid onset of relief
- No long-term relief
- Loss of effectiveness over time

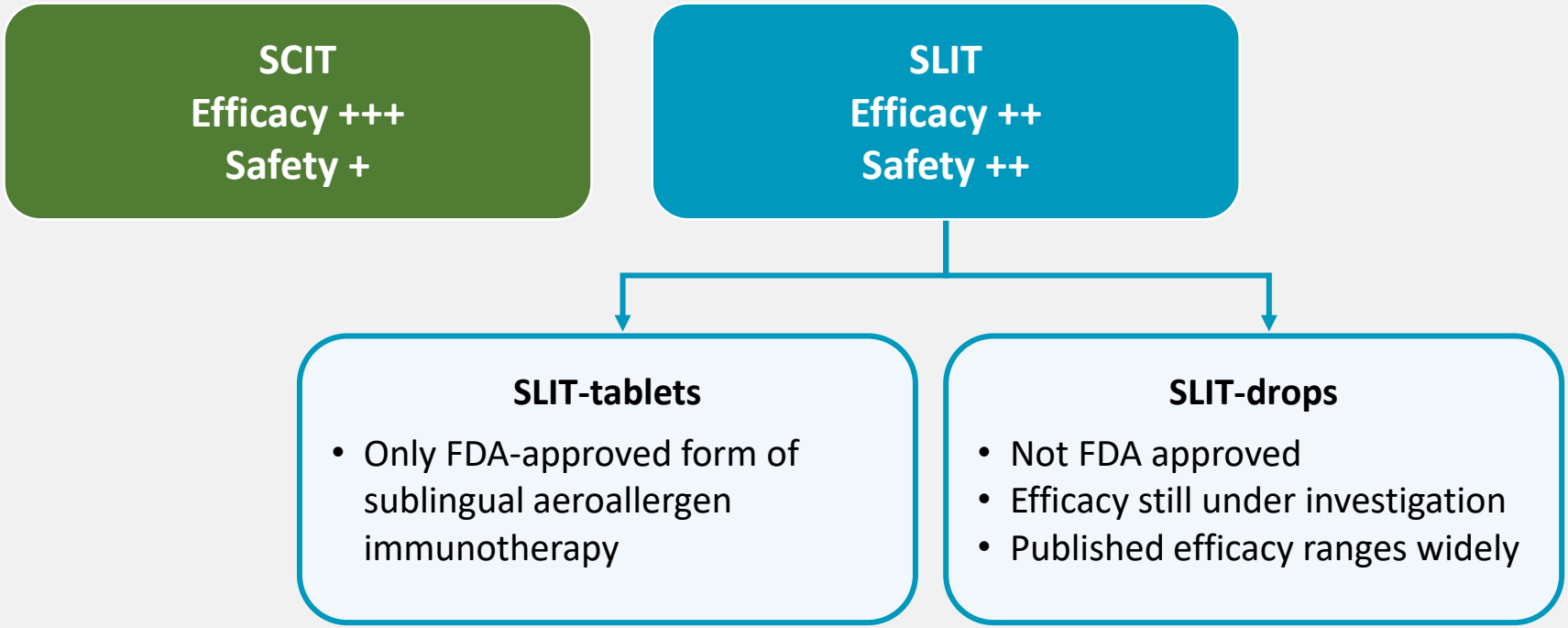
- Bothersome side effects
- Product safety concerns
- Unfavorable attributes (ie, postnasal drip, bad taste)
- Difficulty in administration/ problems with dosing schedule

*Data are from the Pediatric Allergies in America Survey, which included 500 children (aged 4-17 years) with HCP-diagnosed nasal allergies.

HCP, healthcare provider.

Meltzer EO, et al. *J Allergy Clin Immunol*. 2009;124(3 suppl):S43-S70.

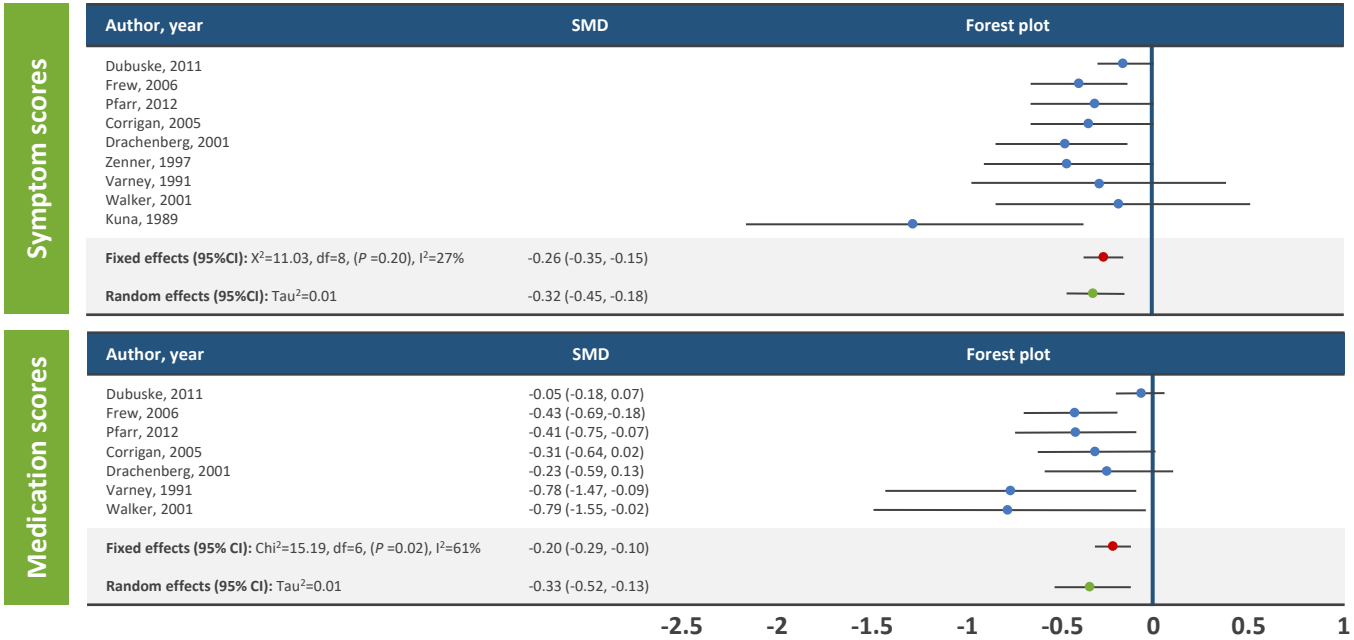
Overview of AIT: SCIT vs SLIT-tablets vs SLIT-drops



AIT, allergy immunotherapy.

Durham SR, et al. *J Allergy Clin Immunol*. 2016;137(2):339-349.e10.

Meta-Analysis of the Efficacy of SCIT Grass Products: Low Heterogeneity Among Studies



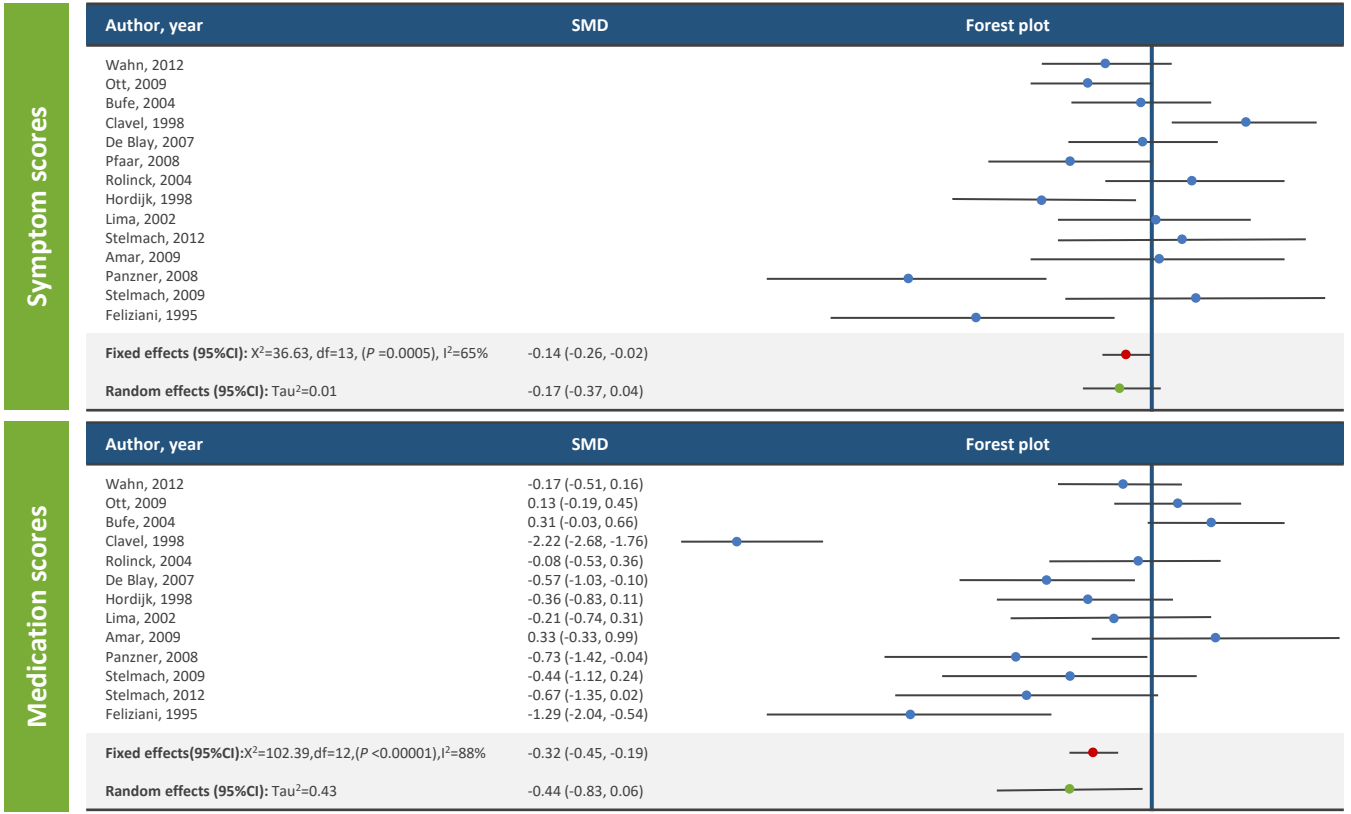
SMD, standardized mean difference

Nelson H et al. *J Allergy Clin Immunol Pract*. 2015;3(2):256-266.e3.

Meta-Analysis of the Efficacy of SLIT-Tablet Grass Products: Low Heterogeneity Among Studies

Nelson H et al. *J Allergy Clin Immunol Pract*. 2015;3(2):256-266.e3.

Meta-Analysis of the Efficacy of SLIT Drops Grass Products: High Heterogeneity Among Studies



Nelson H et al. *J Allergy Clin Immunol Pract*. 2015;3(2):256-266.e3.

Never Starting and Discontinuing SCIT is Common in Pediatric and Adolescent Patients

US Claims Data Analysis of Patients with AR That Had ≥1 AIT Claim

	Children 5-11 Years Old	Adolescents 12-17 Years Old
Patients (no.)	308,873	218,583
Number that Reached Maintenance* (%)	7,417 (2.4%)	5231 (2.4%)
Number with Any AITs (%)	12,867 (4.1%)	10,609 (4.9%)
Number with No AIT Fills (%)	288,589 (93%)	202,743 (92.7%)

Only 2.4% of Children and Adolescents ≥5 Years of Age Reached Maintenance and 93% has no AIT fills.

*Maintenance defined as 25+ AIT fills.

Stone B, et al. *Allergy Asthma Proc*. 2021;42(1):55-64.

Case Discussion

- Discuss the importance of shared decision-making
- What topics would you address with David and his family?
  - Medication and avoidance
  - Allergy shots
  - Allergy immunotherapy tablets and drops

Indications for SLIT-tablet Immunotherapy

SLIT-tablet	AR-inducing allergen*	Ages (years)	Positive skin test or in vitro testing for IgE antibodies	Initiation (weeks prior to season)	Duration of therapy
Grastek®	Grass pollen (Timothy)	5 – 65	Timothy grass or any cross-reactive grass species	12	Prior to and through relevant season (or perennially over 3Y for sustained efficacy)
Oralair®	Grass pollen (sweet vernal, orchard, perennial rye, Timothy, & Kentucky blue)	5 – 65	Any of 5-grass species in the tablet	16	Prior to and through relevant season
Ragwitek®	Short ragweed pollen	5 – 65	Short ragweed	12	Prior to and through relevant season
Odactra®	Dust mite	12 – 65	*Dermatophagoides farinae* or *D. pteronyssinus*	Anytime	Year-round

*Indication is for AR with or without conjunctivitis.

Grastek PI. ALK-Abello; 2022; Odactra PI. ALK-Abello; 2023; Oralair PI. Stallergenes SAS; 2019; Ragwitek PI. ALK-Abello; 2022.

Safety Considerations for SLIT-tablet Immunotherapy

Contraindications

- Severe unstable or uncontrolled asthma
- History of any of the following:
  - Severe systemic allergic reaction
  - Severe local reaction after taking SLIT
  - Eosinophilic esophagitis*
- Hypersensitivity to inactive ingredients

Safety of Treatment Reinitiation After a Missed Dose

- Interruptions for up to 7 days allowed in Grastek®, Ragwitek®, and Odactra® trials
- Data not available for Oralair®

Clinical Trial Inclusion of Asthma Patients

- Grastek® and Oralair®:
  - Not studied in patients with moderate or severe asthma or requiring daily asthma medication
- Ragwitek®:
  - Patients requiring daily low- dose ICS for asthma
- Odactra®:
  - Patients with mild-to-moderate asthma requiring, at most, daily medium-dose ICS for asthma

*There is no evidence that the drug causes it, but SLIT should not be initiated for a patient with the condition.

ICS, inhaled corticosteroid.

Grastek PI. ALK-Abello; 2022; Odactra PI. ALK-Abello; 2023; Oralair PI. Stallergenes SAS; 2019; Ragwitek PI. ALK-Abello; 2022.

JTFPP 2020 Practice Parameter: Guidance on Patient Selection for AIT

- SCIT and SLIT-tablets are both effective for the treatment of AR and may help prevent and/or treat allergic asthma
- Suggest subcutaneous or sublingual tablets be offered through shared decision-making for patients with moderate/severe AR who demonstrate the following:*

Uncontrolled with allergen avoidance and/or pharmacotherapy	Preference for immunotherapy (eg, due to desire to avoid AEs, costs, or long-term use of pharmacotherapy)	Desire for potential benefit of immunotherapy to prevent or reduce severity of comorbid conditions, such as asthma

- Suggest subcutaneous or sublingual tablets be considered for patients with controlled mild/moderate asthma with coexisting AR*

*Conditional recommendation, moderate evidence.
AE, adverse event.

Dykewicz MS, et al. *J Allergy Clin Immunol*. 2020;146:721-767.

Optimizing Treatment Success: Patient Education and Shared Decision-Making

Patient Education

- Provide information on the efficacy and safety of treatments
- Review treatment administration
- Discuss treatment of a systemic reaction

Shared Decision-Making

- Discuss treatment options with parents and patients
- Ascertain preferences:
  - Would they rather have a shot or a tablet?
  - Would they rather continue taking medication?

Case Discussion

- With shared decision making, parents don't want to go the allergist's office for weekly shots as they don't have time in their busy schedules and medication just not working well enough; David is scared of needles.
- SLIT drops aren't covered by insurance
- SLIT-tablets can be prescribed by the pediatrician with first dose in the office and all other doses at home

Sublingual Tablet Immunotherapies for the Treatment of AR/C

Efficacy in Pediatric Populations

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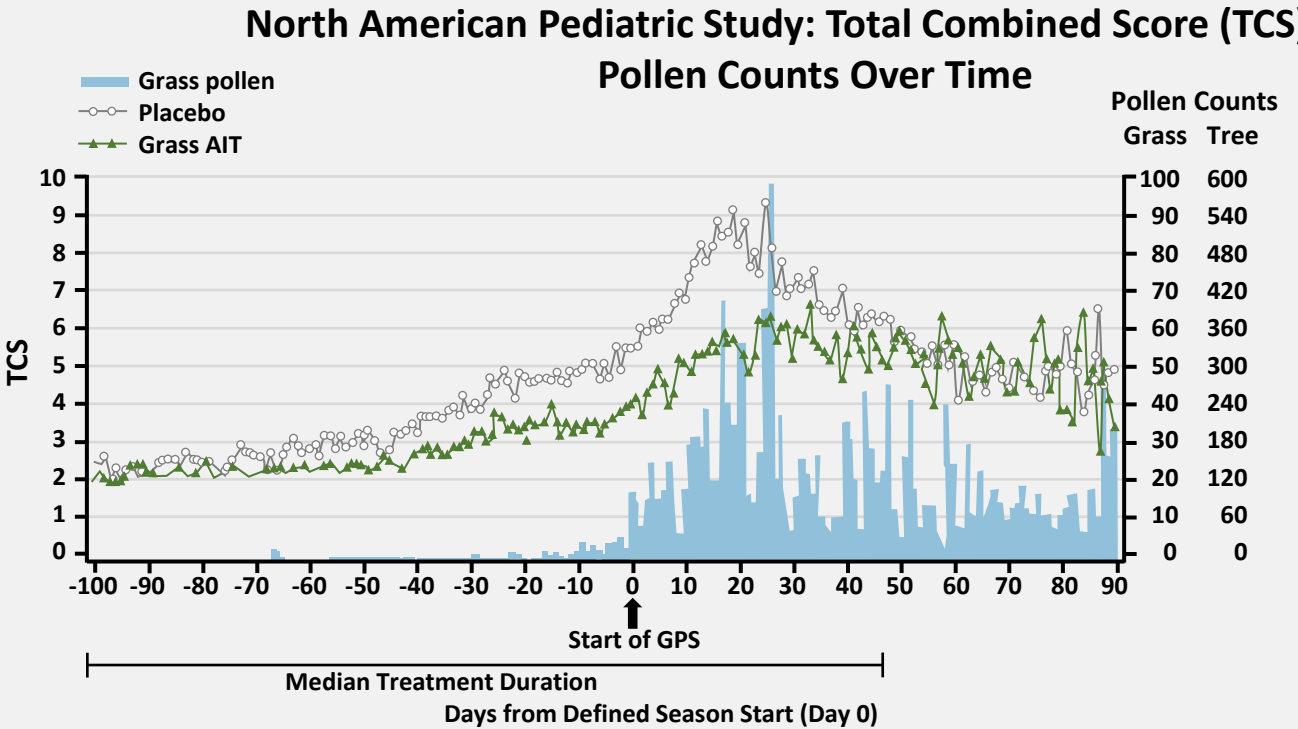
Timothy Grass AIT Effectively Treats Timothy Grass* Pollen-Induced AR/C



- ~24-week study (N=344) pediatric
- 5–17 YOA
- 26% with asthma
- 89% sensitized to other allergens than grass
- Assessed first grass pollen season efficacy of grass AIT vs PBO

Pollen counts (in grains per cubic meter) were weighted by the number of subjects exposed.

*Cross-reactive with Northern Pasture grasses.

PBO, placebo; TCS, Total Combined Score

Blaiss M, et al. *J Allergy Clin Immunol*. 2011;127(1):64-71,71.e1-4.

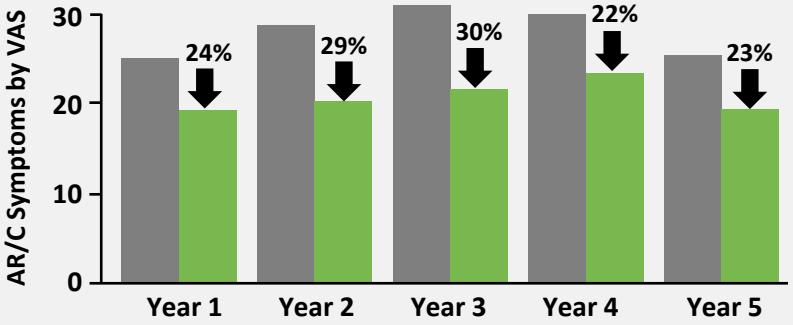
Impact of Sublingual Tablet Immunotherapy on Asthma in Children With Grass Pollen Allergy

GAP Trial

812 children aged 5–12 with grass allergy and no asthma randomized

3 years treatment and 2 years follow-up

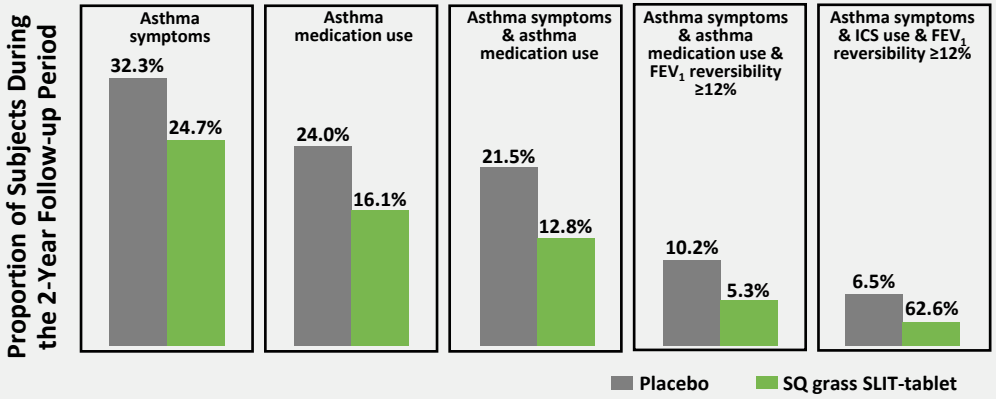
SQ grass SLIT-tablet treatment reduced **allergic rhinoconjunctivitis** symptoms and medication use



Daily AR/C symptoms by VAS, year 5 during GPS
-22%
difference, SQ grass SLIT-tablet to placebo

Daily AR/C medication use, year 5 during GPS
-27%
difference, SQ grass SLIT-tablet to placebo

SQ grass SLIT-tablet treatment reduced **allergic** symptoms and medication use

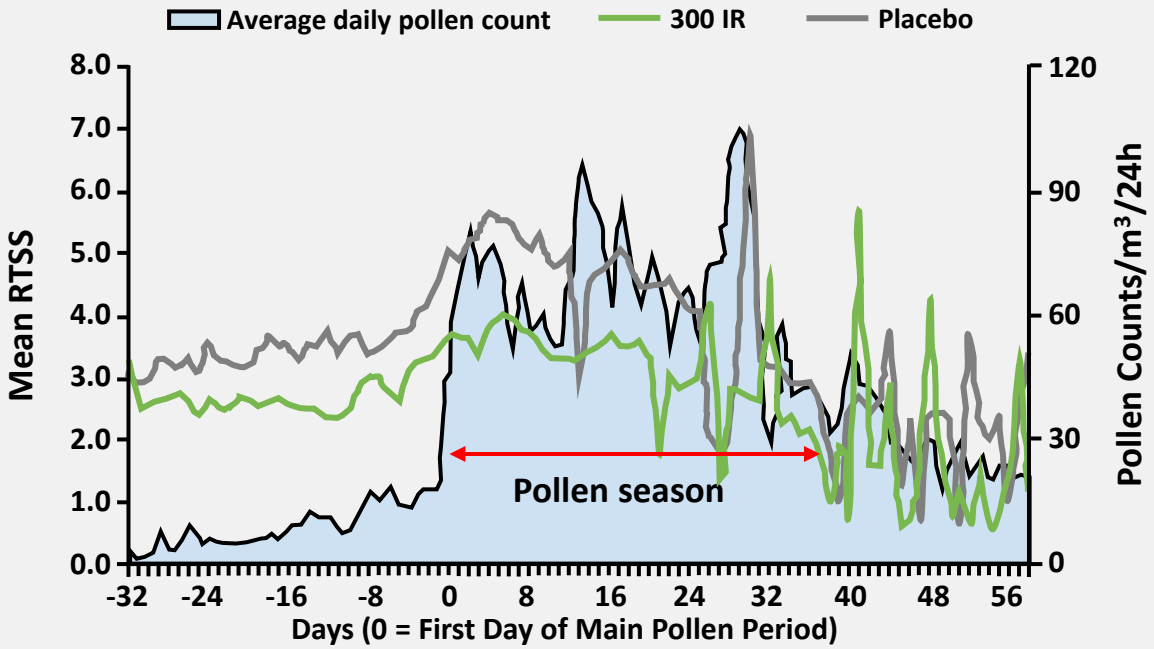


FEV_1, forced expiratory volume in the first second; GPS, grass pollen season; SQ, standardized quality; VAS, visual analogue scale.

Valovirta E, et al. *J Allergy Clin Immunol*. 2018;141:529-538.e13.

Efficacy of 5-Grass-Pollen Sublingual Tablet Immunotherapy in Pediatric AR/C

Daily mean RTSS and pollen counts (ITT population) in relation to daily pollen counts



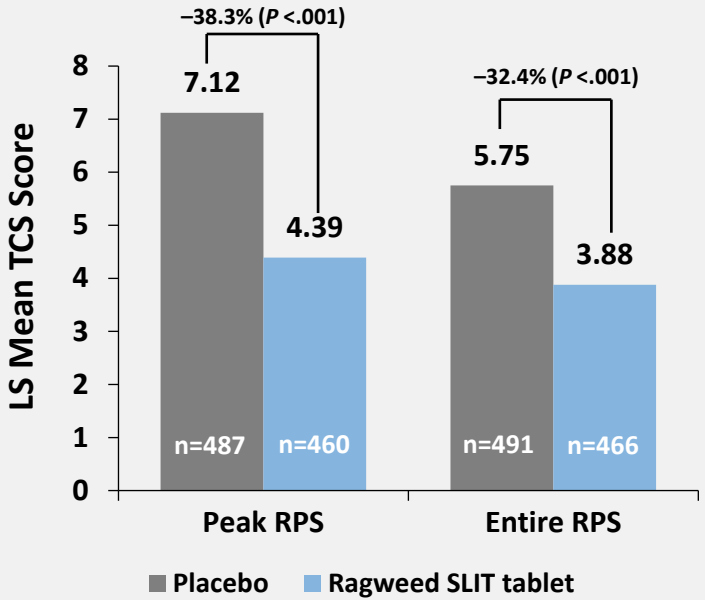
- ~21-week pediatric study (ages 5–17 YOA; N=278)
- Assessed first grass pollen season efficacy of 5-grass AIT vs PBO

IR, index of reactivity; ITT, intent to treat; RTSS, Rhinoconjunctivitis Total Symptom Score.

Wahn U, et al. *J Allergy Clin Immunol*. 2009;123:160-166.e3.

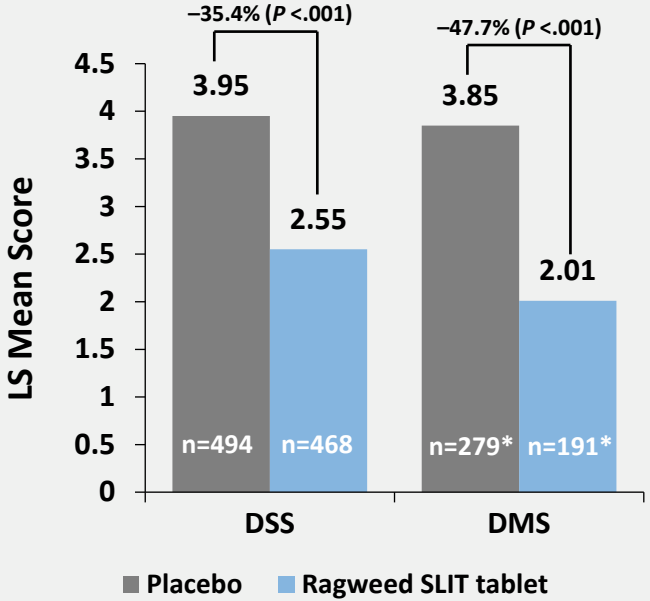
Efficacy of Ragweed SLIT-Tablet in Children With AR/C

TCS During Peak and Entire RPS*



Treatment difference (95% CI) in LS mean during peak RPS was 2.73 (3.45 to 2.00) and during entire RPS was 1.86 (2.46 to 1.27).

DSS and DMS During Peak RPS



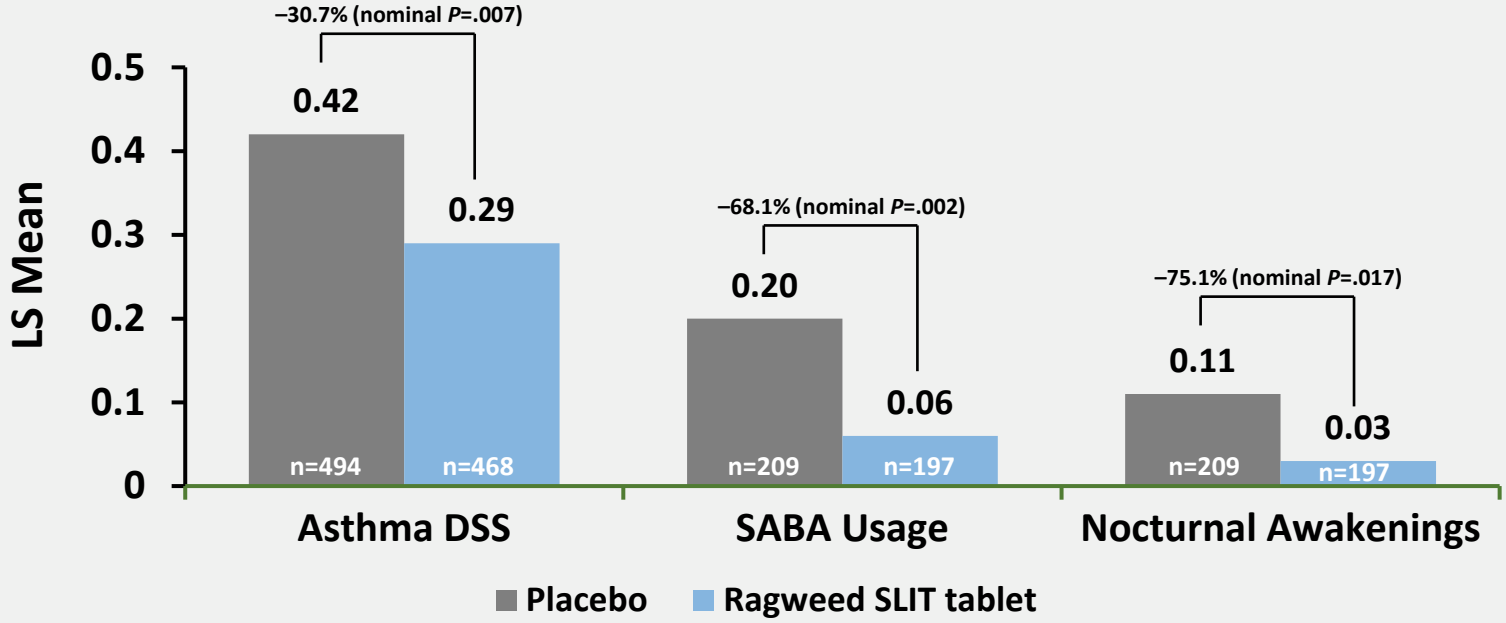
Treatment difference (95% CI) in LS mean for DSS was 1.40 (1.81 to 0.99) and for DMS was 1.84 (2.60 to 1.08).

- ~28-week study of children 5–17 YOA (n=1025)
- 77.7% polysensitized
- Randomized 1:1 to daily ragweed SLIT-tablet or PBO

DMS, Daily Medication Score; DSS, Daily Symptom Score; LS, least squares; RPS, ragweed pollen season.

Nolte H, et al. *J Allergy Clin Immunol Pract*. 2020;8(7):2322-2331.

Impact of Ragweed SLIT-Tablet on Asthma DSS, Daily SABA Usage, and Nocturnal Awakenings From Asthma During RPS

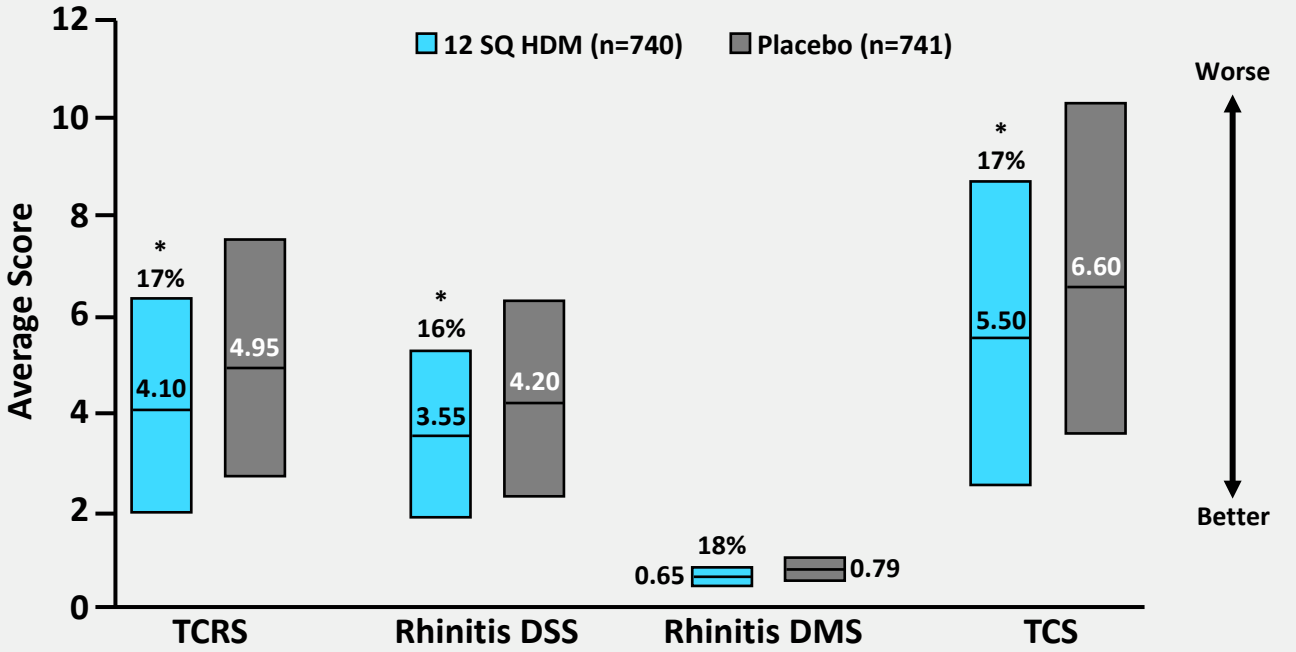


SABA, short-acting beta agonist.

Nolte H, et al. *J Allergy Clin Immunol Pract*. 2020;8(7):2322-2331.

Efficacy of House Dust Mite Sublingual Tablet Immunotherapy

Efficacy Outcomes During Approximately the Last 8 Weeks of Treatment



- ~52-week study of adolescents and adults >12 YOA (N=1482)
- 76% polysensitized
- 31% with asthma
- Randomized to a daily SQ HDM SLIT-tablet or PBO

*P <.001, score improvement compared with placebo.

SQ HDM, standardized quality house dust mite SLIT-tablet; TCRS, Total Combined Rhinitis Score.

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

Symptom Treatment Effect Size for SLIT-Tablets and Pharmacotherapies for SAR and PAR

Treatment	Number of trial subjects, N	Difference in mean: active treatment from placebo (95% CI)	Relative difference from placebo, %
Timothy grass SLIT-tablet	6,3094	-0.46 (-0.60, -0.32)	-16.3
Ragweed SLIT-tablet	2,658	-0.57 (-0.87, -0.26)	-17.1
HDM SLIT-tablet	2,1768	-0.57 (-0.83, -0.31)	-16.1
Cedar SLIT-tablet	Not done	Not done	
Leukotriene receptor antagonist			
SAR	5,3584	-0.40 (-0.54, -0.26)	-5.4
PAR	2,3215	-0.25 (-0.39, -0.12)	-3.7
Oral antihistamine			
SAR	6,1916	-0.59 (-0.79, -0.40)	-8.5
PAR	3,2539	-0.31 (-0.49, -0.13)	-4.8
Intranasal corticosteroid			
SAR	4,958	-1.44 (-1.74, -1.15)	-22.2
PAR	4,1182	-0.58 (-0.77, -0.39)	-11.2

Nolte H, Maloney J. *Allergol Int*. 2018;67(3):301-308.

Meta-Analysis of the Relative Difference in TNSS* From Placebo for SLIT-Tablets and Pharmacotherapies for PAR

Treatment	PAR Relative Difference in TNSS From Placebo	Population (N)
Montelukast (10 mg daily)	3.7%	3215 (2 studies)
Desloratadine (5 mg daily)	4.8%	2539 (3 studies)
Mometasone furoate nasal spray (200 µg daily)	11.2%	1182 (4 studies)
HDM SLIT-tablets (12 SQ-HDM daily)	16.1%†	1768 (2 studies)

Due to a lack of direct comparisons, Durham et al (2016) undertook a pooled data analysis to indirectly compare the treatment effects of SLIT-tablets and pharmacotherapies. This included 11 randomized, double-blind, placebo-controlled trials for PAR, but was limited by study design heterogeneity and the use of rescue medications in SLIT-tablet trials. A fixed effect meta-analysis method was used to estimate the overall effect size.

*Total nasal symptom score = sum of 4 nasal symptoms (rhinorrhea/runny rose, nasal stuffiness/congestion/ blocked nose, nasal itching, and sneezing). Scale of symptom intensity ranges from 0 (none) to 1 (mild), 2 (moderate), and 3 (severe).

†SLIT-tablet trials allowed rescue medication use, whereas most pharmacotherapy trials did not. The observed treatment effect for SLIT-tablets is in addition to background AR rescue medication use.

Durham S et al. *J Allergy Clin Immunol*. 2016;138:1081-1088.

Sublingual Tablet Immunotherapies for the Treatment of AR/C

Safety & Tolerability

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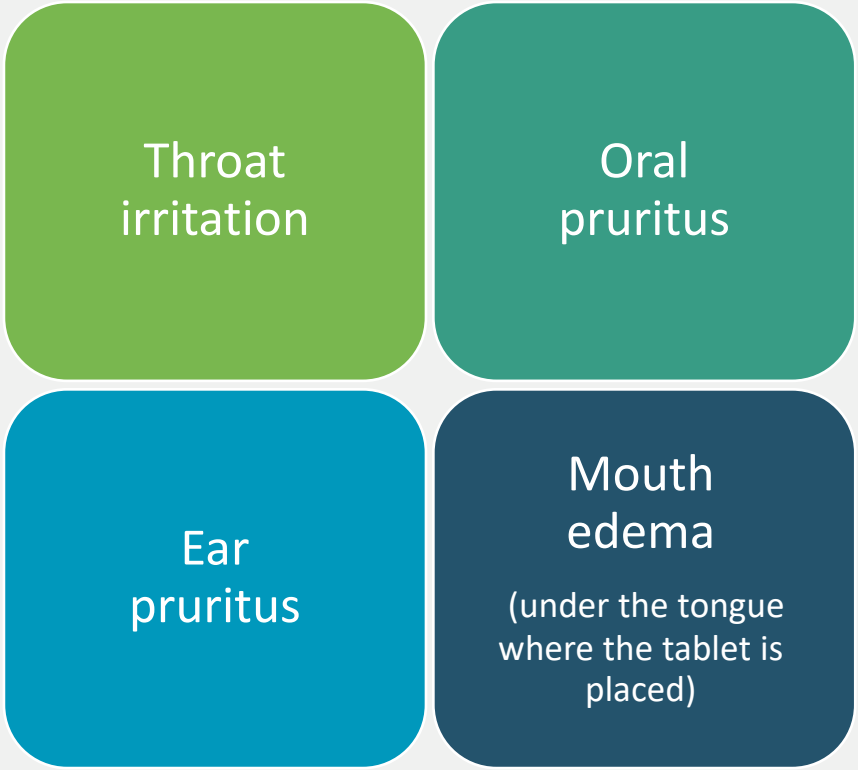
Common AEs Associated With Sublingual Tablet Immunotherapy



Side effects are common, but are **brief in duration**, **not life-threatening**, and **resolve over time**.

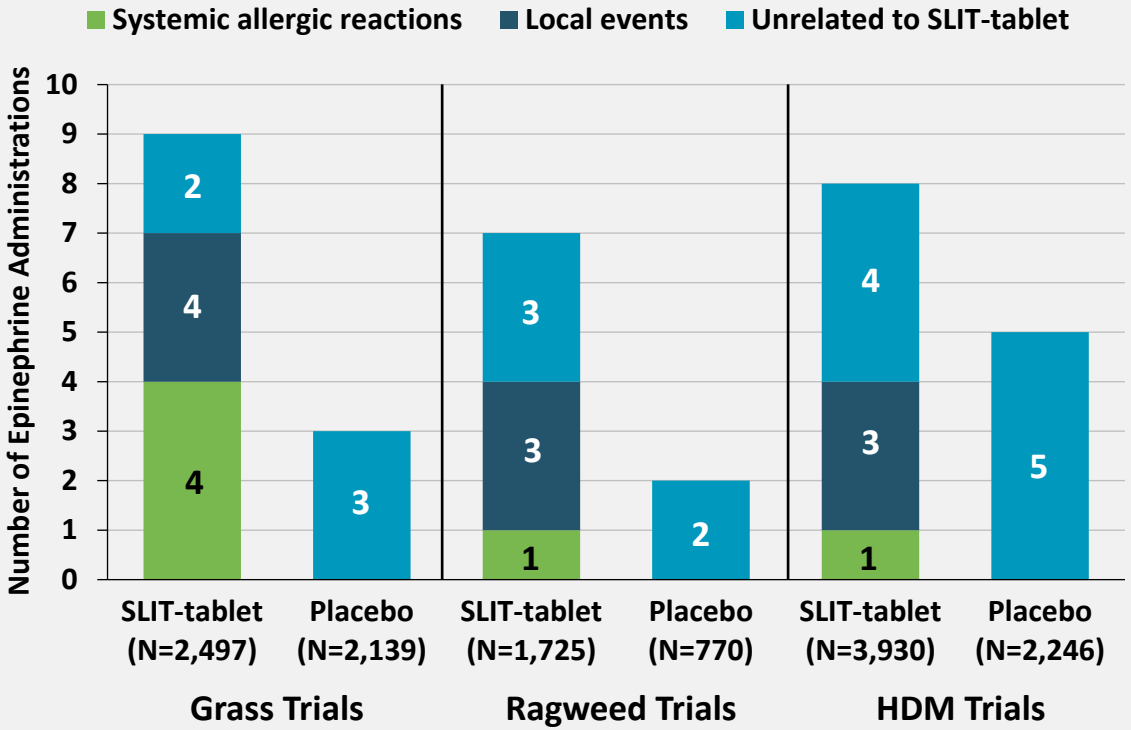
Bernstein DI, et al. *Postgrad Med.* 2017;129:590-597.

FDA Class-Labeling: SLIT Boxed Warning

- SLIT can cause life-threatening allergic reactions such as anaphylaxis and severe laryngopharyngeal restriction
- Do not administer SLIT to patients with severe, unstable, or uncontrolled asthma
- Observe patients in the office for at least 30 minutes following the initial dose
- **Prescribe auto-injectable epinephrine, instruct, and train patients on its appropriate use, and instruct patients to seek immediate medical care upon its use**
- SLIT may not be suitable for patients with certain underlying medical conditions that may reduce their ability to survive a serious allergic reaction
- SLIT may not be suitable for patients who may be unresponsive to epinephrine or inhaled bronchodilators, such as those taking beta-blockers

Grastek PI. ALK-Abello; 2022; Odactra PI. ALK-Abello; 2023; Oralair PI. Stallergenes SAS; 2019; Ragwitek PI. ALK-Abello; 2022.

Epinephrine Administration for TEAEs During Clinical Development of SLIT-tablets*



- Data from 8152 participants in all clinical trial phases
- 16 epinephrine administrations
  - Event rate = 0.2% administrations/subject
  - 6 for systemic allergic reactions
- **No serious AEs**

*Includes Timothy grass, ragweed, and SQ HDM SLIT-tablet development programs.
TEAEs, treatment-emergent adverse events.

Bernstein DI, et al. *Postgrad Med.* 2017;129:590-597.

AEs After SQ HDM SLIT-tablet Treatment Interruption

Duration of interruption	Safety
Short-term (≤2 consecutive days)	• No safety signal for tablet reinitiation – Rate of TEAEs after treatment reinitiation similar between SQ HDM SLIT-tablet (29%) vs PBO (26%) – Most common AEs observed more often in SQ HDM SLIT-tablet group vs PBO group – Most AEs were mild or moderate – No systemic allergic reactions, epinephrine administrations, or severe local swellings – One post-marketing report of anaphylaxis at reinitiation after a 1.5-month treatment interruption – AE profile was consistent with known safety profile of SQ HDM SLIT-tablet
Long-term	• Safety profile after has not been determined

Nolte H, et al. *J Allergy Clin Immunol*. 2015;135:1494-1501; Nolte H, et al. *J Allergy Clin Immunol*. 2016;138:1631-1638.

Adverse Events After SQ HDM SLIT Tablet Treatment Interruption: Methods

- Two randomized, double-blind, placebo-controlled trials were conducted
  - P003: Phase 2 trial of 24 weeks duration in adults assessed efficacy and safety of 6 SQ-HDM and 12 SQ-HDM doses for HDM-induced AR/C using an environmental exposure chamber[1]
  - P001: Phase 3 trial of up to 52 weeks duration in adults and adolescents assessed efficacy and safety of 12 SQ-HDM dose for HDM-induced AR/C[2]
  - Institutional review board approval was obtained for both trials
- Safety data were pooled post-hoc and analyzed for AEs reported at any point after a treatment interruption of ≥2 consecutive days for any reason
  - Data on duration of treatment interruptions was determined based on the daily number of tablets taken by the subject; specific reasons (e.g., due to AEs) for interruptions were not collected
- Data for the Europe/US approved dose 12 SQ-HDM (n=783) and placebo (n=782) are presented

1. Nolte, H. et al. *J Allergy Clin Immunol*.2015;135:1494-501
2. Nolte, H. et al. *J Allergy Clin Immunol*.2016;138:1631-8

Summary of Treatment Interruptions and AEs After Treatment Re-initiation

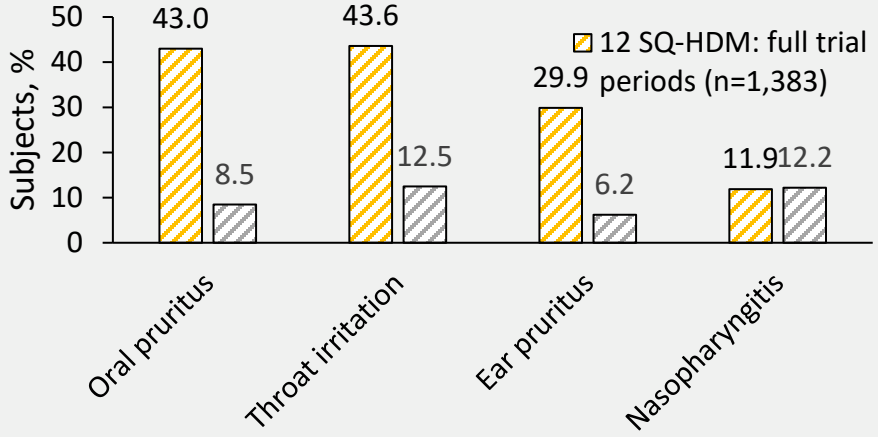
	SQ HDM SLIT-Tablet 12 SQ-HDM (n=783)	Placebo (n=782)
Any treatment interruption, n (%)	476 (61%)	501 (64%)
Duration of treatment interruption, days		
Median (range)	7 (1-142)	8 (1-143)
Mean (SD)	13.4 (16.7)	13.8 (18.3)
Any treatment-emergent AEs after treatment re-initiation, n (%)	226 (29%)	203 (26%)
Systemic allergic reactions, n (%)	0	0
Epinephrine administrations, n (%)	0	0
Severe local swellings, n (%)	0	0

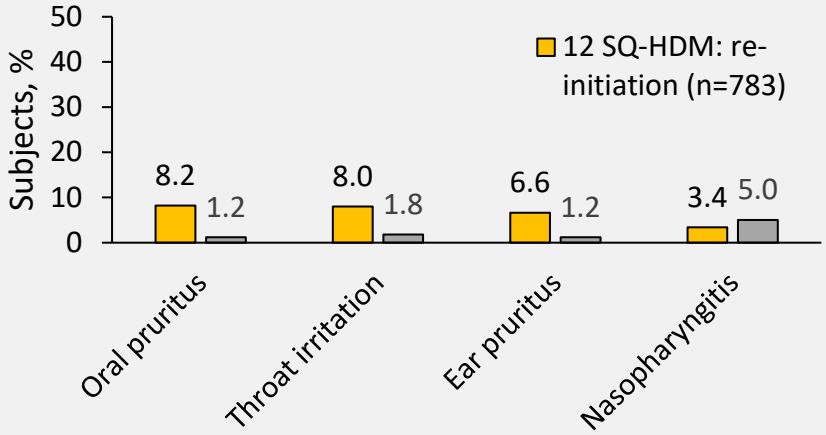
Most AEs after treatment re-initiation were assessed by the investigator as mild or moderate in severity
Of 3321 post-marketing reports, there was one anaphylactic reaction that occurred following a 1.5 month treatment interruption. This event occurred on day 1 of re-initiation.

1. Nolte, H. et al. *J Allergy Clin Immunol*.2015;135:1494-501
2. Nolte, H. et al. *J Allergy Clin Immunol*.2016;138:1631-8

AE Profile After Treatment Re-initiation vs Known AE Profile

- The AE profile after re-initiation was consistent with the known AE profile of SQ HDM-SLIT-tablet, characterized mainly by local application site reactions
- The most common treatment-emergent AEs after treatment re-initiation were the same most common AEs as the full trial periods*





*AE frequencies from pooled data of five phase 2 and phase 3 trials of SQ HDM SLIT-tablet

1. Nolte, H. et al. *J Allergy Clin Immunol*.2015;135:1494-501
2. Nolte, H. et al. *J Allergy Clin Immunol*.2016;138:1631-8

Panel Discussion

- What are the most common questions about safety asked by your patients considering SLIT-tablets?
- What type of reactions do you see in the office with your patients? How do your patients typically do with the treatments?

Implementation of Sublingual Tablet Immunotherapy

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Implementation of Sublingual Tablet Immunotherapy

- **Directions**
  - First dose of SLIT-tablet will be given in a medical professional's office
    - Patient will be observed for ≥ 30 minutes
  - Dose once daily all year round
  - With dry hands, carefully remove the foil and then the tablet from the blister pack
  - Place the tablet under tongue
    - Dissolve in 10 seconds
    - Do not swallow for at least 1 minute
    - Wash your hands after handling the tablet
  - Do not take the tablet with food and beverages
  - Do not eat or drink for at least 5 minutes after taking the tablet
- **Ensure availability of epinephrine autoinjector**
- **Consult physician if ≥ 1 dose is missed**
- **Efficacy expectations**
  - Onset of action: 4 to 8 weeks
  - Long-term expectation: desensitization and reduced need for symptomatic medications

Panel Discussion

- What barriers to SLIT-tablet implementation have you encountered in your own practice, and how do you typically address them?
- What key advice would you offer to clinicians seeking to implement treatment with SLIT-tablets?
  - When to start treatment?
  - Length of treatment?
  - Local reactions are extremely common, but typically resolve rapidly
- When should a patient be referred to an allergist?

Key Points

- AR/C is an inflammatory disorder of the nasal mucosa that has significant negative physical and mental effects in children and adolescents
- Early diagnosis and optimal assessment (including a detailed history, physical exam, and skin prick testing or specific IgE testing) are crucial to limiting the negative impact of symptoms on daily activity and function, as well as contributions to other disease processes
- For the many children and adolescents with poor symptom control despite allergen avoidance and pharmacotherapy, AIT is an effective treatment:
  - Induces long-term clinical tolerance to sensitizing allergens (disease modification)
  - Reduces medication use
  - May prevent other diseases

Key Points *(cont)*

- AIT can be administered via subcutaneous injections (SCIT) or sublingual tablets or drops (SLIT)
- SCIT requires clinician-supervised injections and carries a risk for serious systemic allergic reactions
- SLIT may be self-administered by patients or caregivers and is associated with a reduced risk for allergic reactions
- The only FDA-approved forms of SLIT for AR/C are 5-grass, Timothy grass, ragweed, and house dust mite tablets
- Optimal care requires patients undergoing SLIT-tablet immunotherapy to be educated on its safety and efficacy, proper tablet administration, how to manage potential systemic reactions, and appropriate dosing to ensure optimal safety

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Thank You