

Is the Proof in the Pudding? *Update on Novel Food Allergy Therapies* J. Andrew Bird, M.D.

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UT Southwestern Medical Center

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Olivia

- 8 y/o female with a peanut allergy
 - Ingestion at 14 m/o → diffuse urticaria and vomiting within minutes of ingestion of peanut butter for the first time
 - Recent testing ImmunoCAP peanut-specific IgE 16.3 kU/L and SPT wheal diameter of 12 mm
 - Olivia has had no accidental ingestion and no use of auto-injectable epinephrine since diagnosis
- Mom has heard about OIT. She wants to know if you think it is right for her daughter, and she asks if you think treatment options might change in the next few years.

Objectives

- 1. Describe recent advances in Oral Immunotherapy (OIT), Sublingual Immunotherapy (SLIT) and Epicutaneous Immunotherapy (EPIT)
- 2. Identify advantages and disadvantages of all methods of treatment
- 3. Be prepared to discuss advances, expectations and limitations with your food-allergic patients

Food Allergy Facts and Goals for Immunotherapeutic Intervention

- Food allergies are common
 - ~8% of young children in the US¹ and ~10% of Australian children²

Goal 1: Improve the QOL for food allergic patients with active therapy

- Severe reactions may occur in up to 42% of food allergic children¹
 - Estimate ~25 deaths in US per year
 - More likely to die from:
 - An accident (~1 in 5000)
 - Murder (~1 in 10,000)
 - Fire (~1 in 100,000)
 - Less likely to die from lightning (~1 in 10 million)

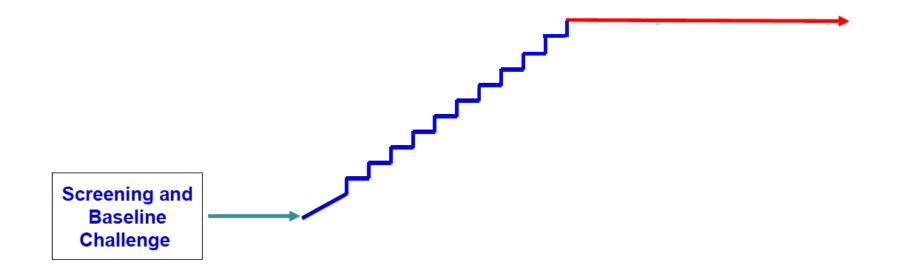
Goal 2: Eliminate reaction severity and life-threatening anaphylaxis

Oral Immunotherapy (OIT)

Oral Immunotherapy (OIT)

- Allergen powder ingested in vehicle
- Antigen is processed in GALT with antigen up-take by mucosal dendritic cells that further modify immune pathways through Tregs dampening Th2-skewed allergic response

OIT Dosing Schematic



Wood RA. J Allergy Clin Immunol 2016;137:973-82.

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Factors Affecting Broad Acceptance/Implementation into Practice

- Efficacy
- Safety concerns
- Long-term data on remission (i.e., sustained unresponsiveness), quality of life, and sustainability
- Medicolegal concerns (e.g., potential dosing errors, product contamination)



AR101 Oral Immunotherapy for Peanut Allergy

The PALISADE Group of Clinical Investigators*

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Phase 3 trial of peanut allergic participant 4 to 55 y/o

Primary Efficacy Endpoint: proportion of participants 4 to 17 y/o who could ingest a challenge dose of 600 mg or more, without dose-limiting symptoms.

Participant Characteristics:

- 551 participants, 486 were 4 to 17 y/o
- Median Maximum Tolerated Peanut Dose at entry: 10 mg (3 30 mg)

Methods:

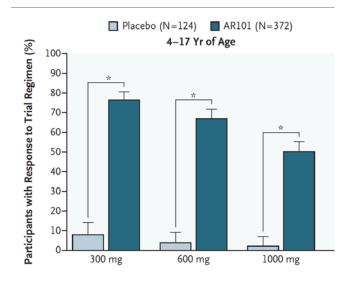
300 mg maintenance dose daily x 24 weeks

Peanut OIT raises the dose-triggering threshold & induces humoral and effector cell responses consistent with desensitization



AR101 Oral Immunotherapy for Peanut Allergy

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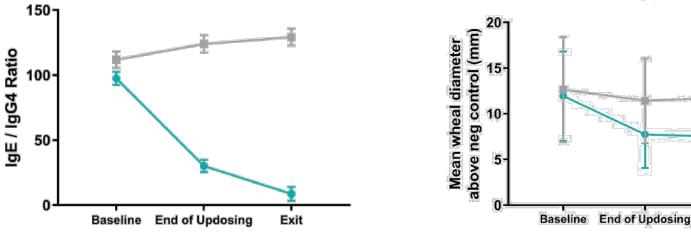


- 67.2% (250/372) in the active-drug group were able to ingest at least 600 mg of peanut protein with no more than mild symptoms compared to 4% (5/124) receiving placebo
- Immunomodulatory activity consistent with desensitization after 34 wks of maintenance

PNsIgE:G4 ratio and PN SPT decrease



Peanut SPT



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Exit

Vickery B, et al. N Engl J Med 2018 Nov 22;379(21):1991-2001

Efficacy Conclusions

Peanut OIT effectively elevates the dose-triggering threshold for most peanut-allergic children and adolescents who are able to complete one year of therapy^{1, 2}

Long-term sustainability unknown

Remission is unclear though data suggests it is unlikely to induce permanent remission for patients other than those for whom it would have naturally developed^{2, 3}

Oral immunotherapy for peanut allergy (PACE): a systematic Is OIT safe? review and meta-analysis of efficacy and safety

| Α | | | | | |
|-------------------------------------|------------------------|-------|----------------|--------------------|--------|
| | OIT (n/N) No OIT (n/N) | | /N) | RR (95% CI) | Weight |
| Proprietary OIT | | | | | |
| STOP II (2014) | 1/49 | 0/50 | | 3.06 (0.13-73.34) | 3 |
| PPOIT (2014) | 3/31 | 1/31 | - | 3.00 (0.33-27.29) | 7 |
| ARC001 (2015) | 1/29 | 0/26 | | 2.70 (0.11-63.52) | 4 |
| PALISADE (2018) | 60/413 | 4/138 | - | 5.01 (1.86–13.54) | 33 |
| Subtotal | 65/522 | 5/245 | \diamond | 4.30 (1.86-9.97) | 47 |
| p=0.0007, I ² =0% | | | | | |
| Non-proprietary OIT | | | | | |
| Varshney et al (2011) ²³ | 2/19 | 1/9 | - <u>+</u> | 0.95 (0.10-9.13) | 7 |
| Narisety et al (2015) ²⁸ | 4/11 | 0/10 | - <u> </u> | 8.25 (0.50-136.33) | 4 |
| PNOIT (2017) | 22/23 | 2/4 | -+- | 1.91 (0.72–5.12) | 34 |
| TAKE-AWAY (2018) | 11/57 | 0/20 | | 8.33 (0.51-135.19) | 4 |
| PITA (2018) | 4/21 | 0/9 | | 4·09 (0·24-68·94) | 4 |
| Subtotal | 43/131 | 3/52 | \diamond | 2.35 (1.07-5.18) | 53 |
| p=0.033, I ² =0% | | | | | |
| Overall | 108/653 | 8/297 | \$ | 3·12 (1·76-5·55) | 100 |
| p=0.0001, I ² =0% | | | i | | |
| Pinteraction=0.31 | | | Favors | | |
| | | | Control | | |
| | | F | avours Favours | | |
| | | | OIT no OIT | | |

Chu DK, et al. Lancet. 2019 Jun 1;393:2222-32.

UT Southwestern Medical Center Oral immunotherapy for peanut allergy (PACE): a systematic review and meta-analysis of efficacy and safety

- Summary of AEs
 - ↑ risk of Anaphylaxis (RR 3.12 (1.76-5.55))
 - ↑ Epinephrine use (RR 2.21 (1.27-3.83))
 - ↑ SAEs (RR 1.92 (1.00-3.66))
 - Vomiting (RR1.79 (1.35-2.38))
 - ▲ ↑ Angioedema (RR 1.36 (1.02-1.81))
 - Peanut OIT → large increase in completing supervised OFC but this does not translate into less reactions outside of clinic (RR 12.42 (6.82-22.61))
 - •OIT did not improve QOL by minimally important difference

Sustained outcomes in oral immunotherapy for peanut allergy (POISED study): a large, randomised, double-blind, placebo-controlled, phase 2 study

- Is the goal to induce long-term remission?
 - No therapies currently under study have been shown to consistently induce remission
 - PALISADE f/up data suggests that daily dosing for the first two years is safer and more effective than non-daily dosing.¹

Sustained outcomes in oral immunotherapy for peanut allergy (POISED study): a large, randomised, double-blind, placebo-controlled, phase 2 study

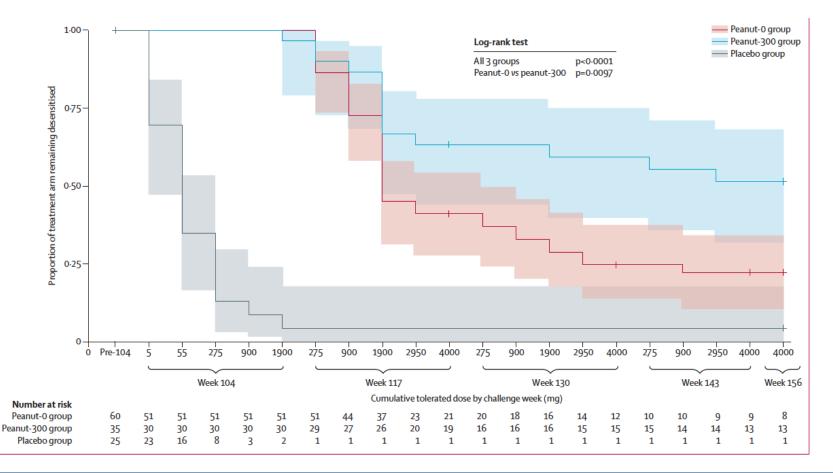
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Is the goal to induce long-term remission?

No therapies currently under study have been shown to consistently induce remission

- Remission (SU) is achieved infrequently (~13%)
- Decreasing dose to 300 mg results in increased likelihood of regaining reactivity



Chinthrajah RS, et al. Lancet. 2019; 392:1437-49.

Is the goal to induce long-term remission?

No therapies currently under study have been shown to consistently induce remission

Does the family want the child to be safer?

 Consider data previously shown; however, most reactions are mild and when they occur the patient is under observation in the family home

GI AEs are most common AE and most common reason for discontinuation (1-5% of participants in trials dx'd with EoE)^{2,3}

- 1217 patients enrolled in Aimmune Phase 2 & 3 trials³
- 62 withdrew due to GI AEs
- 17 had EGD
- 12/17 diagnosed with EoE

• 5/7 with EGD data available after removal of OIT had resolution of EoE

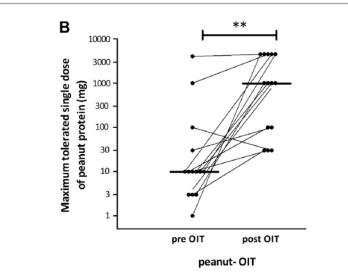
What is the best dose?

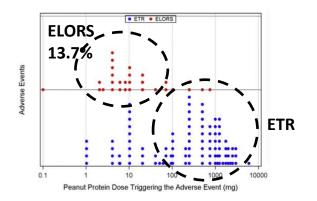
Efficacy, Safety, and Quality of Life in a Multicenter, Randomized, Placebo-Controlled Trial of Low-Dose Peanut Oral Immunotherapy in Children with Peanut Allergy

- Low-dose OIT (125-250mg) may be safer and provide comparable efficacy to higher doses (e.g. ≥300 mg)
- No epinephrine use and no EoE

Real-World Experience with Peanut Oral Immunotherapy: Lessons Learned From 270 Patients

- 3000 mg maintenance then decrease to 2000 mg 1 to 2 times daily
- 114/270 (42%) discontinued, transferred care or lost to f/u
- 100 ETRs in 63/270 (23%) during build-up and 60 ETRs in 28 patients during maintenance
- 13.7% developed EoE-like syndrome





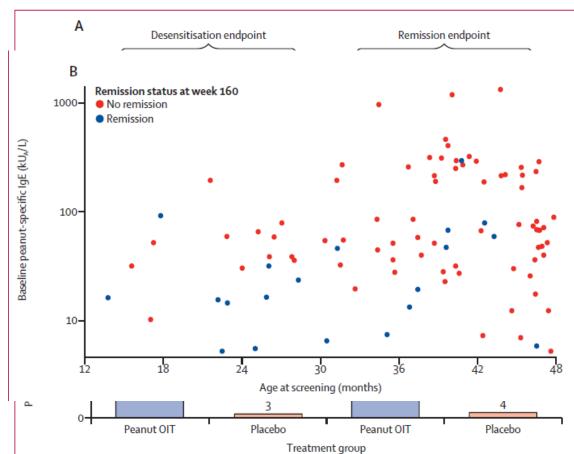
¹Blumchen K, et al. J Allergy Clin Immunol Pract 2019; 7:479-91.². Wasserman RL, et al. J Allergy Clin Immunol Pract 2019;7:418-26.

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What is the best age?

Efficacy and safety of oral immunotherapy in children aged 1–3 years with peanut allergy (the Immune Tolerance Network IMPACT trial): a randomised placebo-controlled study

- Enrolled children 1-4 y/o (96 PnOIT, 50 placebo)
- 2000 mg PnOIT daily x 2 $\frac{1}{2}$ years \rightarrow Desensitization challenge.
- Therapy stopped x 6 mos \rightarrow SU challenge
- Lower baseline peanut-specific IgE predicted better outcome



Is the goal to induce long-term remission?

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Does the family want the child to be safer?

Consider data previously shown; however, most reactions are mild and when they occur the patient is under observation in the family home

Does the family wish to liberalize diet (e.g., ingest "may contain" products)

- Consider low-dose challenges
 - Threshold stability over time has not been well-established

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Patients with significantly impaired QOL tend to report most improvement in QoL¹

Does the Patient have Multiple Food Allergies?

- 30-70% of peanut-allergic patients are allergic to multiple foods^{1, 2}
- Following scenarios might argue for OIT to single allergen in multi-food allergic patient
 - Frequent exposure and/or reactions to one allergen
 - Increased anxiety related to one allergen over others because of perception of risk
- Multi-food OIT is understudied with safety as primary concern.
 - Omalizumab as Monotherapy and as Adjunct Therapy to Multi-Allergen OIT in Food Allergic Children and Adults (OUtMATCH)
 - Protection from Food Induced Anaphylaxis by Reducing the Serum Level of Specific IgE (Protana)
 - Omalizumab to Accelerate a Symptom-driven Multi-food OIT (BOOM)
 - E-B-FAHF-2, Multi OIT and Xolair (Omalizumab) for Food Allergy

Lifestyle considerations

OIT requires up-dosing at least every 2 weeks & daily dosing at home with activity modifications

- Daily dosing following snack or meal (preferably in evening and at the same time every day)
- No exertion or exercise within 3h of dose
- No dosing within 2 h of waking or going to sleep
- No hot showers or baths within 3 hours of dosing
- Dose modification with fever and/or illness or asthma flare
- Risk may increase during menstruation
- Does child live in more than 1 household?
- Are family members supportive and willing to maintain therapy?

OIT for foods other than peanut

- Is FDA approval necessary?
 - Assures quality and safety of the product
 - Precision and consistency in dosing
 - Mitigation of medicolegal concerns for the allergist
- If a child is going to develop natural tolerance, is the risk of reacting with therapy unnecessarily greater than standard avoidance?
 - Diagnostic tools do not adequately predict timing of tolerance development and if it will occur
- Evidence is lacking for foods other than milk, egg, and peanut

How do I approach and discuss OIT with patients?

- 1. Confirm allergy
 - Skin and serum testing, components, and food challenges if necessary
- 2. Discuss patient and family goals of therapy
 - Minimize likelihood of life-threatening anaphylaxis
 - Ad lib consumption of food
 - Ability to eat "may contain" foods
 - Consider low dose challenge
- 3. Review pros and cons
 - Consider lifestyle factors (athletics, siblings, working parents, etc.)
 - Consider potential discontinuation with age
 - Consider family focus and reason for seeking therapy

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Development and acceptability of a shared decision-making tool for commercial peanut allergy therapies Matthew Greenhawt, MD, MBA, MSc^{*}; Marcus Shaker, MD, MS^{†,†}; Tonya Winders, MBA[§]; Don A. Bukstein, MD^{||}; Ray S. Davis, MD[¶]; John Oppenheimer, MD[#]; David M. Fleischer, MD^{*}; Edwin Kim, MD^{**}; Edmond S. Chan, MD^{††}; David R. Stukus, MD^{‡‡}; Daniel Matlock, MD, MPH^{§§,¶¶}

AllergyAndAsthmaRelief.org

Should My Child Try Peanut Allergy Treatment?

Use this discussion guide to help decide if the treatment is right for your child

Welcome

It can be frightening if your child has a peanut allergy. Even when you and your child are doing your best to avoid peanuts, accidental ingestion still can occur. If your child is 4 to 17 years old, a new treatment may help reduce the severity of allergic reactions, including anaphylaxis, that may happen with accidental exposure to peanut. Oral peanut immunotherapy slowly exposes an allergic child to peanuts so their immune system is less likely to react if they accidentally eat something containing a small amount of peanut. Even with this treatment, your child MUST continue to avoid peanuts and carry two epinephrine auto-injectors.

It's important to understand:

 The new treatment is not a cure - your child will still be allergic to peanuts and must avoid them. The goal is to help reduce risk and fear of a life-threatening reaction if your child accidentally ingests any amount of peanut, no matter how small. This may improve quality of life by helping the child (and family) worry less and feel more comfortable in social situations. • It will not enable your child to eat peanuts or peanut products anytime they wish.

• It must be taken daily to maintain the treatment effect. It works only while your child is taking it on a daily basis.

 Your child will need to continue to carry two epinephrine auto-injectors, and you and your child will still need to read food labels.

 Reactions, including anaphylaxis, can occur due to the treatment itself.

For many children with peanut allergy and their parents, the benefits may be worth the drawbacks.

This tool helps you talk with your child's allergist to decide if this treatment might be a good option.

The discussion guide is easy to use:

1 Read about peanut allergy and the therapy.

2 Respond to a few simple statements based on your child's temperament and preferences.

Bring your answers to your child's next appointment.

Your Turn

The next step is to talk about the treatment with your child's allergist. To help you figure out if the treatment might be an option for your child, check the boxes if you **agree** with the following statements.

- My child and I frequently worry they will be exposed to peanuts and have a serious allergic reaction.
- My child avoids peanuts and carries an epinephrine autoinjector but still doesn't feel protected from a reaction.

I would be able to take my child to the allergist every two weeks for six months.

My child is not able to fully enjoy participating in activities such as parties and overnight camp due to their peanut allergy.

- It would not be difficult to plan daily activities such as showering and exercise around the treatment.
- My child would be willing to try this treatment.
- My child would be able to adhere to a daily treatment.
- Being able to afford the treatment is not a concern for me.

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Greenhawt M, et al. Ann Allergy Asthma Immunol 125 (2020): 90-96.

Developmental Transition to Independence



Concerns with alcohol and illicit drug use Comfort with self-administration of epinephrine Food preparation Dating partner awareness of allergy Encouraging self-carry of auto-injectable epinephrine Introduction to reducing risk-taking behaviors Education regarding not sharing food Introduction of label reading and food ordering Introduction of teaching the child she is allergic Introduction of teaching the child to ask if food contains allergen Learning to not share and accept food from strangers Management of impulse control to prevent grabbing

Maintain self-injectable epinephrine and a food allergy action plan

Train others in frequent contact with child to use self-injectable epinephrine

Strict allergen avoidance

Educate persons who prepare the child's food regarding cross-contact and safe food prep

Sublingual Immunotherapy (SLIT)

Summary of Studies to Date

Sublingual immunotherapy for peanut allergy: Clinical and immunologic evidence of desensitization

Edwin H. Kim, MD,^a J. Andrew Bird, MD,^a Michael Kulis, PhD,^a Susan Laubach, MD,^a Laurent Pons, PhD,^a Wayne Shreffler, MD, PhD,^b Pamela Steele, CPNP,^a Janet Kamilaris, RN,^a Brian Vickery, MD,^a and A. Wesley Burks, MD^a Durham, NC, and Boston, Mass

J Allergy Clin Immunol 2011.

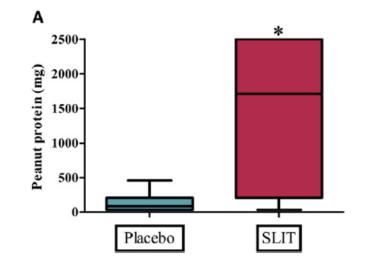
Peanut-eliciting threshold 20 times greater in SLIT vs placebo

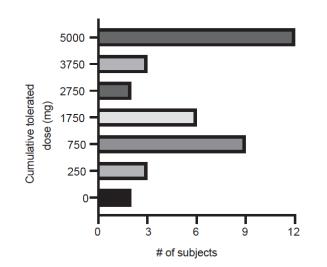
Long-term sublingual immunotherapy for peanut allergy in children: Clinical and immunologic evidence of desensitization

Edwin H. Kim, MD, MS,^a Luanna Yang, MD,^b Ping Ye, PhD,^b Rishu Guo, PhD,^b Quefeng Li, PhD,^c Michael D. Kulis, PhD,^b and A. Wesley Burks, MD^b Chapel Hill, NC

J Allergy Clin Immunol 2019.

- Peanut-allergic children received 2 mg/d x 3-5 years
 - 67% (32/48) successfully consumed ≥ 750 mg pn protein
 - 25% (12/48) successfully consumed ≥ 5000 mg pn protein





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Sublingual immunotherapy for peanut allergy: A randomized, double-blind, placebo-controlled multicenter trial

David M. Fleischer, MD,^a* A. Wesley Burks, MD,^b* Brian P. Vickery, MD,^b Amy M. Scurlock, MD,^c Robert A. Wood, MD,^d Stacie M. Jones, MD,^c Scott H. Sicherer, MD,^e Andrew H. Liu, MD,^a Donald Stablein, PhD,^f Alice K. Henning, MS,^f Lloyd Mayer, MD,^e Robert Lindblad, MD,^f Marshall Plaut, MD,^g and Hugh A. Sampson, MD,^e for the Consortium of Food Allergy Research (CoFAR) Denver, Colo, Chapel Hill, NC, Little Rock, Ark, Baltimore, Rockville, and Bethesda, Md, and New York, NY

J Allergy Clin Immunol 2013.

 70% of SLIT responded with median SCD dose changing from 21 mg → 996 mg vs 15% in placebo group

Sublingual immunotherapy for peanut allergy: Long-term follow-up of a randomized multicenter trial

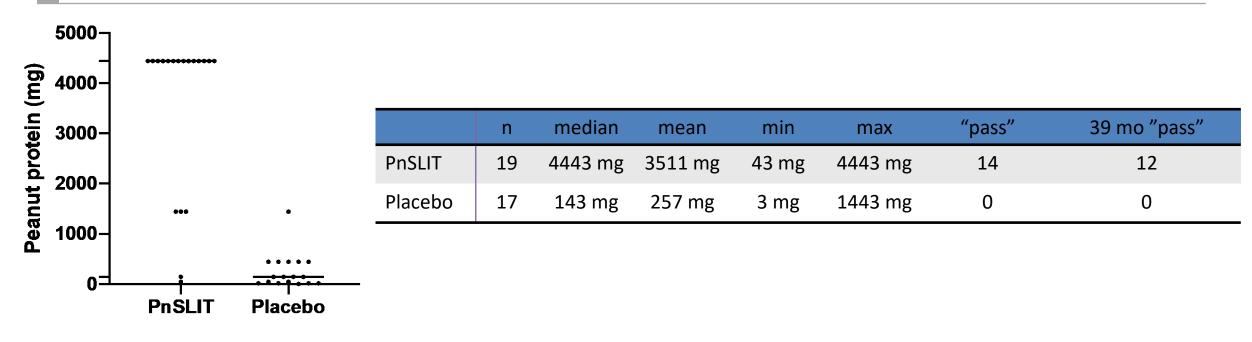
A. Wesley Burks, MD,^a Robert A. Wood, MD,^b Stacie M. Jones, MD,^c Scott H. Sicherer, MD,^d David M. Fleischer, MD,^e Amy M. Scurlock, MD,^c Brian P. Vickery, MD,^a Andrew H. Liu, MD,^f Alice K. Henning, MS,^g Robert Lindblad, MD,^g Peter Dawson, PhD,^g Marshall Plaut, MD,^h and Hugh A. Sampson, MD,^d for the Consortium of Food Allergy Research (CoFAR) Chapel Hill, NC, Baltimore, Rockville, and Bethesda, Md, Little Rock, Ark, New York, NY, and Denver, Colo

- >50% withdrew from study
- Did not appear to be a significant difference in median tolerated dose based on amount of protein in SLIT but unable to fully conclude because of drop-out rate

Safety and efficacy of peanut sublingual immunotherapy in toddleraged peanut-allergic children

- <u>Central hypothesis</u>: PnSLIT as an early intervention will induce clinical desensitization in the majority of participants after 36 months of therapy
- Study Participants
 - Peanut allergic at age 12-48 months
 - Reaction during peanut 1000 mg peanut DBPCFC
- Methods
 - Build-up to 4 mg PN SLIT over 36 mos

Desensitization after 36 months of therapy



Conclusions

- PnSLIT successfully desensitizes peanut-allergic 1-4 yr old children when compared to placebo
- Side effects requiring treatment are uncommon

SLIT Status

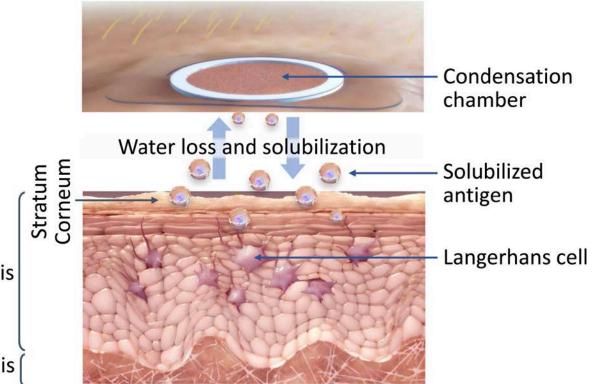
No industry-funded studies underway

 Larger trials needed to confirm if initial treatment with SLIT could improve OIT safety

Epicutaneous Immunotherapy (EPIT)

Epicutaneous Immunotherapy

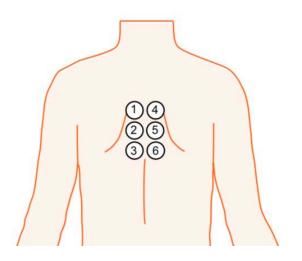
- Patch containing allergenic protein is applied to intact skin
- Skin's natural water loss solubilizes and releases allergen
- Dendrites of Langerhans cells (LCs) take-up the allergen & then Epidermis LCs migrate to regional lymph nodes where they activate immune Dermis response, primarily Tregs



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JAMA | Original Investigation

Effect of Epicutaneous Immunotherapy vs Placebo on Reaction to Peanut Protein Ingestion Among Children With Peanut Allergy The PEPITES Randomized Clinical Trial



Study Population

Peanut-allergic Children, 4-11 years

Efficacy Endpoints

Treatment responder defined by ability to raise eliciting threshold above protective level (e.g. if reactive at <1/30th of peanut, must be able to ingest up to 1 peanut before reacting)

Results: 35.3% responders to treatment in treatment group vs 13.6% in placebo (p<0.001)</p>

-Lower bound of 95% CI 12.4% crossed prespecified lower limit of 15%

Phase 3 trial



Long-term, open-label extension study of the efficacy and safety of epicutaneous immunotherapy for peanut allergy in children: PEOPLE 3-year results David M. Fleischer, MD,^a Wayne G. Shreffler, MD, PhD,^b Dianne E. Campbell, MBBS, PhD,^{c,d} Todd D. Green, MD,^{d,e} Sara Anvari, MD, MSc,^{f,g} Amal Assa'ad, MBBCh,^h Philippe Bégin, MD, PhD,ⁱ Kirsten Beyer, MD,^j J. Andrew Bird, MD,^k Terri Brown-Whitehorn, MD,^{I,m} Aideen Byrne, PhD,ⁿ Edmond S. Chan, MD,^o Amarjit Cheema, MD,^p Sharon Chinthrajah, MD,^q Hey Jin Chong, MD, PhD,^e Carla M. Davis, MD,^g Lara S. Ford, MBBS, MPH,^{c,r} Rémi Gagnon, MD,^s Matthew Greenhawt, MD,^a Jonathan O'B. Hourihane, MD,^{t,u} Stacie M. Jones, MD,^v Edwin H. Kim, MD, MS,^w Lars Lange, MD,[×] Bruce J. Lanser, MD,^Y Stephanie Leonard, MD,^{z,aa} Vera Mahler, MD,^{bb}* Andreas Maronna, MD,^{bb} Anna Nowak-Wegrzyn, MD, PhD,^{ec,dd} Roxanne C. Oriel, MD,^{ee} Michael O'Sullivan, MD,^{ff} Daniel Petroni, MD, PhD,^{gg} Jacqueline A. Pongracic, MD,^{hh} Susan L. Prescott, MBBS, PhD,^{ff,ii} Lynda C. Schneider, MD,^{ji} – Peter Smith, MBBS, PhD,^{kk} Doris Staab, MD,^{II} Gordon Sussman, MD,^{mm} Robert Wood, MD,ⁿⁿ William H. Yang, MD,^{oo} Romain Lambert, MSc,^d Aurélie Peillon, MSc,^d Timothée Bois, MSc,^d and Hugh A. Sampson, MD^{d,ee}



Key Message: EPIT demonstrated durable, long-term clinical benefit with an additional 2 years of treatment in children 4 to 11 y/o

Fleischer D, et al. J Allergy Clin Immunol 2020 Oct;146:863-874.

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EPIT Implementation in Clinical Practice

- August 2020: FDA concerned with impact of patch adhesion and the need for patch modifications.
 - January 2021: FDA agreed modified patch should not be considered new product and asked for 6-month safety and adhesion trial to assess the modified patch
 - December 2021: DBV announced plans for new Phase 3 placebo-controlled efficacy trail similar to PEPITES with a modified patch ~50% larger than the current patch.

"I do not know what food immunotherapy will be like 20 to 30 years from now, but I am hopeful that it will look nothing like the therapies described in this review."

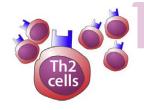
> - Robert A. Wood, MD Food allergen immunotherapy: Current status and prospects for the future J Allergy Clin Immunol 2016;137:973-82

How do we make food IT safer and/or more effective/sustainable?

- Safety is primarily related to effector cell activation
 - Block effector cell activation
 - Minimize exposure to effector cells
 - Directly target antigen uptake
- Sustainability may be related to suppression of Th2 response
 - Inhibit Th2 initiation and promote Th1 expansion

OIT Mechanisms

- B cells
- INCREASE in peanut-specific IgE
 - INCREASE in peanut-specific Ig4
 - Specific Ig4 stays elevated & specific IgE decreases over time



- First exposures promote Th2 & suppress T reg
 - Increase in IL-10 production & exhaustion/deletion of Th2 cells
 - T reg cell differentiation



- Increased T regs, though not antigen specific, which diminish in periphery over time
- Enhanced epigenetic modifications associated with SU

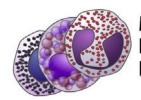
- Mast cells Eosinophils Basophils
- Continuous allergenic stimulation leads to deprivation of preformed mediators through continuous degranulation
 - IgE endocytosis and actin rearrangement render cells hyporesponsive
 - Induction of inhibitory signaling prevents degranulation

Future Therapeutics

Block activation Omalizumab

Anti-IL-33 (ANB020)

IL-33 acts upstream of IgE and mediates B-class switching to IgE

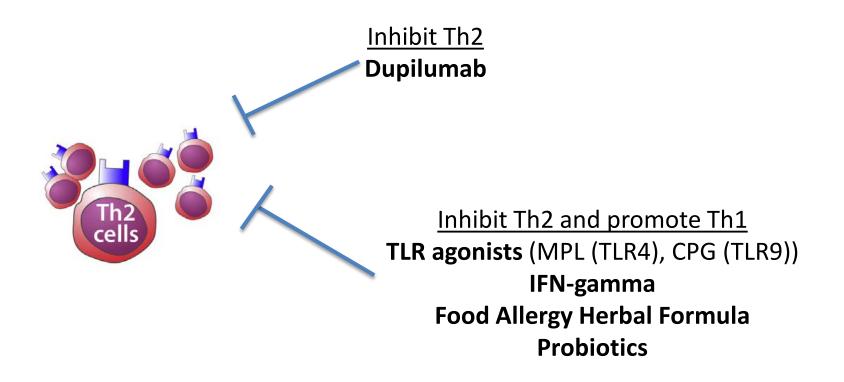


Mast cells Eosinophils Basophils

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| | |
| <u>Block in</u> | <u>flammatory mediators</u> |
| | Ketotifen |
| | |
| | ITRAs |

Minimize Exposure to Effector Cells Nanoparticles DNA plasmid (Ara h1-3 tied to LAMP-1) Modified peanut extract (HAL MPE) PVX108 (synthetic T-cell binding epitopes for Ara h1&2)

Future Therapeutics



Peanut OIT + Probiotic

Probiotic peanut oral immunotherapy versus oral immunotherapy and placebo in children with peanut allergy in Australia (PPOIT-003): a multicentre, randomised, phase 2b trial

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Primary aim: Efficacy and safety of PPOIT at inducing 8-week SU compared to placebo and PnOIT alone.

- •<u>Methods</u>: 1-10 y/o children built up to 2000 mg of PnOIT
- •<u>Results</u>: No efficacy advantage in PPOIT compared to PnOIT alone.
 - 1-5 y/o children had higher rate of SU than 6-10 y/o children

Conclusions

- Peanut OIT is FDA-approved but may not be right for all patients
- •SLIT and EPIT may offer potential efficacy with fewer AEs
- Current therapies may elevate dose-triggering threshold but unlikely to induce permanent remission

 Children 1 to 55 years-old with peanut allergy + at least 2 other food allergies (milk, egg, wheat, cashew, hazelnut or walnut)

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