Consensus report from the Food Allergy Research & Education (FARE) 2019 Oral Immunotherapy for Food Allergy Summit

Amber N. Pepper, MD,[a] Amal Assa'ad, MD,[b] Michael Blaiss, MD, FACAAI,[c] Emily Brown,[d] Sharon Chinthrajah, MD,[e] Christina Ciaccio, MD, MSc,[f] Mary Beth Fasano, MD, MSPH,[g] Ruchi Gupta, MD, MPH,[h,i] Nurry Hong, BA,[j] David Lang, MD,[k] Todd Mahr, MD,[l] Erin Malawer, BA,[m] Anita Roach, MS,[j] Wayne Shreffler, MD, PhD,[n] Scott Sicherer, MD,[o] Kathleen Vickers, MS,[j] Brian P. Vickery, MD,[p] Richard Wasserman, MD, PhD,[q] Kimberley Yates, BA,[r] and Thomas B. Casale, MD[s] *Tampa, Fla, Cincinnati and Cleveland, Ohio, Augusta, Ga, Kansas City, Mo, Stanford and Redwood City, Calif, Chicago, Ill, Iowa City, Iowa, McLean, Va, LaCrosse, Wis, Dallas, Tex, Boston, Mass, and New York, NY*

Food allergy is a major health problem affecting 5% to 10% of the population in developed nations, including an estimated 32 million Americans. Despite the large number of patients suffering from food allergies, up until the end of January 2020, no treatment for food allergies had been approved by the US Food and Drug Administration. The only options were avoidance of food allergen triggers and acute management of allergic reactions. A considerable body of data exists supporting oral immunotherapy (OIT) as a promising, novel treatment option, including that for the now Food and Drug Administration–approved peanut OIT product Palforzia (Aimmune Therapeutics, Brisbane, Calif). However, data for long-term quality-of-life improvement with OIT varies, depending on the measures used for analysis. Like many therapies, OIT is not without potential harms, and burdens, and the evaluation of patient-specific risk-benefit ratio of food OIT produces challenges for clinicians and patients alike, with many unanswered questions. Food Allergy Research & Education organized the Oral Immunotherapy for Food Allergy Summit on November 6, 2019, modeled after the PRACTALL sessions between the European Academy of Allergy and Clinical Immunology and the American Academy of Allergy, Asthma & Immunology to address these critical issues. Health care providers, patient representatives, researchers, regulators, and food allergy advocates came together to discuss OIT and identify areas of common ground as well as gaps in existing research and areas of uncertainty and disagreement. The purpose of this article was to summarize that discussion and facilitate collaboration among clinicians and patients to help them make better-informed decisions about offering and accepting OIT, respectively, as a therapeutic option. (J Allergy Clin Immunol 2020;146:244-9.)

Key words: *Oral immunotherapy, Food allergy, Peanut allergy*

Food allergy affects 5% to 10% of the population in developed nations.[1-3] Established clinical management, namely avoidance of food allergen triggers and immediate availability of epinephrine, is less than ideal for some patients and families with food allergy. The need for treatment options that offer an opportunity for more normal daily living is well established among the food allergy community. Oral immunotherapy (OIT) is one such therapy, and a considerable body of data is building to show its promise for improving the long-term quality of life (QOL) for a select population of food-allergic patients.[1] Patients and families are actively seeking out this treatment option, and a product for peanut OIT,

From [a]the Division of Allergy and Immunology, Department of Internal Medicine, University of South Florida Morsani College of Medicine, Tampa; [b]Cincinnati Children's Hospital Medical Center, Cincinnati; [c]the Medical College of Georgia at Augusta University, Augusta; [d]the Food Equality Initiative, Kansas City; [e]Sean N. Parker Center for Allergy and Asthma Research, Stanford University, Stanford; [f]The University of Chicago, Department of Pediatrics, Chicago; [g]the University of Iowa Carver College of Medicine, Iowa City; [h]the Center for Food Allergy and Asthma Research, Northwestern University Feinberg School of Medicine, Chicago; [i]Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago; [j]FARE (Food Allergy Research & Education), McLean; [k]the Department of Allergy and Clinical Immunology, Respiratory Institute, Cleveland Clinic, Cleveland; [l]Gundersen Health System, La Crosse; [m]AllergyStrong, McClean; [n]Food Allergy Center, Departments of Pediatrics and Medicine, Massachusetts General Hospital, Boston; [o]the Department of Pediatrics, Jaffe Food Allergy Institute, Icahn School of Medicine at Mount Sinai, New York; [p]Food Allergy Center at Emory + Children's, Atlanta; [q]Allergy Partners of North Texas, Dallas; [r]Latitude Food Allergy Care, Redwood City; and [s]Food Allergy Research & Education (FARE), University of South Florida, Tampa.

Food Allergy Research & Education hosted the meeting that produced this document and provided support for writing the manuscript.

Disclosure of potential conflict of interest: A. N. Pepper and T. B. Casale are investigators on Aimmune-sponsored studies. B. P. Vickery reports grants and personal fees from Aimmune Therapeutics, personal fees from AllerGenis, grants and personal fees from Food Allergy Research & Education (FARE), grants from Genentech, grants from DBV Technologies, grants from NIH-NIAID, and grants from Regeneron, outside the submitted work. W. Shreffler has received payment from FARE, Aimmune Therapeutics, Buhlmann Laboratories AG, and Sanofi Pasteur. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication March 23, 2020; revised May 14, 2020; accepted for publication May 15, 2020.

Available online June 4, 2020.

Corresponding author: Thomas B. Casale, MD, Food Allergy Research & Education (FARE), University of South Florida, 12901 Bruce B Downs Blvd, MDC19, Tampa, FL 33612. E-mail: tbcasale@usf.edu.

0091-6749/$36.00

https://doi.org/10.1016/j.jaci.2020.05.027

Abbreviations used
EoE: Eosinophilic esophagitis
FDA: Food and Drug Administration
ICER: Institute for Clinical and Economic Research
OIT: Oral immunotherapy
PALISADE: Peanut Allergy Oral Immunotherapy Study of AR101 for Desensitization
QOL: Quality of life

Palforzia (Aimmune Therapeutics, Brisbane, Calif), was approved by the US Food and Drug Administration (FDA) on January 31, 2020. Much like therapeutic interventions for other diseases, OIT is not without potential harms and burdens, and the evaluation of patient-specific risk-benefit ratio of food OIT produces challenges for clinicians and patients alike. Food Allergy Research & Education organized the Oral Immunotherapy for Food Allergy Summit on November 6, 2019, to address these critical issues. Health care providers, patient representatives, researchers, regulators, and food allergy advocates came together to discuss this therapy and produce consensus documents identifying areas of common ground as well as gaps in existing research and areas of uncertainty and disagreement. The goal of this article was not to recommend any particular treatment or OIT product, but to help physicians make informed decisions about accepting and offering OIT in their clinical practices. The OIT for Food Allergy Summit was modeled after the PRACTALL sessions between the European Academy of Allergy and Clinical Immunology and the American Academy of Allergy, Asthma & Immunology producing published articles for physician guidance. The summit focused on 4 areas: (1) OIT from the Practicing Physician Perspective; (2) OIT from the Patient Perspective; (3) OIT from the Institute for Clinical and Economic Research (ICER) Perspective; and (4) OIT from the Regulatory Perspective. All authors participated in addressing the critical areas discussed at the summit and had the opportunity to review the statements in this article.

PATIENT CONSIDERATIONS

Candidate selection

OIT is an emerging option for the treatment of food allergy, but it is not appropriate for all patients with a history of allergic reactions to food. European food allergy guidelines published in 2018 have recommended the use of OIT in "highly specialized clinical centers with expertise and facilities to safely deliver this therapy" for milk, egg, or peanut, whereas the older US practice guidelines recommend against its use and need to be updated, especially with the approval of Palforzia.[4] Patients must have confirmed IgE-mediated food allergy to undergo OIT. This should be determined through a thorough history with supportive allergen-specific IgE blood and/or skin testing. If the history is unclear, an oral food challenge is needed for diagnosis. The summit participants recognize that food challenges are not without risks and potential harms and the need for alternative methods to confirm food allergy is pressing. OIT is not appropriate for the treatment of food intolerances, food sensitivity without confirmed allergy, or other non–IgE-mediated indications. In addition, OIT may not be appropriate for patients with a high likelihood of spontaneous food allergy resolution, such as some young children with cow's milk or hen's egg allergy for which FDA-approved OIT products are not currently available. Other allergic diseases, especially asthma, should be well controlled before OIT initiation and during OIT treatment.[1] Because a history of eosinophilic esophagitis (EoE) may create additional risks and added complexity in interpreting symptoms during OIT, providing OIT to patients with EoE should be avoided until data support an alternative view.[1]

OIT is most beneficial for fully informed, motivated patients and families who desire enhanced normalcy and a reduced influence of food allergy in their lives, and who are willing to accept the added potential harms and burdens of the treatment. The psychosocial impact of food allergy before, and anticipated changes during and after OIT treatment, should be explored for each family, with engagement of mental health services as needed before, during, and after OIT. Food aversion, its implications for OIT dosing, and apprehension over epinephrine use must be addressed in advance. Access to mental health services has been shown to be a substantial gap in care that caregivers strongly prioritize.[5,6] Summit participants agreed that better measures for the impact of OIT on patient-centered outcomes such as QOL and enhanced normalcy in food-allergic subjects are needed in research studies. The participants agreed that the conclusion by ICER, based largely on the Peanut Allergen immunotherapy, Clarifying the Evidence systematic review, that OIT has no impact on QOL may be premature, given the problems in the analysis reviewed in a recent publication.[7-9] In a small subset of Peanut Allergy Oral Immunotherapy Study of AR101 for Desensitization (PALISADE) trial participants, all parents and 86% of children felt the advantages of peanut OIT using Palforzia outweighed the disadvantages. In addition, 5 key areas of QOL impacted by peanut allergy improved after Palforzia treatment (emotional functioning, social and leisure activities, daily activities, relationships, and independence/supervision).[10] Studies show significant improvement in QOL after OIT, but more robust data are needed.[9,11,12]

Goals of therapy

The detailed discussion of patient goals and expectations of OIT should be documented in the medical record before treatment initiation. OIT is a treatment for food allergy. It is not a cure. OIT induces desensitization and may, in a subset of patients, induce sustained unresponsiveness.[1,13,14] There is limited evidence that OIT provides long-lasting unresponsiveness after discontinuation in only a subset of patients.[15] Patients must understand that treatment may be indefinite. The most robust data published on the efficacy of OIT for desensitization are for peanut allergy. In the phase 3 PALISADE trial, in which participants' maximum tolerated amount of peanut protein at baseline was less than 100 mg, 67.2% of the active treatment group tolerated 600 mg of peanut protein at the exit double-blind placebo-controlled food challenge as compared with only 4% in the placebo group.[16] In the The Peanut Oral Immunotherapy Study: Safety, Efficacy and Discovery (POISED), 85% achieved desensitization to 4000 mg of peanut after 2 years of OIT. After 3 months of discontinuation, only 35% were able to successfully pass the challenge to previously tolerated doses; an individual's ability to ingest approximately 1 g versus 4 g varied over time.[15] The optimal maintenance regimen for OIT is yet to be defined. OIT is effective in children

and in some studies with mixed-age populations. Efficacy in adults alone is not well established.[1]

It is likely that there are multiple phenotypes of food allergy that influence sensitivity (eg, the dose of allergen eliciting a reaction), and the severity of the ensuing reaction, among other influences. Reliable identification of each phenotype before starting therapy remains a substantial research goal, and great strides are being made on this front.[17] In addition, there may be variability among patients/caregivers about their goals for therapy, for example, protection against cross-contamination ("may contain" foods); protection from larger accidental exposures ("bite-proof protection"); or regular ingestion of the food ("free eating"). As much as possible, each family's treatment goal and the individualized maintenance dose of OIT required to achieve that goal should be clarified in advance for non–FDA-approved products. Much more research is needed in this area, including among the patients currently receiving therapy in community patient care centers where products used for OIT may need better oversight with accurate labeling.

Shared decision making and consent

Discussion of harms and side effects. Patients must be aware of the benefits, potential harms, and burdens of OIT as well as alternatives. A shared decision-making process is critical. The decision on whether to pursue OIT should reside between the patient, their families, and all legal guardians of a pediatric patient if applicable, following a thorough discussion of the harms and burdens of OIT to the treating physician's best ability. Care should be taken to avoid any possibility of coercion. A written informed consent is recommended to document this process and ensure that the discussion with each participant is comprehensive, but it should be noted that informed consent is an ongoing process. Age-appropriate assent may be pursued per local standards to ensure that minor patients understand and agree to the treatment. If a non–FDA-approved product is used for OIT, this should be communicated clearly and stated in the consent as should the alternatives to OIT. Physicians should also discuss that non–FDA-approved products may lead to an increased risk of adverse events.

Allergic reactions to foods are estimated to cause 4 to 10 deaths per year in the United States. Peanut has been reported to be associated with food allergy death in 35 of 91 persons from 2010 to 2019.[18] OIT has not been associated with death to date. However, in the PALISADE trial for peanut OIT (Palforzia), systemic allergic reactions and epinephrine use were higher in the treatment group as compared with the placebo group (14.2% vs 3.2% and 14.0% vs 6.5%, respectively).[16] In a real-world peanut OIT review, 23.3% of patients experienced epinephrine-treated reactions during immunotherapy.[19] Because of this increase in systemic allergic reactions and epinephrine use with OIT as compared with avoidance (risk ratio, 3.12 and 2.21, respectively), and what was perceived to be inadequate evidence of QOL benefit, ICER concluded that the evidence for peanut immunotherapy, including OIT, was inadequate to demonstrate a superior net health benefit compared with strict peanut avoidance.[7,8] The POISED study showed that allergic reactions to doses decreased over the course of 3 years of OIT, and the rate of reactions to accidental ingestions to peanut also decreased with continued peanut OIT.[15] Patients must be aware of the risk of systemic reactions and be willing to treat any that may occur. Palforzia carries a black box warning for anaphylaxis. All patients and families should be knowledgeable about and comfortable with the recognition of food allergy reactions and the administration of epinephrine.

In addition, withdrawals from OIT treatment are common. In the PALISADE trial, withdrawal rates due to therapy effects were 11.6% and 2.4% in the treatment and placebo groups, respectively.[16] Dropout rates in a real-world peanut OIT study were 18% overall, but 81% reached the target maintenance dose.[19] Gastrointestinal symptoms (abdominal pain, nausea, vomiting) are common adverse events, occurring in 37% to 52% of participants.[16,19] EoE may occur with OIT. In a review, 13.7% experienced EoE-like symptoms.[19] Patients and families should be warned about this risk and a plan developed to evaluate and manage EoE and EoE-like symptoms should these occur.

Financial discussion. OIT may be cost-prohibitive to some patients and families. A 2013 study estimated that childhood food allergy in the United States costs $24.8 billion annually ($4184 per year per food-allergic child). Of this, $4.3 billion is due to direct medical costs and $20.5 billion is due to impacts on caregiver productivity and the out-of-pocket costs of allergen-free foods, epinephrine autoinjectors, special childcare arrangements, and other expenses.[20] These estimates do not reflect increases in the cost of living since 2013. A discussion of financial costs should include estimated total costs of OIT with or without health insurance. The impact of Palforzia on overall financial costs to patients for peanut OIT remains uncertain. ICER estimated the incremental cost-effectiveness ratio at $88,000 per quality-adjusted life-year, meaning that ICER did not find this treatment to meet its criteria of cost-effectiveness related to cost for each quality-adjusted life-year obtained. ICER estimated the cost of Palforzia at $4200 per year.[7] The announced cash price of Palforzia is approximately $9840 per year ($820 per month). In addition, the cost of OIT in practice with non–FDA-approved products varies substantially and is often not reimbursed by insurers. Additional OIT costs may include epinephrine autoinjectors, office visits, and, in some cases, emergency department or urgent care services. OIT should be discussed in context of the cost of allergen-free foods and special childcare arrangements, which can be a significant cost and QOL burden for families.[21] These factors should be considered when discussing whether OIT is the best treatment choice for a patient, especially considering that OIT is not curative and ongoing precautions around allergen exposure will still be required for many patients.

Social and family dynamics discussion. Social and family dynamics should also be evaluated before OIT because the therapy requires a significant time commitment and other constraints on day-to-day family functioning. Adherence to the treatment plan is vital to ensure the safety and enhance the efficacy of OIT. Patients and families who wish to undergo OIT must be motivated and reliable. All family members should be committed to the process. During build-up, patients return frequently for monitored dose increases in clinic (eg, Palforzia requires 11 updosing visits). Home doses must also be monitored. A discussion of the social supports available to help facilitate travel to/from office visits as well as for home dosing is needed. Dose adjustments may be needed during illnesses, asthma exacerbations, and other situations. Restrictions on exercise and other activities surrounding home and in-office dosing should also be discussed in advance to assist patients and families in evaluating whether OIT is a good fit for their lifestyles. Patients

should be strongly cautioned not to attempt to self-administer OIT. For Palforzia, patients must also still avoid peanuts in their diet. Those who are unable to adhere to the treatment protocols as directed should be discontinued from OIT.[1]

Although OIT may not be the ideal course of treatment for all patients with food allergy, it should, ideally, be available to all patients regardless of socioeconomic status or location. Familiarity about OIT in the general US food-allergic population is low (29%) but is greater among families with higher household incomes and education levels.[22] Considerations must be made for low-income patients or those living in rural areas, because their access to OIT may be more limited.

PHYSICIAN/FACILITY CONSIDERATIONS

Centers or clinical practices that offer OIT should be competent in the diagnosis and treatment of food allergy, the administration of oral food challenges, and the management of systemic allergic reactions, including anaphylaxis. The FDA approval of Palforzia stipulated a Risk Evaluation and Mitigation Strategy. Because of the risks of acute allergic reactions during OIT, this therapy should be performed under the supervision of a board-certified or board-eligible allergist/immunologist. All staff should be trained and experienced in the recognition and treatment of anaphylaxis. Adequate infrastructure, staff, medications, and supplies must be available on site to treat anaphylaxis.

OIT PRODUCT CONSIDERATIONS

Any product used for OIT should have clearly labeled protein content and information about the manufacturing facility's risk for cross-contamination. This is especially important if the product is not pharmaceutical grade. The amounts of major allergens may also vary if these are not included in the label contents, especially between products.[23] FDA-approved products such as Palforzia will be dosed on measurements of protein content and of representative allergens that, to minimize lot-to-lot variability, must meet specified acceptance criteria. Non–FDA-approved products must be continuously monitored to ensure consistency of protein content and manufacturing process. Food manufacturers may change label contents and manufacturing practices at any time. Microbial contamination of non–FDA-approved products is another concern. One study, which proposes methods for microbial contamination testing of OIT products, found low levels of potentially harmful microbes in 4 separate lots of peanut flour.[24] In addition, the appropriate protein content for maintenance doses is needed to ensure that the goals set with patients at the beginning of therapy are met. Safety and efficacy may be less predictable among practices that use products that are not FDA-approved. Some practices offer OIT for multiple foods concurrently although the published efficacy and safety data for this approach are much less robust.[1] It is up to each patient, family, and physician, after a thorough discussion of potential harms, benefits, alternatives, and other pertinent information as discussed previously, to select which product(s) to use for OIT.

REGULATORY CONSIDERATIONS

The legal definition of a drug is "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease."[25] According to this definition, food administered to a patient for OIT can be considered a drug. Therefore, any prospective studies examining OIT for food allergy treatment would likely require an investigational new drug application through the FDA. The FDA framework facilitates a systematic approach to address key questions that remain regarding OIT. However, there are both perceived and real burdens associated with this regulatory framework. Summit participants discussed that obtaining an investigational new drug approval and pursuing rigorous clinical trials for every possible food and combination of foods is impractical for most. The easy availability of food protein, in conjunction with the expansion of OIT in clinical practice, may lead to reductions in available financial support for research.

TABLE I. Unmet needs in OIT research

• Accepted standard definition of desensitization, or adoption of another term that more accurately reflects the changes in clinical and immunologic status with OIT
• Improved methods of measuring the impact of OIT on QOL and enhanced normalcy for patients and families
• Assessment of OIT effectiveness and safety for patients of differing socioeconomic status, race, and ethnicities
• Optimal dose and duration for maintenance therapy including the minimum frequency of maintenance dosing to maintain desensitization
• Optimal initiation dose for OIT buildup (standard protein dose or based on oral food challenge reactivity)
• If/when patients who have reached maintenance OIT can ever forgo avoiding the allergenic food
• More data on the efficacy and safety of multiple food OIT
• Demonstration of reductions, following OIT, in allergic reactions to food and health care utilization linked to accidental exposure
• Comparative data from shelf-bought OIT products with pharmaceutical-grade products, such as peanut powder and Palforzia, for buildup and maintenance, as regulatory considerations permit

UNMET NEEDS

There were several deficiencies in knowledge surrounding OIT identified and discussed at the summit (Table I). The acceptance of a standard definition of desensitization or the adoption of a better term that more accurately reflects the changes in clinical and immunologic status that result after OIT would be beneficial. Clinical trials and studies of OIT should examine effectiveness across patients of differing socioeconomic status, race, and ethnicity. Most published OIT studies examine a predominantly white and male study population with the resources available to attend frequent study visits.[16] In addition, more robust methods of measuring the impact of OIT on patients and families with food allergy, in terms of patient-centered outcomes such as QOL and enhanced normalcy, would be helpful because current assessments do not adequately reflect the complex and far-reaching influence of OIT on the lives of food-allergic patients and their families. New instruments may need to be developed to measure these impacts. Research studies are needed that document reductions, following OIT, in allergic reactions to food and health care utilization linked to accidental exposures. Direct comparisons between Palforzia and widely available peanut foods, such as shelf-bought peanut flour, would be valuable to help physicians and their patients who are being treated with non–FDA-

TABLE II. Summary of key points

- OIT is an emerging option for the treatment of persistent IgE-mediated food allergy. It is efficacious in inducing desensitization but is not without potential harms and burdens, and it is not curative.
- OIT is an option for motivated families with appropriate social support to maintain strict adherence to the office visits and restrictions surrounding dosing.
- OIT is not appropriate for all food-allergic patients. Physicians and patients should use a shared decision-making process to determine whether OIT is the appropriate treatment option for individual patients and families. Physicians should document the decision-making process per local regulations, which should include the signing of a written informed consent stating the potential harms, benefits, alternatives, and other pertinent information.
- OIT should be performed under the supervision of a board-certified or board-eligible allergist/immunologist with experience diagnosing and treating food allergy, including administering oral food challenges.
- All facilities offering OIT must have appropriate staff and infrastructure to manage systemic allergic reactions and anaphylaxis.
- Products used for OIT must have clearly labeled protein content and manufacturing information on potential cross-contamination. Allergen content is rarely included on labels and may vary, especially between products, making dosing standardization and regulation difficult.
- Physicians, other health care professionals, insurance companies, and federal and state governments should work to ensure OIT is available to all patients who desire access to this treatment option.
- Further research is needed to answer many remaining questions about the OIT process, but OIT is a promising first step toward addressing the high burden of disease on patients and families.

approved peanut OIT plan buildup and/or maintenance dosing. However, this direct comparison is difficult to achieve because of the regulatory considerations discussed above. Other unmet needs are listed in Table I.

SUMMARY

OIT is an emerging option for the treatment of persistent IgE-mediated food allergy. Key points about OIT are listed in Table II. It is efficacious in inducing desensitization but is not without potential harms and burdens, and it is not curative. OIT is an option for motivated families with appropriate social support to maintain strict adherence to the office visits and restrictions surrounding dosing. Physicians and patients should use a shared decision-making process to determine whether OIT is the appropriate treatment option for individual patients and families. Physicians should document the decision-making process per local regulations, which should include the signing of a written informed consent stating the potential harms, benefits, alternatives, and other pertinent information. OIT should be performed under the supervision of a board-certified or board-eligible allergist/immunologist with experience diagnosing and treating food allergy, including administering oral food challenges. All facilities offering OIT must have appropriate staff and infrastructure to manage systemic allergic reactions and anaphylaxis. Whether or not they are FDA-approved, products used for OIT must have clearly labeled protein content and manufacturing information on potential cross-contamination. Allergen content is rarely included on labels and may vary, especially between products, making dosing standardization and regulation difficult. The full impact of FDA-approved products, such as Palforzia for peanut OIT, remains uncertain. Food used for OIT can legally be considered a drug. Physicians, other health care professionals, insurance companies, and federal and state governments should work to ensure OIT is available to all patients who desire access to this treatment option. Further research is needed to answer many remaining questions about the OIT process, but OIT is a promising first step toward addressing the high burden of disease on patients and families.

We thank Daniel Rotrosen, Alkis Togias, and Ronald Rabin for their participation and helpful review of this article and Roberta Slivensky for logistical support.

Clinical implications: The validation of food OIT and the FDA approval of a peanut product are important steps in the management of food allergies. We provide guidance on the implementation of OIT in clinical practice and identify information gaps for OIT.

REFERENCES

1. Pajno GB, Fernandez-Rivas M, Arasi S, Roberts G, Akdis CA, Alvaro-Lozano M, et al. EAACI Guidelines on allergen immunotherapy: IgE-mediated food allergy. Allergy 2018;73:799-815.
2. Gupta RS, Warren CM, Smith BM, Blumenstock JA, Jiang J, Davis MM, et al. The public health impact of parent-reported childhood food allergies in the United States. Pediatrics 2018;142:e20181235.
3. Gupta RS, Warren CM, Smith BM, Jiang J, Blumenstock JA, Davis MM, et al. Prevalence and severity of food allergies among US adults. JAMA Netw Open 2019;2:e185630.
4. Boyce JA, Assa'ad A, Burks AW, Jones SM, Sampson HA, Wood RA, et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. J Allergy Clin Immunol 2010;126:S1-58.
5. Herbert LJ, Marchisotto MJ, Sharma H, Gupta R, Bilaver LA. Availability of mental health services for patients with food allergy. J Allergy Clin Immunol Pract 2019;7:2904-5.
6. Bilaver LA, Sharma HP, Gupta RS, Herbert LJ, Marchisotto MJ, Aktas ON, et al. Food allergy research priorities: results from a patient-centered study. J Allergy Clin Immunol Pract 2019;7:2431-3.e4.
7. Institute for Clinical and Economic Review. Oral immunotherapy and Viaskin Peanut for peanut allergy: effectiveness and value. July 2019. Available at: https://icer-review.org/wp-content/uploads/2018/12/ICER_PeanutAllergy_Final_Report_071019.pdf. Accessed November 27, 2019.
8. Chu DK, Wood RA, French S, Fiocchi A, Jordana M, Waserman S, et al. Oral immunotherapy for peanut allergy (PACE): a systematic review and meta-analysis of efficacy and safety. Lancet 2019;393:2222-32.
9. Eiwegger T, Anagnostou K, Arasi S, Begin P, Ben-Shoshan M, Beyer K, et al. ICER report for peanut OIT comes up short. Ann Allergy Asthma Immunol 2019;123:430-2.
10. Assa'ad A, Welch M, Acaster S, Gallop K, DeVries J, Griffin N, et al. Treatment satisfaction with AR101 peanut allergy oral immunotherapy: a mixed methods study. Ann Allergy Asthma Immunol 2018;121:S53.
11. Epstein-Rigbi N, Goldberg MR, Levy MB, Nachshon L, Elizur A. Quality of life of food-allergic patients before, during, and after oral immunotherapy. J Allergy Clin Immunol Pract 2019;7:429-36.e2.
12. Blackman AC, Staggers KA, Kronisch L, Davis CM, Anagnostou A. Quality of life improves significantly following real-world oral immunotherapy for peanut-allergic children. Ann Allergy Asthma Immunol 2020. S1081-1206(20)30193-9. https://doi.org/10.1016/j.anai.2020.03.028.
13. Nurmatov U, Dhami S, Arasi S, Pajno GB, Fernandez-Rivas M, Muraro A, et al. Allergen immunotherapy for IgE-mediated food allergy: a systematic review and meta-analysis. Allergy 2017;72:1133-47.
14. Jones SM, Burks AW, Keet C, Vickery BP, Scurlock AM, Wood RA, et al. Long-term treatment with egg oral immunotherapy enhances sustained unresponsiveness that persists after cessation of therapy. J Allergy Clin Immunol 2016;137:1117-27.e10.
15. Chinthrajah RS, Purington N, Andorf S, Long A, O'Laughlin KL, Lyu SC, et al. Sustained outcomes in oral immunotherapy for peanut allergy (POISED study): a large, randomised, double-blind, placebo-controlled, phase 2 study. Lancet 2019;394:1437-49.
16. Vickery BP, Vereda A, Casale TB, Beyer K, du Toit G, Hourihane JO, et al. AR101 Oral immunotherapy for peanut allergy. N Engl J Med 2018;379:1991-2001.

17. Tsai M, Mukai K, Chinthrajah RS, Nadeau KC, Galli SJ. Sustained successful peanut oral immunotherapy associated with low basophil activation and peanut-specific IgE. J Allergy Clin Immunol 2020;145:885-96.e6.
18. National Food Death Allergy Registry. 2019. Available at: https://www.nationalfoodallergydeathregistry.org/the-registry. Accessed November 27, 2019.
19. Wasserman RL, Hague AR, Pence DM, Sugerman RW, Silvers SK, Rolen JG, et al. Real-world experience with peanut oral immunotherapy: lessons learned from 270 patients. J Allergy Clin Immunol Pract 2019;7:418-26.e4.
20. Gupta R, Holdford D, Bilaver L, Dyer A, Holl JL, Meltzer D. The economic impact of childhood food allergy in the United States. JAMA Pediatr 2013;167:1026-31.
21. Bilaver LA, Kester KM, Smith BM, Gupta RS. Socioeconomic disparities in the economic impact of childhood food allergy. Pediatrics 2016;137.
22. Roach A, Warren C, Hong N, Gupta R, Casale T. Awareness of oral immunotherapy (OIT) among a nationally-representative sample of food allergy patients/caregivers is critically lacking. Presented at: the American Academy of Allergy, Asthma & Immunology Annual Meeting, Philadelphia, PA, March 16, 2020.
23. Filep S, Block DS, Smith BRE, King EM, Commins S, Kulis M, et al. Specific allergen profiles of peanut foods and diagnostic or therapeutic allergenic products. J Allergy Clin Immunol 2018;141:626-31.e7.
24. Berglund JP, Szczepanski N, Penumarti A, Beavers A, Kesselring J, Orgel K, et al. Preparation and analysis of peanut flour used in oral immunotherapy clinical trials. J Allergy Clin Immunol Pract 2017;5:1098-104.
25. U.S. Food and Drug Administration Center for Drug Evaluation and Research. Investigational new drug applications (INDs)—determining whether human research studies can be conducted without an IND. September 2013. Available at: https://www.fda.gov/media/79386/download. Accessed December 2, 2019.