



Editorial

The need for change

Lessons learned from Food and Drug Administration-approved peanut oral immunotherapy



Peanut allergy (PA) affects 1% to 2% of individuals in the United States, significantly affecting quality of life (QoL).¹ Management has expanded from strict avoidance with prompt treatment of accidental exposures to include the option of peanut oral immunotherapy (POIT). In January 2020, the US Food and Drug Administration (FDA) approved peanut (*Arachis hypogaea*) allergen powder-dnfp, the first oral immunotherapy (OIT) indicated for individuals aged 4 to 17 years.² An FDA-approved product for peanut OIT (POIT) offers highly regulated manufacturing techniques leading to precise dosing, is studied through rigorously conducted, double-blind, randomized controlled trials showing safety and efficacy, and affords the ability to provide a uniform POIT dosing protocol across various practice settings.

Although the clinical development of FDA-approved POIT has included multiple trials reporting many patient outcomes, including patient QoL,³ there remain limited data on individuals treated in real-world settings. In this month's issue of the *Annals of Allergy, Asthma & Immunology*, Portnoy et al⁴ report on the experience of 118 children treated with FDA-approved POIT. The median age of the cohort when initiating therapy was 9 years, with 93.4% continuing it 24 weeks after initial dose escalation. Food and Drug Administration-approved POIT was well tolerated, with the frequency of adverse events being lower than in the clinical trials. This improved tolerability in the real-world setting is likely because children were allowed to use concomitant medications, such as H₁ and H₂ blockers, for prophylaxis or rescue of adverse effects. In addition, in the real-world setting, treating allergists have the liberty to make dose adjustments based on individual tolerability. It is also possible that the improved safety profile is related to treatment of patients without allergies.

In addition to differences in adverse-effect profile for FDA-approved POIT in the real-world setting compared with clinical trials, there were important differences in the diagnosis of PA. Of the 118 children in the study, 48 (40.7%) were diagnosed on the basis of clinical history and either skin prick test result (n = 28) or peanut-specific immunoglobulin E (n = 20). Fewer than half (n = 58) had a peanut component test, and most strikingly, only 8 (6.8%) underwent an oral food challenge (OFC). Despite the increasing use of diagnostic tools such as allergen component testing and epitope mapping, OFCs remain the reference standard for diagnosis of food allergy. In addition, in an era of OIT, OFCs are the

only tool to establish an individual's threshold dose to elicit a clinically meaningful allergic reaction. Knowledge of threshold dosing is likely to affect a family's decision to pursue OIT because individuals with lower threshold doses may be the ones to benefit most from OIT. Importantly, in addition to providing essential diagnostic information, OFCs have been shown to be safe, and also improve QoL.^{5,6} Nevertheless, the utilization of OFCs in clinical practice remains unacceptably low owing to a variety of reasons, including lack of proper training, lack of office space, limited staffing, inadequate reimbursement, and risk of adverse event.⁷ Not surprisingly, barriers to implementation of OIT are similar to those reported for OFCs.⁸

Although we, as allergists, want to ensure that our patients have access to the newest and most effective treatment options, insufficient OFC utilization before offering OIT poses noteworthy concerns. The limitations of our diagnostic testing modalities are well documented, with sensitization not equating to clinical allergy, even in the setting of significant skin test reactivity or elevated specific immunoglobulin E levels. In this real-life study, it is highly probable that individuals who did not have PA were unnecessarily treated with FDA-approved POIT. Because OIT is a labor-intensive, time-consuming, long-term, and potentially costly procedure, allergists must ensure that only patients with allergies are offered OIT. Previously, an inaccurate diagnosis led to unnecessary avoidance, and now, with the option of OIT, the stakes are even higher, with an accurate diagnosis being more important than ever. Although the decision to complete an OFC before OIT depends on a myriad of variables, including shared decision making with the family, it is the responsibility of all allergists offering OIT to ensure all patients can access an OFC if desired.

Despite being a highly efficacious and generally well-tolerated therapy, integration of FDA-approved POIT remains low in real-world clinical practice. The study by Portnoy et al reports that the 43 participating physicians each estimated prescribing FDA-approved POIT to 5 of 190 eligible candidates (2.6%), which is even lower than the uptake of approximately 10% reported by Patrawala et al.⁹ Importantly, although FDA-approved POIT increases the threshold dose of peanut allergen required to elicit a clinically meaningful allergic reaction, it is not believed to facilitate the resolution of PA when used for the approved ages of 4 to 17 years. In the IMPACT study, Jones et al showed initiation of POIT in children 1 to 3 years of age not only provided desensitization but was well tolerated, and increased the likelihood of facilitating potential remission of PA.¹⁰

The potential to intervene at a younger age during a window of opportunity to provide disease modification of PA makes for a very different risk/benefit discussion in the setting of shared decision

Disclosures: Dr Mustafa is on the speaker's bureau for Genentech, Teva, AstraZeneca, Regeneron, and CSL Behring.

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Funding: The authors have no funding sources to report.

making compared with offering FDA-approved POIT that provides desensitization alone in an older age group, with minimal likelihood of disease resolution. Therefore, to increase the uptake of FDA-approved POIT, it is imperative to complete ongoing clinical trials indicating efficacy in younger children. In the interim, given emerging literature and what we know to date, withholding POIT in infants and younger children owing to a lack of regulated product could be seen as abandoning our ethical obligation to “first, do no harm” because younger children have the most to gain from this intervention. Families with young children who have a meaningful chance of disease remission are more likely to pursue POIT than are families with children aged 4 to 17 years, whose goal is solely risk mitigation from accidental exposure.

The arrival of FDA-approved POIT has advanced the management of PA while highlighting the need for change, namely, increasing utilization of OFCs in clinical practice and POIT being offered to children 1 to 3 years of age in hopes of facilitating resolution of PA.

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