

Peanut Oral Immunotherapy: Data from a Real-World Clinical Practice



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Peanut allergy affects up to 2% of the general population, is often a life-long allergy, and is a well-known cause of anaphylaxis.¹⁻⁴ The ubiquity of peanut in common foods can cause significant anxiety and alterations in social activities because constant vigilance is required from patients to maintain avoidance and minimize the risk for allergic reactions.⁵⁻⁷ There is thus much interest in the development of new treatments for peanut allergy to reduce its impact on our patients. Despite the number of studies examining the safety and efficacy of oral immunotherapy (OIT) in recent decades, concerns remain about its safety and the current lack of a standardized (Food and Drug Administration [FDA]-approved) product is a barrier to widespread clinical adoption. At this time, there is no therapeutic approach that is recommended for routine clinical practice by current US guidelines.^{8,9}

In this issue, Wasserman et al¹⁰ report on their experience with peanut OIT in the largest cohort to date, from a single site. This is a retrospective review of patients who have undergone treatment over the past 8.5 years; they report a high rate of patients completing dose escalation that is consistent with previously published peanut OIT studies,¹¹⁻¹⁴ adding to the body of evidence in support of OIT.

A major strength of this report is their demonstration of the feasibility of peanut OIT on a large scale, within a single allergy and immunology practice. Patients underwent OIT with informed consent in a clinical practice setting, in contrast to a rigorous clinical trial protocol adopted by a majority of published OIT studies. This clinical practice setting mirrors a real-world situation that most practitioners and patients would encounter. Thus, this study provides evidence that OIT is implementable in a clinical practice.

The authors adapted their treatment protocol over time with increased clinical experience, a process often used in clinical practice. Given the flexibility of their approach, personalized endpoints and maintenance doses were permitted to accommodate patient preferences. In addition, they report that several forms of

peanut protein for OIT were successfully used, potentially providing more options to clinicians and families. Given the authors' integration of OIT into clinical practice, they have been able to capture follow-up for 105 patients who were on maintenance for at least 3 years. Their study provides long-term safety data, which have not been extensively examined in other studies.

The authors acknowledge certain limitations given the retrospective nature of their data. For example, baseline food challenges were not performed so the magnitude of efficacy remains uncertain. Unlike clinical trials, prespecified patient characteristics to define eligibility for treatment and clinical endpoints were not stated at the outset, potentially allowing for selection bias. Furthermore, a formal process for capturing data on a regular basis, such as symptom logs for adverse events (AEs), was not put in place before patients began treatment. Therefore, key safety information such as the frequency and range of AEs cannot be reported, and comparison with published information from clinical trials is difficult.

Although AEs were not formally collected, the results presented demonstrate the potential risks of OIT. Consistent with other peanut OIT studies,¹¹⁻¹⁴ allergic symptoms related to OIT dosing are common, including reactions that required treatment with epinephrine during both escalation and maintenance phases, in the office and at home. Furthermore, reactions to peanut OIT can occur even after several years on maintenance OIT. Although no AEs were reported even when changing the peanut protein sources in this study, recent studies have demonstrated significant variability in peanut protein content across products.^{15,16} To date, uncertainty exists regarding whether the variability of protein content measured is clinically relevant or poses safety concerns. Thus, practices implementing OIT will need to be experienced in managing anaphylaxis and focus on patient education to ensure preparedness against unpredictable reactions inside and outside the office.

Notably, this group reports that 13.7% (n = 37) patients had what the authors term eosinophilic esophagitis—like oral immunotherapy—related syndrome (ELORS), the majority of whom were diagnosed clinically without undergoing endoscopic evaluation. Based on the work suggesting that reducing the OIT dose and slowing the escalation process is an option for these patients,¹⁷ more than half of the patients with ELORS did continue daily OIT. How ELORS is related to eosinophilic esophagitis is unclear, and the long-term outcomes of continuing OIT in these patients experiencing symptoms are not known.

The authors report the use of a nonstandardized, non-FDA-approved product provided to patients within their practice, an approach other practices may find challenging to adopt due to their unwillingness to use a nonapproved OIT product and/or lack of sufficient personnel and resources.¹⁸ The medicolegal implications associated with off-label OIT, a

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treatment that is currently not recommended by evidence-based guidelines, as well as lack of Current Procedural Terminology (CPT) billing code and insurance coverage are additional concerns for widespread adoption of OIT. Therefore, the development of well-characterized products from Good Manufacturing Practices (GMP) facilities is ultimately worthwhile to allow more patients and practices to have access to this therapeutic approach and inform patients about benefits and risks.

This is not the only practice offering OIT to their patients,¹⁸ and currently there are a paucity of data regarding the safety and efficacy of off-label OIT. Advancing OIT into routine clinical practice will require a balance between rigorous placebo-controlled studies and large retrospective studies of this kind. Continued work is needed to bring more clarity regarding the side-effect profile of OIT, particularly the risk of immediate systemic reactions and recurrent/persistent GI symptoms, as well as to determine whether OIT can be disease modifying. Additional large-scale, longitudinal studies will hopefully identify patient-specific factors and biomarkers that reliably predict both safety and efficacy outcomes that will be essential to weigh the benefits versus risks of this therapy in a precision medicine approach.

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