Peanut Allergy Patients Reap Continuing Benefits Past First Year, Palforzia Study Shows

Esther Landhuis

August 16, 2021

A recent analysis of 142 peanut-allergic children treated for 1.5 to 2 years with a licensed oral immunotherapy (OIT) product confirms what various smaller studies have shown: maintaining treatment for longer periods improves protection and reduces adverse effects. The findings offer some reassurance regarding the controversial approach, which has become available at a small number of clinics, yet faces an uncertain future.

The new study, published July 28 in *Allergy,* included a subset of patients who chose to complete an extension of the phase 3 PALISADE trial of Palforzia, a proprietary set of premeasured peanut flour capsules developed by Aimmune Therapeutics.

Palforzia was approved last year for children aged 4 to 17 years with peanut allergy — one of the most common food allergies, affecting around 2% of children in the United States and Europe. The treatment is not a cure — patients must still watch what they eat and carry epinephrine for emergency reactions — but it helps build protection through daily ingestion of gradually increasing amounts of the allergen over a period of months.

In the 1-year PALISADE trial, which enrolled 496 peanut-allergic children at 66 sites in North America and Europe, participants received daily doses of study drug or placebo. The dose of the drug was escalated from 3 mg to 300 mg over 6 months; the 300-mg dose was then maintained for another 6 months. By the end of the study, about two thirds of the children who underwent treatment could safely consume at least 600 mg of peanut protein, about the equivalent of two peanuts.

Could protection be increased with further treatment, and what would be required to sustain it? To address these questions, PALISADE patients who successfully reached the 600-mg threshold, along with those from the placebo group, were invited to participate in Aimmune's open-label follow-on study. The extension study also explored whether protection could be maintained with less frequent dosing.

Among the 358 eligible participants who opted into the 1-year extension study, 256 came from the PALISADE treatment arm. These children were assigned to five cohorts to continue for 6 months or 12 months with daily or less frequent doses. Within the 6-month group, all started with the 300-mg daily dose. A subset received two doses a week. Within the 12-month group, some patients maintained daily dosing throughout; others received doses every other day, twice weekly, or once every 2 weeks.

The children who continued daily maintenance dosing the longest gained the most protection. Those in less-frequent dosing groups experienced more adverse events than those who received doses every day, the company reported last December in *The Journal of Allergy and Clinical Immunology: In Practice.*

Dr Mohamed Yassine

More than a quarter (97 of 358, or 27.1%) of participants failed to complete the extension. Families could withdraw anytime for any reason. Participating in an OIT trial is demanding — it requires office visits for dosing adjustments and blood tests, rest periods, keeping symptom logs in which daily doses are recorded, and possible allergic reactions from the treatment itself. "A common reason for 'withdrawal of consent' in clinical studies is the inconvenience of remaining in a long-term study," Mohamed Yassine, MD, Aimmune's senior vice present of medical affairs, told *Medscape Medical News* via email.

Attrition was concentrated within certain subgroups. Most participants in (88.7%; 102 of 115) PALISADE who received placebo elected to enter the open-label extension; nearly half did not finish. Dropout rates were also high (29.2%) for non–daily dosing participants who had come from the PALISADE treatment arm.

The authors did not report on those high-dropout groups. Instead, they focused their analysis on the 142 treated PALISADE participants who continued daily dosing through the extension — 110 patients for a total of about 1.5 years and 32 patients for about 2 years. In a subgroup analysis, 48.1% of children in the 1.5-year group upped their tolerance to 2000 mg peanut protein, and even more (80.8%) in the 2-year group reached that threshold — all while taking a 300-mg maintenance dose.

Those who remained on treatment longer also had fewer adverse events. At the exit food challenge, 24% of the 1.5-year participants had reactions that required epinephrine, but among 2-year participants, only 3.8% needed the rescue medication.

Continuing therapy past the first year seemed to have additional benefits, Sandra Hong, MD, director of the Cleveland Clinic Food Allergy Center of Excellence, in Cleveland, Ohio, said in an interview with Medscape. Hong was not involved in the new research and has no financial ties with Aimmune or other food allergy companies. "Not only can you ingest more, but your reaction when you do react is going to be less," she says.

Palforzia is only available through a risk evaluation and mitigation strategy (REMS) program, which educates patients, healthcare professionals, and pharmacies about immunotherapy risks and precautionary measures. As of last summer, before Aimmune was acquired by Nestlé Health Science, about 100 allergists in the United States had enrolled patients in the REMS program. Families can find allergists who are certified to prescribe Palforzia using the website's Certified Participant Locator.

Dr Richard Wasserman

Although the field at large remains apprehensive about OIT and other forms of immunotherapy, an estimated 200 or more US clinics are administering home-grown OIT using commercial food products, says Richard Wasserman, an OIT pioneer whose clinic in Dallas, Texas, has treated allergies to about 20 foods since the practice started offering the therapy in 2008. OIT practitioners have treated more than 15,000 food allergy patients nationwide, Wasserman told Medscape via email, yet they make up just a tiny fraction of the more than 6000 board-certified allergists in the United States.

Whether using Palforzia or nonproprietary food products, oral immunotherapy requires a lot of time and effort — not just for patients but also practitioners. "You need more space. You need more staffing. Patients doing oral challenges stay in your office for 4 to 5 hours, and we have one-to-one nursing care for them," said Hong. "So it's a lot of resources."

Her team has treated about 20 children with Palforzia since the Cleveland Clinic began offering the therapy last summer. Hong and coworkers have administered OIT using commercial peanut flour and peanut butter to some 80 peanut-allergic toddlers younger than 4 years who are too young to receive for the US Food and Drug Administration (FDA)–approved treatment. Their early data, which were presented at the annual meeting of the American Academy of Allergy, Asthma and Immunology in February, suggests that toddlers get complete OIT more quickly with fewer side effects than older children, Hong says. A recent study of preschoolers in Canada also found that nonproprietary OIT is very safe and effective in this younger set and could be cost-saving in the long run.

By comparison, Palforzia, which has a list price of $890 per month, was judged to be less cost-effective in analyses by academic allergists and by the Institute for Clinical and Economic Review. But through a copay savings program, depending on their insurance coverage, some eligible families can pay as little as $20 per month for the FDA-approved treatment.

Edwin Kim

Because the therapy is time consuming for families and is resource intensive for practices, questions remain as to how long and how frequently patients need to remain on treatment to sustain protection. Do they need to keep taking Palforzia, or "can we switch them to an equivalent amount of food and not bother with the study drug?" said Edwin Kim, director of the UNC Food Allergy Initiative, Chapel Hill, North Carolina, and study investigator for several Palforzia trials, in an interview with Medscape.

The Food Allergy Support Team, a nonprofit group started by Wasserman and colleagues, publishes best practices and meets annually to discuss research and protocols. However, the best maintenance dose, the best dosing frequency, and the duration of daily dosing that yields the best outcomes are not known, Wasserman says.

"We think the best way to answer that question is with a regulated, pharmaceutical-grade form of peanut protein," Yassine said.

The field's experience with Palforzia raises a dilemma: Does its approval legitimize oral immunotherapy in general, or will rigorous, multi–million dollar trials be needed to approve products for each food or combination of foods? About 32 million people in the United States have food allergies — about 1 in 10 adults and 1 in 13 children.

Dr Stacie Jones

"I think the field has always grappled with that, honestly," said Stacie Jones, MD, professor of pediatrics and chief of allergy and immunology at the University of Arkansas for Medical Sciences and Arkansas Children's Hospital, Little Rock, Arkansas, in an interview with Medscape. Home-grown OIT is "easier to do when you have high control of your small patient volumes or you're in a clinical trial," said Jones, who has served as an investigator on Palforzia trials and last year received more than $30,000 in consulting fees from Aimmune. "It becomes a very different situation when it becomes a national or an international recommended therapy."

The Canadian Society of Allergy and Clinical Immunology has published clinical practice guidelines and provides practical information on its website on how to implement OIT — including protocols for dozens of foods and diary sheets for patients to log doses and symptoms.

However, US professional societies still consider OIT investigational and suggest that it will not be approved by the FDA. "As a field, are we willing to wait 4 to 5 more years for an egg product? Should we? Are we willing?" said Kim. "These are tough questions."

Stacie M. Jones reports advisory board fees, Aimmune Therapeutics, FARE; personal fees, DBV Technologies; clinical trials grants, Aimmune Therapeutics, DBV Technologies, Astellas, Sanofi, Regeneron, FARE, Genentech, and NIH-NIAID. Edwin Kim reports consultancy with Aimmune Therapeutics, Allako, AllerGenis, Belhaven Pharma, DBV Technologies, Duke Clinical Research Institute, and Nutricia; advisory board membership with ALK, DBV Technologies, Kenota Health, and Ukko; grant support from the NIH's National Institute of Allergy and Infectious Diseases, National Center for Complementary and Integrative Health and Immune Tolerance Network; Food Allergy Research and Education, and the Wallace Research Foundation. Richard Wasserman receives consulting fees from Aimmune Therapeutics and DBV Technologies. Mohamed Yassine is employed by Aimmune Therapeutics.

Sandra Hong has disclosed no relevant financial relationships.

Allergy. Published online July 28, 2021. Abstract

For more news, follow Medscape on Facebook, Twitter, Instagram, and YouTube.

Send news tips to news@medscape.net.

Cite this: Peanut Allergy Patients Reap Continuing Benefits Past First Year, Palforzia Study Shows - *Medscape* - Aug 16, 2021.