Original Article

Efficacy and Safety of Epicutaneous Immunotherapy in Peanut-Allergic Toddlers: Open-Label Extension to EPITOPE

Matthew Greenhawt, MD[a], Deborah Albright, MD[b], Sara Anvari, MD[c], Nicolette Arends, MD[d], Peter D. Arkwright, MD, PhD[e], Philippe Bégin, MD[f], Katharina Blümchen, MD[g], Terri Brown-Whitehorn, MD[h], Heather Cassell, MD[i], Edmond S. Chan, MD[j], Christina E. Ciaccio, MD[k], Antoine Deschildre, MD[l], Amandine Divaret-Chauveau, MD[m,n], Stacy Dorris, MD[o], Morna Dorsey, MD[p], George Du Toit, MBBCh[q], Thomas Eiwegger, MD[r,s,t,u], Michel Erlewyn-Lajeunesse, DM[v], David M. Fleischer, MD[a], Lara S. Ford, MBBS[w], Maria Garcia-Lloret, MD[x], Jonathan O'B. Hourihane, MD[y], Nicola Jay, MBBS[z], Stacie M. Jones, MD[aa], Edwin H. Kim, MD, MS[bb], Kirsten Kloepfer, MD[cc], Stephanie Leonard, MD[dd], Guillaume Lezmi, MD[ee], Jay Lieberman, MD[ff], Jeanne Lomas, DO[gg], Melanie Makhija, MD[hh], Michael O'Sullivan, MBBS[ii], Christopher Parrish, MD[jj], Jane Peake, MBBS[kk], Kirsten P. Perrett, MBBS[ll,mm,nn], Daniel Petroni, MD[oo,pp], Jacqueline A. Pongracic, MD[hh], Patrick Quinn, MBBS[qq], Rachel G. Robison, MD[o,hh], Georgiana Sanders, MD[rr], Lynda Schneider, MD[ss], Hemant Sharma, MD[tt], Sayantani B. Sindher, MD[uu], Juan Trujillo, MD[vv], Paul J. Turner, MD[ww], Katherine Tuttle, MD[xx], Julia Upton, MD[yy], Pooja Varshney, MD[zz], Brian P. Vickery, MD[aaa], Christian Vogelberg, MD[bbb], Brynn Wainstein, MBChB, PhD, FRACP[ccc,ddd], Julie Wang, MD[eee], Robert Wood, MD[fff], Katharine J. Bee, PhD[ggg], Dianne E. Campbell, MD[w,ggg], Todd D. Green, MD[b,ggg], Rihab Rouissi, MD[ggg], Henry T. Bahnson, MPH[ggg], Timothée Bois, MSC[ggg], Hugh A. Sampson, MD[eee], and A. Wesley Burks, MD[bb] *Aurora, Colo; Pittsburgh and Philadelphia, Pa; Houston and Dallas, Texas; Little Rock, Ark; Chapel Hill, NC; Tucson, Ariz; Chicago, Ill; Nashville and Memphis, Tenn; San Francisco, Los Angeles, San Diego, and Palo Alto, Calif; Clarence and Rochester, NY; Seattle, Wash; Durham, NC; Ann Arbor, Mich; Boston, Mass; Washington, DC; Atlanta, Ga; Rotterdam, the Netherlands; Manchester, London, Southampton, and Sheffield, United Kingdom; Montreal, QC; Vancouver, BC; and Toronto, ON, Canada; Frankfurt and Dresden, Germany; Lille, Vandœuvre-lès-Nancy, Montrouge, and Paris, France; St Pölten and Krems an der Donau, Austria; Sydney, NSW; Nedlands, WA; Brisbane, QLD; Melbourne and Parkville, VIC; North Adelaide, SA; and Randwick, Australia; Dublin, Ireland; and Cork, Ireland*

What is already known about this topic? In the EPITOPE study, 12 months of treatment with the VIASKIN patch containing 250 μg of peanut protein (VP250) versus placebo resulted in a statistically significant treatment effect (desensitization) in peanut-allergic children aged 1 through 3 years with a well-tolerated safety profile consistent with prior clinical trials.

What does this article add to our knowledge? After 24 months of VP250 treatment, there was continued enhancement of the treatment effect without additional reports of treatment-related anaphylaxis. Results of the original placebo-treated participants mirrored the initial EPITOPE findings after 12 months of VP250 treatment.

How does this study impact current management guidelines? Data from open-label extension and placebo crossover participants demonstrate the potential of VP250 to be a safe and efficacious treatment option for the management of young peanut-allergic children, if approved.

[a]Section of Allergy and Immunology, Department of Pediatrics, Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, Colo
[b]UPMC Children's Hospital of Pittsburgh, University of Pittsburgh School of Medicine, Pittsburgh, Pa
[c]Department of Pediatrics, Division of Immunology, Allergy, and Retrovirology, Texas Children's Hospital/Baylor College of Medicine, Houston, Texas
[d]Department of Pediatrics, Division of Allergy and Pulmonology, Erasmus MC Sophia Children's Hospital, Rotterdam, the Netherlands
[e]Lydia Becker Institute of Immunology and Inflammation, University of Manchester, Manchester, United Kingdom
[f]Section of Allergy, Immunology, and Rheumatology, Department of Pediatrics, CHU Sainte-Justine and Université de Montréal, Montreal, QC, Canada
[g]Department of Pediatrics, Division of Pneumology, Allergology, Infectious Diseases and Gastroenterology, Goethe University Frankfurt, Frankfurt, Germany
[h]Children's Hospital of Philadelphia, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pa
[i]Pediatric Allergy and Immunology, Banner—University Medical Center, Tucson, Ariz
[j]Department of Pediatrics, Division of Allergy, British Columbia Children's Hospital, the University of British Columbia, Vancouver, BC, Canada
[k]Departments of Pediatrics and Medicine, the University of Chicago, Chicago, Ill

Abbreviations used
AE- Adverse event
CI- Confidence interval
DBPCFC- Double-blind, placebo-controlled food challenge
ED- Eliciting dose
EPIT- Epicutaneous immunotherapy
FDA- Food and Drug Administration
M- Month
OIT- Oral immunotherapy
OLE- Open-label extension
PA- Peanut allergy
TEAE- Treatment-emergent adverse event
VP250- VIASKIN patch, 250 μg of peanut protein

BACKGROUND: The pivotal phase 3 EPITOPE trial, a 12-month, double-blind, placebo-controlled study of epicutaneous immunotherapy with the VIASKIN patch containing 250 μg of peanut protein (VP250), previously reported significant treatment response versus placebo in peanut-allergic toddlers aged 1 through 3 years.

OBJECTIVE: To assess the interim efficacy and safety of VP250 from the first year of the EPITOPE open-label extension (OLE) study.

METHODS: Eligible participants enrolled in the OLE study for up to 3 years of total treatment with annual double-blind, placebo-controlled food challenges (DBPCFCs) and safety assessments; here we report the first-year OLE (year 2) results.

RESULTS: A total of 266 EPITOPE participants enrolled in the OLE study; 244 underwent month 24 DBPCFC (n = 166 VP250; n = 78 placebo). After 24 months of VP250, 81.3% reached an eliciting dose (ED) ≥1000 mg, 63.8% reached an ED ≥2000 mg, and 55.9% completed the DBPCFC (cumulative dose: 3444 mg) without meeting stopping criteria. No treatment-related anaphylaxis or serious treatment-related adverse events occurred during year 2 in this treatment arm. Local application-site reactions occurred less frequently in year 2 versus year 1. In placebo-treated EPITOPE participants, outcomes after 1 year of open-label VP250 were consistent with EPITOPE treatment results: 62.7% reached an ED ≥1000 mg, 36.5% reached an ED ≥2000 mg, and 28.4% completed the DBPCFC without meeting stopping criteria; and there was 1 treatment-related anaphylaxis event.

CONCLUSIONS: Two years of VP250 in young peanut-allergic children demonstrated continued increases in treatment effect without new safety signals. This supports the potential of VP250 as a safe and effective treatment for peanut allergy in young children.

[l]Université de Lille, INSERM Unit 1019, CNRS UMR 9017, CHU Lille, Institut Pasteur de Lille, Center for Infection and Immunity of Lille, Lille, France
[m]Pediatric Allergy Unit, Children's Hospital, Centre Hospitalier Universitaire de Nancy, Vandœuvre-lès-Nancy, France
[n]EA 3450 DevAH, Faculty of Medicine, Université de Lorraine, Vandœuvre-lès-Nancy, France
[o]Department of Pediatrics, Division of Allergy Immunology and Pulmonology, Vanderbilt University Medical Center, Nashville, Tenn
[p]University of California San Francisco, San Francisco, Calif
[q]Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom
[r]Division of Paediatrics and Adolescent Medicine, University Hospital St Pölten, St Pölten, Austria
[s]Karl Landsteiner University of Health Sciences, Krems an der Donau, Austria
[t]Division of Clinical Immunology and Allergy, Department of Paediatrics, The Hospital for Sick Children, Toronto, ON, Canada
[u]Department of Immunology, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada
[v]Paediatric Allergy and Immunology, Southampton Children's Hospital, University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom
[w]The Children's Hospital at Westmead, University of Sydney, Sydney, NSW, Australia
[x]Department of Pediatrics, UCLA David Geffen School of Medicine, Los Angeles, Calif
[y]Pediatrics and Child Health, Royal College of Surgeons in Ireland and Children's Health Ireland, Dublin, Ireland
[z]Sheffield Children's NHS Foundation Trust, Sheffield, United Kingdom
[aa]Department of Pediatrics, Division of Allergy and Immunology, University of Arkansas for Medical Sciences and Arkansas Children's Hospital, Little Rock, Ark
[bb]Department of Pediatrics, Division of Pediatric Allergy and Immunology, University of North Carolina School of Medicine, Chapel Hill, NC
[cc]Division of Pulmonology, Allergy/Immunology and Sleep Medicine, Indiana University and Riley Hospital for Children at Indiana University Health, Indianapolis, Ind
[dd]Department of Pediatrics, University of California San Diego, San Diego, Calif
[ee]Department of Pediatric Pulmonology and Allergy, AP-HP, Hôpital Necker-Enfants Malades, Université Paris Cité, Paris, France
[ff]Department of Pediatrics, the University of Tennessee Health Science Center and Le Bonheur Children's Hospital, Memphis, Tenn
[gg]Division of Pediatric Allergy and Immunology, University of Rochester, Clarence, NY
[hh]Ann and Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, Ill
[ii]Immunology Department, Perth Children's Hospital and Honorary Research Associate, Telethon Kids Institute, Nedlands, WA, Australia
[jj]Departments of Pediatrics and Internal Medicine, Division of Allergy and Immunology, the University of Texas Southwestern Medical Center and Children's Medical Center, Dallas, Texas
[kk]Queensland Paediatric Immunology and Allergy Service, Queensland Children's Hospital and University of Queensland, Brisbane, QLD, Australia
[ll]National Allergy Centre of Excellence, Population Allergy Group, Murdoch Children's Research Institute, Melbourne, VIC, Australia
[mm]Department of Paediatrics, University of Melbourne, Melbourne, VIC, Australia
[nn]Department of Allergy and Immunology, Royal Children's Hospital, Parkville, VIC, Australia
[oo]Seattle Allergy and Asthma Research Institute, Seattle, Wash
[pp]Clinical Development, BioCryst Pharmaceuticals, Inc, Durham, NC
[qq]Department of Allergy and Clinical Immunology, Women's and Children's Hospital, North Adelaide, SA, Australia
[rr]Division of Allergy and Clinical Immunology, Department of Internal Medicine, University of Michigan, Ann Arbor, Mich
[ss]Allergy and Asthma Program, Department of Pediatrics, Boston Children's Hospital, Harvard Medical School, Boston, Mass
[tt]Division of Allergy and Immunology, Children's National Hospital, Washington, DC
[uu]Sean N. Parker Center for Allergy and Asthma Research, Stanford University, Palo Alto, Calif
[vv]HRB Clinical Research Facility University College Cork, Irish Centre for Maternal and Child Health Research (INFANT), Cork University Hospital, University College Cork, Cork, Ireland
[ww]Paediatric Allergy and Clinical Immunology, National Heart and Lung Institute, Imperial College London, London, United Kingdom
[xx]Division of Pediatric Allergy and Immunology, University of Rochester School of Medicine and Dentistry, Golisano Children's Hospital, Rochester, NY
[yy]Department of Paediatrics, Division of Immunology and Allergy, the Hospital for Sick Children, University of Toronto, Toronto, ON, Canada
[zz]Department of Pediatrics, Dell Medical School at the University of Texas at Austin, Dell Children's Medical Center, Austin, Texas
[aaa]Department of Pediatrics, Emory University School of Medicine and Children's Healthcare of Atlanta, Atlanta, Ga
[bbb]Department Pediatric Pneumology and Allergology, University Hospital Dresden and Faculty of Medicine Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany
[ccc]Department of Immunology, Sydney Children's Hospital, Randwick, NSW, Australia
[ddd]School of Clinical Medicine, University of New South Wales, Sydney, NSW, Australia
[eee]Department of Pediatrics, Division of Allergy and Immunology, Icahn School of Medicine at Mount Sinai, New York, NY

CLINICALTRIALS.GOV: NCT03859700. **(J Allergy Clin Immunol Pract 2025;13:1176-87)**

Key words: *Peanut allergy; Epicutaneous immunotherapy; VIASKIN patch; Anaphylaxis; Desensitization; Open-label study; Pediatrics*

Peanut allergy (PA) affects approximately 2% to 3% of children globally, with evidence suggesting that disease prevalence has steadily increased in the past 20 years.[1-5] PA tends to be persistent, often diagnosed in very early childhood, but outgrown by less than approximately 30% by age 6 to 10 years.[6,7] The burden of PA can be significant, often associated with unhealthy coping strategies, poor quality of life, and anxiety related to perpetual vigilance for accidental exposures to peanut.[1,8] It is also costly to manage, with direct costs recently estimated at US$6500 per patient each year.[9] The ubiquity of peanut in the diet makes avoidance difficult, and accidental peanut exposure is common and often results in severe reactions.[10]

Treatment options for PA remain limited. Peanut oral immunotherapy (OIT) using a proprietary peanut flour preparation is approved by the Food and Drug Administration (FDA) and European Medicines Agency in children aged 1 to 17 years .[11,12] Omalizumab is also FDA-approved for use in peanut and other food allergies in children and adults aged 1 year and older.[13] However, both treatments come with drawbacks, including side effects, multiple restrictions on daily activities associated with OIT, and a requirement for regular

[fff]Julie and Neil Reinhard Pediatric Allergy and Immunology, Pediatrics and International Health, Eudowood Division of Allergy, Immunology, and Rheumatology, Pediatric Clinical Research Unit, Institute for Clinical and Translational Research, the Johns Hopkins University School of Medicine, Baltimore, Md

[ggg]DBV Technologies SA, Montrouge, France

Funding for this research, including design and conduct of the study and collection, management, analysis, and interpretation of the data, was provided by DBV Technologies. Editorial support for manuscript preparation was provided by Red Nucleus and funded by DBV Technologies.

Conflicts of interest: M. Greenhawt reports receiving financial support from DBV Technologies, Takeda, Griffols, Nutricia, Novartis, Aquestive, Allergy Therapeutics, AstraZeneca, ALK-Abello, ARS, Bryn, Genentech, and Prota; has served on the advisory board of the International Food Protein Induced Enterocolitis Syndrome Association, the Asthma and Allergy Foundation of America, and the National Peanut Board; and is associate editor of the *Annals of Allergy, Asthma, and Immunology*. S. Anvari reports receiving grants or contracts from the National Institutes of Health (NIH)/National Institute of Allergy and Infectious Diseases (NIAID) for the SUNBEAM study and DBV Technologies for the EPITOPE, EPOPEX, and VITESSE studies; consulting fees from DBV Technologies; received honoria as an invited speaker for American Academy of Pediatrics (AAP) Annual Congress and American College of Allergy, Asthma, Immunology (ACAAI) Webinar; participated in an advisory board for DBV Technologies; and received support for attending NIAID/NIH SUNBEAM Study Steering Committee. N. Arends reports receiving payment for presentations for ALK and Nutricia and support for attending Pediatric Allergy and Asthma Meeting (PAAM) from ALK. P. Bégin reports receiving consultation and research grants to institution from DBV Technologies; grants or contracts to institution from Novartis, Regeneron Pharmaceuticals Inc, and Sanofi; consulting fees from Novartis, Sanofi, and ALK; payment for presentations from Pfizer, ALK, Bausch Health, and AstraZeneca; and has a leadership or fiduciary role in Food Allergy Canada (scientific advisory board), Canadian Allergy, Asthma, and Immunology Foundation (board of directors), Canadian Society of Allergy and Clinical Immunology (board of directors), and L'Association des Allergologues et Immunologues du Québec (board of directors). K. Blümchen reports institutional grants from Novartis Pharma GmbH, Aimmune Therapeutics, DBV Technologies, and HiPP GmbH; consulting fees from Novartis Pharma GmbH, Nestlé, Bencard Allergie, Aimmune Therapeutics, and DBV Technologies; payment for lectures, presentations, speaker bureaus, manuscript writing, or educational events from Aimmune Therapeutics, DBV Technologies, Novartis Pharma GmbH, Thermo Fisher Scientific, Viatris Healthcare GmbH, Allergopharma, and ALK; support for attending meetings from DBV Technologies, Novartis Pharma GmbH, and Aimmune Therapeutics; participation on a data safety monitoring board or advisory board and receiving payment from Novartis Pharma GmbH, Aimmune Therapeutics, DBV Technologies, Nestlé, and Bencard Allergie, and no payment from Charité, Department of Pediatrics; and a leadership or fiduciary role in West German consortium pediatric allergology and pneumology (board member, no payment). T. Brown-Whitehorn reports receiving grants or contracts from DBV Technologies as principal investigator and Regeneron as subinvestigator, consulting fees from DBV Technologies, and support for attending a meeting for poster presentation from DBV Technologies. E. S. Chan reports receiving grants from DBV Technologies as a site clinical trial investigator for research expenses; is an advisory board member for Pfizer, Miravo Healthcare, Medexus Pharmaceuticals Inc, Leo Pharma, Kaléo, DBV Technologies, Allergenis, Sanofi Genzyme, Bausch Health, Avir Pharma, AstraZeneca, ALK, and Alladapt Immunotherapeutics; and has a leadership or fiduciary role in Canadian Society of Allergy and Clinical Immunology (CSACI) (board and executive member), Canadian Paediatric Society (allergy section-executive member), and Food Allergy Canada (healthcare advisory board). C. E. Ciaccio reports receiving research support to institution from DBV Technologies and Genentech; payment for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Genentech; has a leadership or fiduciary role in Food Allergy Research and Education (FARE); and has stock or stock options in Siolta Therapeutics and ClostraBio. A. Deschildre reports receiving support for the present manuscript from DBV Technologies; consulting fees from Novartis, ALK, GSK, Sanofi, Regeneron, AstraZeneca, Aimmune Therapeutics, Nestlé Health Science, Stallergenes Greer, and Viatris; support for attending meetings from ALK, Sanofi, Stallergenes Greer, Novartis, AstraZeneca, Aimmune Therapeutics, and Celltrion; and participation on a data safety monitoring board for the BOOM study (I14BOOM study ClinicalTrials.gov identifier: NCT04045301 Lead Investigator: Philippe Bégin [Montreal]). A. Divaret-Chauveau reports receiving grants/contracts from the French public agency Agence Nationale de Sécurité Sanitaire (2018 to 2021), Don du Souffle for the PASTURE 16-year visit (University Hospital of Besançon), Fondation du Souffle for the PASTURE 16-year visit (University Hospital of Besançon), Novartis (University Hospital of Besançon), and Association Régionale d'Aide aux Insuffisants Respiratoires de Lorraine (University of Lorraine); consulting fees from Aimmune Therapeutics as a speaker at symposium at the European Academy of Allergy and Clinical Immunology (EAACI) Congress in 2019 and at the French Allergy Congress in 2019, Novartis as a speaker at symposium at the Pulmonology and Allergy Paediatric congress in France in 2020, and ALK as a speaker at symposium at a Paediatric congress in France in 2023; support for attending meetings from Nutricia for EAACI Congress 2019 and Mead Johnson for PAAM 2019; and has stock or stock options in EssilorLuxottica. M. Dorsey reports receiving support for the present manuscript from DBV Technologies and grants or contracts from Aimmune Therapeutics. G. D. Toit reports receiving grants or contracts for clinical trials from DBV Technologies and Aimmune Therapeutics; consulting fees for an Aimmune Therapeutics scientific board; payment or honoraria from Aimmune Therapeutics and DBV Technologies; support for attending meetings from DBV Technologies and Aimmune Therapeutics; participating on a data safety monitoring board or advisory board for the DREAM study (UK) and OUtMATCH trial (USA) and a scientific board for DBV Technologies; and has a leadership or fiduciary role for the EAACI team drafting guidelines. T. Eiwegger reports receiving support for the present manuscript from DBV Technologies; grants or contracts from ALK, Stallergenes Greer, and Novartis; consulting fees from ALK; honoraria from Aimmune Therapeutics, Thermo Fisher Scientific, Nutricia/Danone, ALK, Novartis, and MADx; payment for expert testimony from Aimmune Therapeutics; support for attending meetings from Sanofi; participation on a data safety monitoring board or advisory board from ALK, Aimmune Therapeutics, Stallergenes Greer, and Nutricia/Danone; leadership or fiduciary for EAACI; and receipt of equipment, materials, drugs, medical writing, gifts, or other services from MADX. M. Erlewyn-Lajeunesse reports receiving grants or contracts from Aimmune Therapeutics, DBV Technologies, Abbott Nutrition; consulting fees from Novartis, Aimmune Therapeutics, DBV Technologies, and Allergy Therapeutics; honoraria from DBV Technologies; and has a leadership or fiduciary role in BSACI Registry for Immunotherapy. D. M. Fleischer reports receiving grants from DBV Technologies and ARS

injections and unknown long-term safety in young children with omalizumab.[12-17]

Early introduction and regular consumption of peanut in the diet of infants has been shown to reduce the risk of developing PA compared with delayed introduction.[18-20] However, not all infants benefit from early introduction, with some developing PA regardless of the age of introduction.[21] A cross-sectional analysis in Australia found that in a 1-year study conducted shortly after implementing updated guidelines recommending early peanut introduction, this change had not significantly reduced the prevalence of PA in the population.[21] Furthermore, these recommendations for early peanut introduction and regular ingestion have not been universally adopted. In addition, the average age of PA diagnosis is becoming younger, and evidence continues to emerge suggesting that the developing immune system in infants and toddlers may be more responsive to immunomodulation compared to older children.[22-29] These factors emphasize the importance of developing new treatment options for children with PA, especially at a very young age.

Epicutaneous immunotherapy (EPIT) for PA with the VIASKIN patch (VP250) is a nonoral, noninjectable investigational treatment currently in clinical development. VP250 aims to induce desensitization to peanut through the daily application of a patch containing 250 μg of peanut protein (1/1000th of 1 peanut), worn on the backs of children.[30] The phase 3 EPITOPE trial of VP250 met its primary endpoint, with 67% of the treatment group meeting responder criteria at 12 months (vs 33.5% placebo, $P < .001$).[27] VP250 was well tolerated, with mild application-site reactions being the most common adverse events (AEs) and a low rate of treatment-related anaphylaxis (1.6%).

Pharmaceuticals; royalties from UpToDate; participated on an advisory board for ARS Pharmaceuticals, Bryn Pharma, Aquestive Therapeutics, DBV Technologies, Nasus, and Genentech; and has stock options in Grow Happy. L. S. Ford reports a leadership or fiduciary role in Australasian Society of Clinical Immunology and Allergy (ASCIA) Paediatric Practice Committee as a chair and ASCIA council member. M. Garcia-Lloret reports receiving honoraria from Grifols. J. O'B. Hourihane reports receiving support for the present manuscript from DBV Technologies; and grants or contracts from DBV Technologies, the City of Dublin Skin and Cancer Hospital Charity, Johnson and Johnson, National Children's Research Centre, Ireland, and Children's Health Ireland at Temple Street. S. M. Jones reports receiving support for the present manuscript from DBV Technologies; and grants or contracts from DBV Technologies, Regeneron Inc, Novartis, Inc, Astellas Pharma Inc, Aimmune Therapeutics, Genentech, FARE, NIH-NIAID, Immune Tolerance Network, ALK-Abelló, Aravax, and LAmAb Bio, Inc. E. H. Kim reports receiving consulting fees from ALK-Abelló, Ukko Inc, Cellergy Pharma, DBV Technologies, Genentech, Hanimune Therapeutics, Novartis, Phylaxis Bioscience, and Revolo Biotherapeutics; participated on a data safety monitoring board or advisory board for Allergy Therapeutics; and has stock or stock options in Cellergy Pharma. K. Kloepfer reports receiving grants from NIAID (development of allergy in offspring is enhanced by maternal eicosanoids and lung microbiota composition dysbiosis), National Heart, Lung, and Blood Institute (scientific innovation for personalized severe asthma management), and NIAID (preventing asthma in high-risk kids); honoraria from Regeneron; and has an unpaid leadership or fiduciary role in Indiana Allergy and Immunology Society (President) and American Academy of Allergy, Asthma & Immunology (AAAAI) (Microbes in Allergy Committee Chair). S. Leonard reports receiving support for the present manuscript from DBV Technologies; a grant or contract from Hanimune Therapeutics; consulting fees from DBV Technologies and Aimmune Therapeutics; honoraria from Washington State Society of Allergy, Asthma, and Immunology, San Diego Allergy Society, ACAAI, and Annenberg Center for Health Sciences at Eisenhower; participation on a data safety monitoring board or advisory board for COUR Pharmaceuticals and International FPIES Association; and has stock or stock options in Hanimune Therapeutics. G. Lezmi reports receiving consulting fees from ALK-Abelló, Stallergenes Greer, and Meenuts; honoraria from ALK-Abelló, GSK, and Sanofi; support for attending meetings from ALK-Abello; and participation on a data safety monitoring board or advisory board for ALK Abelló and Stallergenes Greer. J. Lieberman reports receiving a grant or contract from Novartis; consulting fees from ARS and Bryn; honoraria from Novartis, Genentech, and FARE; participation on a data safety monitoring board or advisory board for Siolta Therapeutics and Aquestive Therapeutics; and has a leadership or fiduciary role in American Board of Allergy and Immunology, ACAAI, and Joint Task Force for Practice Parameters. J. Lomas reports receiving consulting fees from Lightship (clinical trials) and participation on a data safety monitoring board or advisory board for Dupixent Respiratory TLL Regional Insight Meeting. M. Makhija reports receiving support for the present manuscript from DBV Technologies, honoraria from Aimmune Therapeutics, and participation on an advisory board for DBV Technologies. M. O'Sullivan reports receiving grants or contracts from Channel 7 Telethon Trust, Government of Western Australia Department of Health, and Raine Medical Research Foundation; and has a leadership or fiduciary role in the ASCIA. C. Parrish reports receiving support for the present manuscript from DBV Technologies; grants or contracts from Sanofi/Regeneron, Aimmune therapeutics, and NIH/NIAID; consulting fees from Magellan Rx Management; honoraria from Sanofi; support for attending meetings from DBV Technologies; and participation on a data safety monitoring board or advisory board for Takeda and Sanofi. J. Peake reports receiving support for the present manuscript from DBV Technologies and has a leadership role of director of the ASCIA (honorary position, unpaid). K. P. Perrett reports receiving National Health and Medical Research Council Investigator Grant and Melbourne Children's Clinician-Scientist Fellowship for support of the present manuscript; research grants to institution from DBV Technologies, Aravax, Siolta, and Novartis; consulting fees from Aravax; is chair of the scientific advisory board for AllergyPal (chief scientific officer); is director of the National Allergy Centre of Excellence and nonexecutive director of Omnisova Pty Ltd; and has stock or stock options in AllergyPal. D. Petroni reports receiving grants for clinical trials from DBV Technologies and Alladapt and consulting fees from Aimmune, DBV Technologies, and Roche Genentech for advisory boards and Alladapt for protocol creation. J. A. Pongracic reports receiving grants to institution for conduct of clinical trials from DBV Technologies and Aimmune Therapeutics, consulting fees from DBV Technologies as global principal investigator on a different clinical trial, support for attending meetings from FARE, participated in a data safety monitoring board and received payment from DBV Technologies and Regeneron, participated in a FARE advisory board, and received provision of study drug and study materials to institution to conduct clinical trials from DBV Technologies and Aimmune Therapeutics. P. Quinn reports receiving support for the present manuscript from DBV Technologies; grants or contracts from DBV Technologies, Aravax, Novartis, National Health and Medical Research Council, and Women's and Children's Hospital Foundation; support for attending meetings from DBV Technologies, ASCIA, and National Allergy Council; has a leadership or fiduciary role in Australian Medical Association and ASCIA. R. G. Robison reports receiving support for the present manuscript from DBV Technologies, grants or contracts from Aimmune Therapeutics, and participation on a data safety monitoring board or advisory board for Genentech and Aimmune Therapeutics. G. Sanders reports receiving support for the present manuscript from DBV Technologies; grants or contracts from Nestlé, Alladapt Immunotherapeutics, Novartis, and Siolta Therapeutics; and receipt of equipment, materials, drugs, medical writing, gifts, or other services from DBV Technologies, Nestlé, Alladapt Immunotherapeutics, Novartis, and Siolta Therapeutics. L. Schneider reports receiving support for the present manuscript from DBV Technologies; grants or contracts from Regeneron; consulting fees from DBV Technologies; participation on a data safety monitoring board or advisory board for NIAID, Alladapt Immunotherapeutics, Ukko Inc, and Amagma Therapeutics; and has a leadership or fiduciary role in the National Eczema Association advisory board. H. Sharma reports receiving honoraria from the American Academy of Pediatrics National Conference and Exhibition 2023 as a speaker. S. B. Sindher reports receiving grants or contracts from NIH, Regeneron, DBV Technologies, Aimmune Therapeutics, Novartis, CoFAR, and FARE; consulting fees from DBV Technologies; and support for attending meetings from PAAM and FARE. J. Trujillo reports receiving honoraria from ALK-Abelló, Thermo Fisher Scientific, and Menarini Group; payment for expert testimony from Aimmune Therapeutics and ALK-Abelló; and support for attending meetings from Menarini Group. P. J. Turner reports receiving grants or contracts from MRC, NIHR Imperial Biomedical Research Centre, and the JM Foundation; consulting fees from Allergenis, Aquestive Therapeutics, and Novartis; participation on a data safety monitoring board or advisory board for Aimmune Therapeutics and UK Food Standards

Participants, including those who received placebo, who successfully completed 12 months of EPITOPE were invited to participate in an open-label extension (OLE) study with VP250 for a total of up to 36 months of active treatment (NCT03859700). Herein, we present the interim safety and efficacy results of the first year of the OLE study, including the first year of active treatment for placebo crossover participants.

METHODS

Trial design

The study design for the 12-month phase 3 EPITOPE trial has been previously published.[27] In brief, 362 participants with an eliciting dose (ED) ≤300 mg of peanut protein were randomized 2:1 to receive 12 months of VP250 or placebo. A dose-ranging substudy was conducted before initiating the EPITOPE study. This substudy enrolled 51 peanut-allergic participants aged 1 through 3 years who were randomized 2:2:1 to receive the VIASKIN patch for 12 months at a dose of 100 μg or 250 μg of peanut protein or placebo. The 250 μg dose was approved by an independent data and safety monitoring board and selected for use in EPITOPE. Eligible participants were invited to enter the OLE, where all participants received the 250 μg dose for a total of up to 36 months of active treatment (Figure E1, available in this article's Online Repository at www.jaci-inpractice.org). The full study protocol is provided in this article's Online Repository at www.jaci-inpractice.org.

After 1 year of open-label treatment with VP250, double-blind, placebo-controlled food challenges (DBPCFCs) were performed at month 24 (M24), with M0 defined as EPITOPE baseline.

Standardized DBPCFCs were conducted in accordance with the Practical Allergy (PRACTALL) consensus report guidelines using a standardized food matrix. Increasing doses of peanut protein were administered every 30 minutes (1 mg, 3 mg, 10 mg, 30 mg, 100 mg, 300 mg, 1000 mg, and 2000 mg; cumulative dose of 3444 mg). The challenge was stopped when objective signs and symptoms met prespecified stopping criteria, the details of which can be found in the study protocol in this article's Online Repository at www.jaci-inpractice.org. The ED is defined as the dose that triggered symptoms meeting prespecified stopping criteria, and the cumulative reactive dose is defined as the sum of all tolerated doses and the ED.

The study is being conducted in accordance with the International Council for Harmonisation Good Clinical Practice Guidelines, the Declaration of Helsinki, and all applicable regulatory requirements. The description of trial conduct, protocol approval, informed consent, and the principal investigators involved has been previously published.[27]

Eligibility and participant populations

The description of inclusion and exclusion criteria for initial enrollment in the EPITOPE trial and study treatment has been previously reported.[27] To be eligible for the OLE study, participants completed 12 months of treatment in EPITOPE, including performing the M12 DBPCFC. Because of the potential risks associated with future DBPCFCs, participants were ineligible for the OLE study if they had developed a severe anaphylactic reaction (requiring intubation or leading to cardiac arrest and/or coma) during the M12 DBPCFC or had uncontrolled asthma. Participants were enrolled in the OLE study before unblinding of EPITOPE.

The OLE study consists of 2 participant populations based on initial randomization at EPITOPE baseline:

- VP250 + VP250 group: participants who were initially randomized to VP250
- Placebo + VP250 group: participants who were initially randomized to placebo

Outcomes are presented by participant population, as defined above, with efficacy results focusing on the patient population initially randomized to VP250 in the pivotal EPITOPE trial. Efficacy and safety results, which include participants from the dose-

Agency; and has a leadership or fiduciary role in the World Allergy Organization and British Society for Allergy and Clinical Immunology. K. Tuttle reports receiving support for the present manuscript from DBV Technologies and the AAAAI Educator Development Grant. J. Upton reports receiving support for the present manuscript from DBV Technologies; grants or contracts from Regeneron, Sanofi, ALK-Abelló, CIHR, SickKids Food Allergy and Anaphylaxis Program, and Innovation Fund Denmark; honoraria from Pear Healthcare, AstraZeneca, and Pfizer; participation on a data safety monitoring board or advisory board for Pfizer, Bausch Health, Pharming, and ALK-Abelló; has a leadership or fiduciary role in Food Allergy Canada, CSACI, *Allergy* (editorial board), and *AACI* (associate editor); and receipt of drug (omalizumab) from Novartis for research study. P. Varshney reports receiving support for the present manuscript from DBV Technologies; grants or contracts from Aimmune Therapeutics, Siolta Therapeutics, Dell Medical School, and Health Transformation Research Institute; support for attending meeting from DBV Technologies; participation on the advisory board for DBV Technologies; and has a leadership or fiduciary role in State Health Department, Stock Epinephrine Advisory Committee (unpaid). B. P. Vickery reports receiving support for the present manuscript from DBV Technologies; grants or contracts from DBV Technologies, NIH-NIAID, Genentech, Aimmune Therapeutics, Aravax, Alladapt Immunotherapeutics, AstraZeneca, Moonlight Therapeutics, Novartis, Regeneron, and Siolta Therapeutics; consulting fees from Aimmune Therapeutics, Aravax, DBV Technologies, Genentech, IgGenix, Novartis, Parexel, Reacta Healthcare, Regeneron, Revolo Biotherapeutics, Sanofi, and Stallergenes Greer; and has stock or stock options in Moonlight Therapeutics. C. Vogelberg reports receiving support for the present manuscript from DBV Technologies, research grants from Boehringer Ingelheim, participation on a data safety monitoring board for Allergy Therapeutics, and honoria or contracts from DBV Technologies, Aimmune Therapeutics, Sanofi Aventis, LETI Pharma, AstraZeneca, ALK, Bencard Allergie, Orion Pharma, AbbVie, and Allergopharma. B. Wainstein reports receiving support for the present manuscript from DBV Technologies, honoraria from ALJESAL Educational Services, support for attending meetings from travel and education allowance from NSW Health, participation of a probiotic and peanut oral immunotherapy data safety monitoring board for Murdoch Research Institute Melbourne, and has a leadership or fiduciary role in Allergy & Anaphylaxis Australia.. J. Wang reports receiving support for the present manuscript from DBV Technologies; grants or contracts from NIH, Aimmune Therapeutics, Regeneron, and Siolta Therapeutics; honoraria from Medscape and DBV Technologies; support for attending AAAAI, ACAAI, and AAP meetings; participation on a data safety monitoring board or advisory board for ALK-Abelló, Jubilant HollisterStier, and Novartis; and has a leadership or fiduciary role in AAP (immediate past chair, executive committee, Section on Allergy and Immunology) and AAAAI (vice chair, annual meeting programming committee). R. Wood reports receiving support for the present manuscript from DBV Technologies; grants or contracts from Aimmune Therapeutics, Genentech, ALK, Novartis, Aravax, and FARE; and consulting fees from Genentech. A. W. Burks reports consulting fees from Allergy Therapeutics, Aimmune Therapeutics, Consortia TX, DBV Technologies, and Ukko Inc; grants to his institution from Burroughs Wellcome Fund; research grant from the NIH; and royalties from UpToDate. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication August 7, 2024; revised January 21, 2025; accepted for publication February 7, 2025.

Available online February 14, 2025.

Corresponding author: Matthew Greenhawt, MD, Children's Hospital Colorado, 13123 East 16th Ave, Box 518, Aurora, CO 80045. E-mail: Matthew.Greenhawt@childrenscolorado.org.

2213-2198

https://doi.org/10.1016/j.jaip.2025.02.004

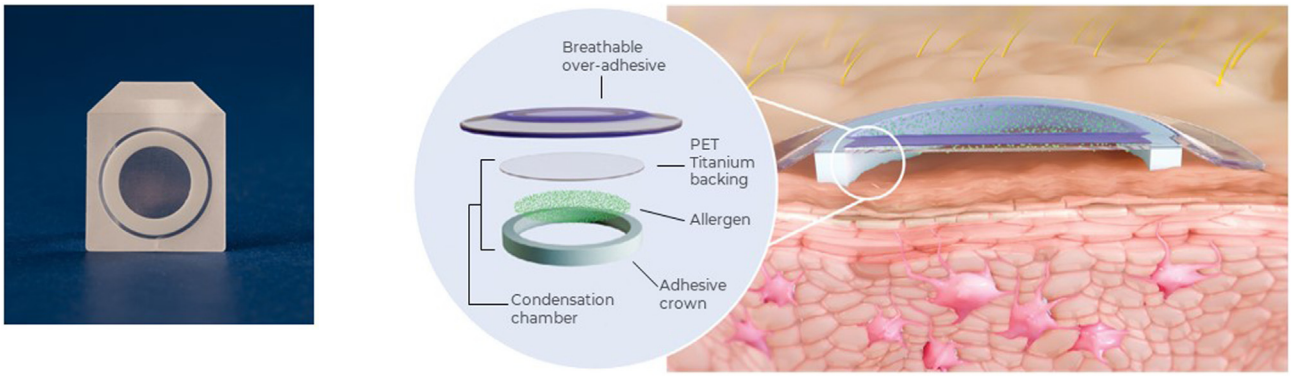

FIGURE 1. VIASKIN patch design. The peanut patch contains 250 μg of dried peanut protein on a film disc that is placed on top of a double-sided adhesive foam ring. When placed on the skin, the film disc and foam ring, which are held in place by an adhesive overlay, form a condensation chamber. Natural water loss from the skin leads to solubilization of the peanut allergen, which is taken up by antigen-presenting cells, such as Langerhans cells, in the superficial layers of the nonvascularized epidermis. *PET*, Polyethylene terephthalate.

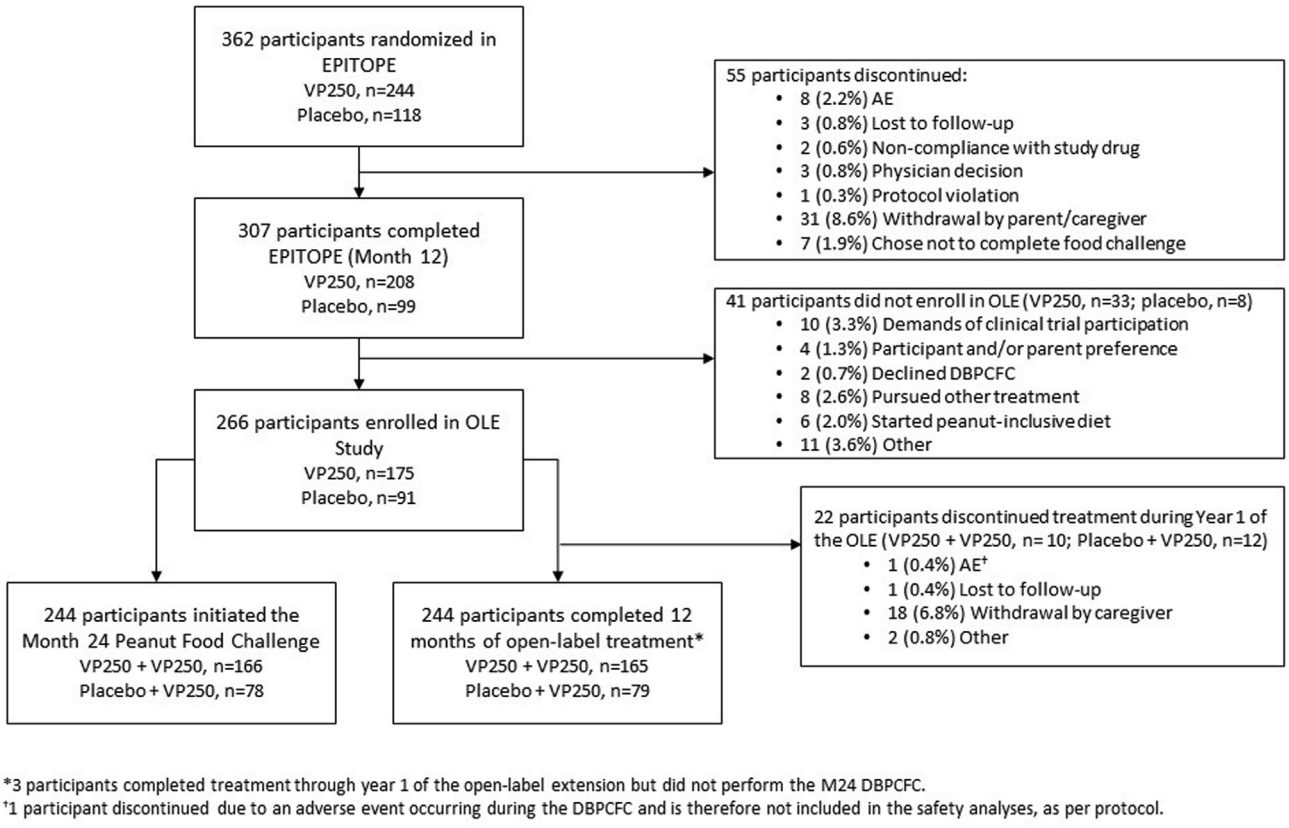

FIGURE 2. Participant disposition. Enrolled participants underwent randomization in a 2:1 ratio to receive epicutaneous immunotherapy with VP250 or to receive placebo for 12 months. Eligible participants were invited to enter the open-label extension study to receive up to 3 years of open-label treatment with VP250. *AE*, Adverse event; *DBPCFC*, double-blind, placebo-controlled food challenge; *OLE*, open-label extension; *VP250*, VIASKIN patch containing 250 μg of peanut protein.

ranging substudy, are presented in detail in this article's Online Repository at www.jaci-inpractice.org.

Intervention

The VIASKIN patch is an epicutaneous system containing unmodified lyophilized peanut protein within an occlusive condensation chamber (Figure 1). Treatment initiation, instructions, and guidelines have been previously outlined[27] and are provided within the study protocol in this article's Online Repository at www.jaci-inpractice.org. In brief, 1 patch is applied daily on the interscapular area of the back, with a new patch applied each day after the removal of the previously applied patch. The daily duration of patch

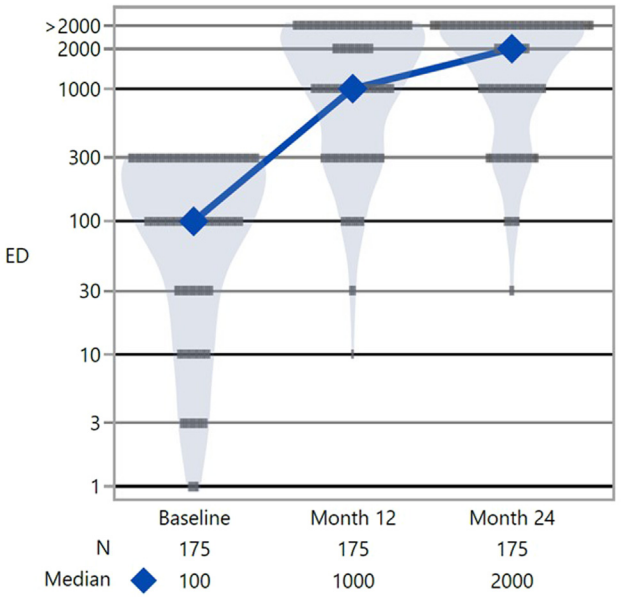

FIGURE 3. Median eliciting dose over time in participants who received 24 months of VP250. The figure illustrates changes in the median eliciting dose (ED) over time after 24 months of VP250 treatment in children aged 1 to 3 years. Each marker represents the ED of an individual participant, with the width of the marker band proportional to the number of participants at each ED. Median values at each timepoint are shown as blue diamonds. The light blue shaded area represents a smoothed kernel density estimation of the ED distribution at each timepoint. Participants who tolerated 2000 mg without meeting the stopping criteria are indicated at the top of the figure as ">2000," whereas other values represent the dose that caused a reaction, leading to the cessation of the food challenge. *ED*, Eliciting dose; *VP250*, VIASKIN patch containing 250 μg of peanut protein.

wear time is progressively increased at home over the first 4 weeks of treatment to reach a full day by week 5. No restrictions on daily activities are required while wearing the patch.

Outcomes

Assessments for evaluating treatment response at M24 included the percentage of participants who reached an ED ≥1000 mg and ≥2000 mg, and the percentage of participants who completed the DBPCFC without meeting the prespecified stopping criteria. Efficacy was also assessed according to the treatment responder criteria from EPITOPE, defined as participants achieving an M12 ED of ≥300 mg (if baseline ED ≤10 mg) or ≥1000 mg (if baseline ED >10 mg). The change from baseline to M24 in reaction severity during the DBPCFC was also assessed.

Key assessments of global safety included AEs, assessment of local application-site reactions, physical examinations, and clinical laboratory assessments. AEs were assessed by the investigator according to seriousness, severity, duration, and relationship to treatment. Anaphylactic reactions were defined, as in EPITOPE,[27] according to the criteria of the Food Allergy & Anaphylaxis Network/National Institute of Allergy and Infectious Diseases or by investigator report.[31] Treatment compliance was assessed by the total number of patches used (dispensed minus returned) during the active treatment period divided by the number of days in the active treatment period.

Statistical methods

This interim analysis included available data as of September 25, 2023.

The main efficacy analyses were performed on evaluable (eg, nonmissing) endpoints.

Participants who discontinued before the M24 DBPCFC were excluded from the main analyses. However, participants who began the M24 DBPCFC but did not complete the food challenge were included if the specific endpoint could be defined. For example, if a participant experienced no allergic symptoms but stopped the DBPCFC after completing the 1000 mg dose (for any reason, as was permissible per study protocol), their endpoint would be analyzed as an ED ≥1000 mg. Conversely, the 2000 mg endpoint for this participant would be considered unevaluable and missing because they stopped before attempting the final dose. As a result, the sample size for different efficacy endpoints may vary slightly when using the complete-case analysis methodology. Imputation strategies were implemented to address missing data.

For participants completing both the M12 and M24 DBPCFCs, differences in response rates between the 2 time points were computed using paired binomial methodology. The 95% confidence intervals (CIs) were calculated using the Newcombe method based on Wilson score intervals with continuity correction and are considered statistically significant when not spanning 0%.

RESULTS

Participant disposition and baseline characteristics

Overall, 307 participants completed EPITOPE (VP250, n = 208; placebo, n = 99), and of these, 266 (86.6%) participants enrolled in the EPITOPE OLE study (VP250 + VP250, n = 175; placebo + VP250, n = 91) and 244 initiated the M24 DBPCFC (VP250 + VP250, n = 166; placebo + VP250, n = 78) (Figure 2). The median age of participants at the time of enrollment in the OLE was 3.8 years in both VP250 + VP250 and placebo + VP250 groups. Additional characteristics of those who enrolled in the OLE and those who did not enroll are presented in Table E1 in this article's Online Repository at www.jaci-inpractice.org.

Between the start of the OLE study and the M24 DBPCFC, 22 participants discontinued treatment (VP250 + VP250, n = 10; placebo + VP250, n = 12). Reasons for study discontinuation during this time were as follows: 18 (6.8%) participants whose caregiver withdrew consent for further participation, 1 (0.4%) who was withdrawn due to an AE (a serious AE that occurred during the DBPCFC), 1 (0.4%) who was lost to follow-up, and 2 (0.8%) who were withdrawn for other reasons. In total, 244 participants started the M24 DBPCFC, and of these, 226 had evaluable data for all doses given, with 18 participants (VP250 + VP250, n = 14; placebo + VP250, n = 4) partially completing the M24 DBPCFC. For this reason, the denominators reported in the efficacy outcomes vary to reflect the number of participants with evaluable data at each dose given during the DBPCFC.

Of the participants who completed the dose-ranging substudy, 38 of 42 (90.5%) (VP250, n = 16; VP100, n = 14; placebo, n = 8) entered the OLE study. Further details on these participants are included in this article's Online Repository at www.jaci-inpractice.org.

Demographics and characteristics of the participants' baseline PA status have been previously reported.[27]

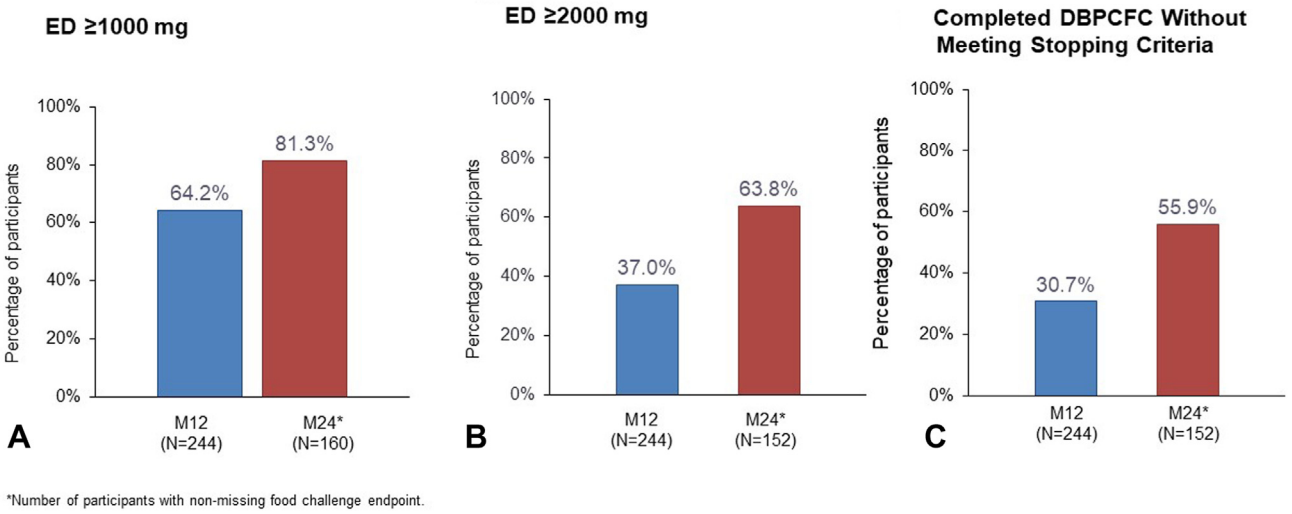

FIGURE 4. Efficacy outcomes for participants treated with VP250 for 24 months. (**A**,**B**) Patients achieving ED ≥1000 mg and ≥2000 mg, respectively, at M12 and M24. (**C**) Participants completing the M12 and M24 DBPCFC who successfully ingested the cumulative dose of 3444 mg of peanut protein without displaying dose-limiting symptoms. (*) Indicates the number of participants with nonmissing DBPCFC data. *DBPCFC*, Double-blind, placebo-controlled food challenge; *ED*, eliciting dose; *M*, month.

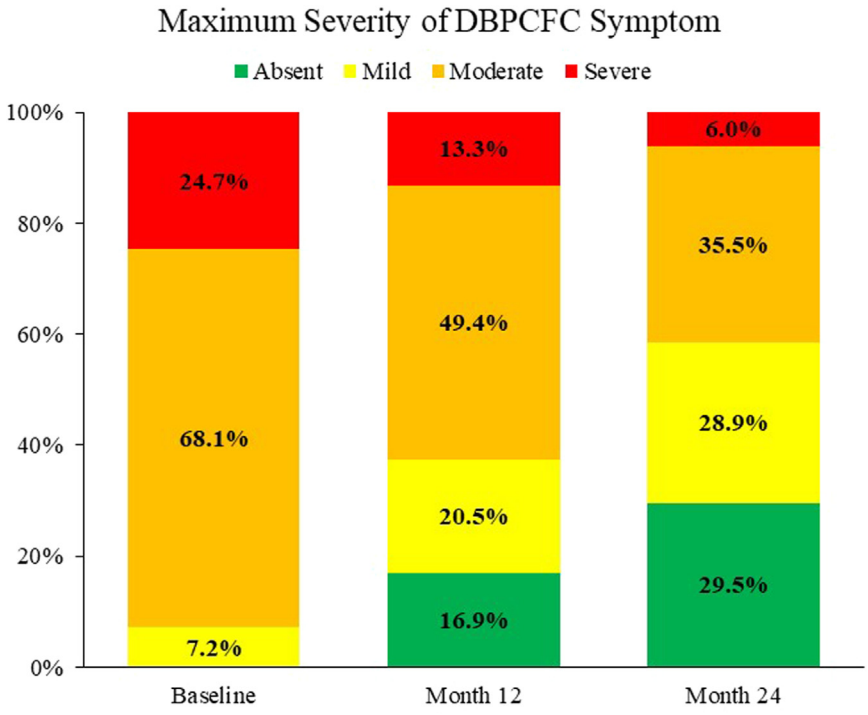

FIGURE 5. Changes in reaction severity during the DBPCFC in participants who received 24 months of VP250. The severity of reactions during the DBPCFC was graded by the investigator according to PRACTALL scoring as absent, mild, moderate, or severe in toddlers aged 1 through 3 years in EPITOPE and the open-label extension study from baseline, month 12, and month 24 for participants who initiated the M24 DBPCFC (n = 166). *DBPCFC*, Double-blind, placebo-controlled food challenge; *M*, month; *PRACTALL*, practical allergy; *VP250*, VIASKIN patch containing 250 μg of peanut protein.

Efficacy of VP250 after 24 months (VP250 + VP250 group)

For all efficacy endpoints, an additional 12 months of VP250 treatment resulted in increased treatment benefit. After 24 months of VP250 treatment, the median ED increased over time, from 100 mg at baseline to 1000 mg at M12 and to 2000 mg at M24 (Figure 3). A total of 81.3% (130 of 160) of participants reached an ED ≥1000 mg and 63.8% (97 of 152)

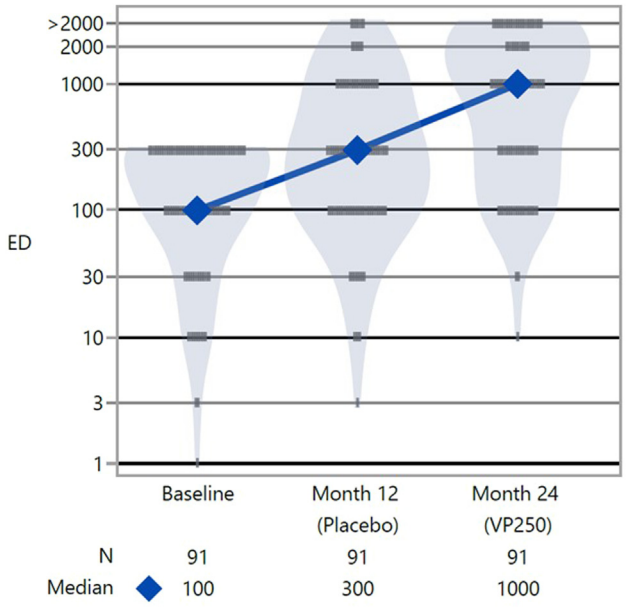

FIGURE 6. Median eliciting dose over time in EPITOPE placebo participants who received 12 months of VP250 during the open-label extension study. The figure illustrates changes in the median eliciting dose (ED) over time after 12 months of placebo treatment followed by 12 months of VP250 treatment in children aged 1 to 3 years. Each marker represents the ED of an individual participant, with the width of the marker band proportional to the number of participants at each ED. Median values at each timepoint are shown as blue diamonds. The light blue shaded area represents a smoothed kernel density estimation of the ED distribution at each timepoint. Participants who tolerated 2000 mg without meeting the stopping criteria are indicated at the top of the figure as ">2000," whereas other values represent the dose that caused a reaction, leading to the cessation of the food challenge. *VP250*, VIASKIN patch containing 250 μg of peanut protein.

reached an ED ≥2000 mg (Figure 4, *A* and *B*). A total of 158 participants had evaluable data at both M12 and M24 for the ED ≥1000 mg endpoint. The percentage of participants who achieved this endpoint increased significantly from 74.7% to 81%, Δ[M24-M12] = 6.3% (95% CI: 0%; 12.8%). Similarly, an additional 25 participants achieved an ED ≥2000 mg at M24 who had not reached this endpoint at M12, representing a significant increase of 12.9% (95% CI: 5.6%; 20.0%), from 52.4% to 65.3% (among the 147 participants with evaluable data at both M12 and M24 for the ED ≥2000 mg endpoint).

At the M24 DBPCFC, 85 of 152 (55.9%) participants ingested the full cumulative peanut protein dose (3444 mg) without meeting the prespecified stopping criteria (Figure 4, *C*). Among 147 participants with this endpoint evaluable at both M12 and M24 DBPCFC, a significantly greater proportion of participants achieved this endpoint at M24 than those at M12 (57.1% vs 39.5%, respectively; Δ[M24-M12] = 17.7% [95% CI: 9.3%; 25.6%]). In addition, at the M24 DBPCFC, the proportion of participants meeting the treatment responder criteria, as defined in EPITOPE, was 83.9% (135 of 161).

Analyses of imputed endpoints demonstrated results generally consistent with the main analyses (Figure E2, available in this article's Online Repository at www.jaci-inpractice.org).

The reactions elicited during the M24 DBPCFC decreased in severity compared with the M12 DBPCFC (Figure 5). At M24, severe reactions were reported in 6.0% (10 of 166) of VP250 participants compared with 13.3% (22 of 166) of VP250 participants at M12. The proportion of participants with absent or mild symptoms during the DBPCFC increased from 37.4% at M12 to 58.4% at M24.

Similar efficacy outcomes were observed for all endpoints at M24 when including participants who received active treatment during the dose-ranging substudy and received a second year of treatment in the OLE study (Table E2, available in this article's Online Repository at www.jaci-inpractice.org).

Efficacy of VP250 after 12 months among participants initially randomized to placebo (placebo + VP250 group)

For participants who received 12 months of placebo in EPITOPE, the median ED was 100 mg at baseline and 300 mg at M12. After 12 months of VP250 in the OLE study, the median ED increased to 1000 mg (Figure 6), and 62.7% (47 of 75) of participants reached an ED ≥1000 mg (Table I). A total of 36.5% (27 of 74) participants reached an ED ≥2000 mg and 28.4% (21 of 74) ingested the full cumulative peanut protein dose (3444 mg) of the M24 DBPCFC without meeting the prespecified stopping criteria. In addition, 68.0% (51 of 75) were treatment responders according to EPITOPE study criteria.

There was an increase in the proportion of participants who achieved an ED ≥1000 mg from 30.1% (22 of 73) at M12 to 63.0% (46 of 73) at M24 (Δ[M24-M12] = 32.9% [95% CI: 20.5%; 43.5%]). Similarly, an additional 20 participants achieved an ED ≥2000 mg at M24 who had not reached this endpoint at M12, representing an increase from M12 to M24 of 27.8% (95% CI: 16.9%; 38.5%), from 9.7% to 37.5% among 72 participants. The proportions of mild, moderate, and severe reactions occurring during the DBPCFC shifted toward less severe reactions after 12 months of VP250 in participants who received placebo in EPITOPE. At the M24 DBPCFC, 38.5% of participants had absent or mild symptoms compared with 18.0% at M12.

Similar efficacy outcomes were observed at M24 when including participants who received placebo for 12 months during the dose-ranging substudy (Table E2, available in this article's Online Repository at www.jaci-inpractice.org).

Analyses of imputed endpoints demonstrated results consistent with the main analyses (Figure E3, available in this article's Online Repository at www.jaci-inpractice.org).

Adverse events

At M24, the median (first quartile, third quartile) active treatment exposure duration was 25.6 months (24.8, 27.1), with a mean compliance of 95.3% for participants initially randomized to VP250, and 12.6 months (12.2, 12.7), with a mean compliance of 94.1% for participants initially randomized to placebo.

For all participants initially randomized to VP250 who enrolled in the OLE study (n = 175), 100% reported a treatment-emergent AE (TEAE), regardless of treatment-relatedness, over the 2 years of treatment. The most commonly reported treatment-related TEAEs were local application-site reactions observed in 100% of participants, which were predominantly mild or moderate in severity. A summary of TEAEs

TABLE I. Efficacy outcomes for EPITOPE placebo participants who received 12 months of VP250 during the OLE study

	ED ≥1000 mg (n = 75)	ED ≥2000 mg (n = 74)	Completed DBPCFC without meeting stopping criteria (n = 74)	Treatment responder (n = 75)
Participants, n (%)	47 (62.7)	27 (36.5)	21 (28.4)	51 (68.0)

DBPCFC, Double-blind, placebo-controlled food challenges; *ED*, eliciting dose; *OLE*, open-label extension; *VP250*, VIASKIN patch containing 250 μg of peanut protein.

TABLE II. Adverse events in participants who enrolled in the OLE study and were initially randomized to VP250, by the year of active treatment

	VP250 + VP250 (N = 175)	
Adverse event category, n (%)	Year 1 of treatment	Year 2 of treatment
TEAEs	175 (100)	171 (97.7)
Mild	175 (100)	169 (96.6)
Moderate	160 (91.4)	129 (73.7)
Severe	43 (24.6)	13 (7.4)
Treatment-related TEAEs	175 (100)	160 (91.4)
Serious TEAEs	17 (9.7)	7 (4.0)
Treatment-related serious TEAEs	1 (0.6)	0
TEAEs leading to permanent study treatment discontinuation	0	0
Treatment-related local TEAEs	175 (100)	160 (91.4)
Severe treatment-related local TEAEs	37 (21.1)	9 (5.1)
Treatment-emergent local AESI	40 (22.9)	25 (14.3)
Anaphylactic reaction	11 (6.3)	11 (6.3)
Treatment-related anaphylactic reaction	3 (1.7)	0
TEAE leading to epinephrine use	16 (9.1)	10 (5.7)
Treatment-related TEAE leading to epinephrine use	2 (1.1)	0

AESI, Adverse event of special interest; *TEAE*, treatment-emergent adverse event; *VP250*, VIASKIN patch containing 250 μg of peanut protein.

by year of active treatment is provided in Table II. The number of TEAEs decreased by 31.5% in year 2 compared with year 1.

During the second year of VP250 treatment, there were 7 serious TEAEs reported, including 3 anaphylactic reactions, none of which were assessed as related to treatment, and no study discontinuations due to an AE were reported. Overall, fewer participants experienced treatment-related local skin reactions during year 2 than those during year 1 (91.4% vs 100%), including a reduction in severe treatment-related local TEAEs. As determined by investigators, most local skin reactions during year 2 were assessed as grade 1 (erythema, or erythema and infiltration) or grade 2 (erythema and few papules), and the distribution of grades decreased in severity from year 1 to year 2 (Table E3, available in this article's Online Repository at www.jaci-inpractice.org).

Among participants who received placebo during the first year of study treatment (n = 91), the safety profile during the first 12 months of VP250 treatment in the OLE study was consistent with that reported in EPITOPE. TEAEs occurred in 98.9% (90 of 91) of participants, and treatment-related TEAEs occurred in 95.6% (87 of 91) of participants. Two participants (2.2%) experienced a serious TEAE, one of which was assessed as treatment-related (cough and acute conjunctival tearing, which resolved without the use of epinephrine reported as moderate anaphylaxis and deemed as an important medical event by the investigator) (Table E4, available in this article's Online Repository at www.jaci-inpractice.org). No study discontinuations due to an AE were reported.

Overall, including both participants initially randomized to VP250 or placebo, between M12 and M24, there were 17 cases of anaphylaxis reported in 17 participants (VP250 + VP250, n = 11; placebo + VP250, n = 6), one of which was assessed as related to treatment (placebo + VP250 participant, as described above). All other anaphylaxis events were considered unrelated, and all but one were mild or moderate in severity. No cases of treatment-related epinephrine use were reported during the first year of the OLE (year 2).

Similar safety outcomes were observed among participants in the dose-ranging substudy (Table E5, available in this article's Online Repository at www.jaci-inpractice.org). One participant initially randomized to placebo discontinued the study due to an AE that was unrelated to treatment. One serious TEAE considered unrelated to treatment was reported in 1 participant initially randomized to placebo.

DISCUSSION

The interim results of the first year of the EPITOPE OLE study demonstrate that 2 years of treatment with VP250 provided gains in efficacy beyond those achieved with 12 months of treatment, alongside a reduction in treatment-related TEAEs. There were significant increases in the number of participants reaching ED ≥1000 mg, ED ≥2000 mg, and completing the full DBPCFC after 2 years versus after 1 year of VP250 treatment. Furthermore, there was a steady increase in median ED from 100 mg at baseline to 1000 mg at M12 to 2000 mg at M24. Among participants treated with VP250 for 2 years, 4 of 5 reached an ED ≥1000 mg (equivalent to 3-4 large peanuts), and nearly two-thirds had an ED ≥2000 mg (approximately 6-8 large peanuts). Moreover, more than half of the participants completed the DBPCFC without reaching stopping criteria, ingesting approximately 12 to 14 peanuts. These represent substantial gains among a population with a median pre-intervention baseline ED of 100 mg (approximately one-third of a large peanut), and these amounts are well beyond what would be likely encountered in an accidental exposure, suggesting that treatment with VP250 could potentially provide a meaningful level of protection to patients.

Efficacy results from participants who received placebo in EPITOPE and 1 year of open-label VP250 replicate the primary outcome results from the EPITOPE study. Among this placebo-crossover group, the percentage of participants meeting the EPITOPE responder criteria (68%) was essentially identical to those initially randomized to VP250 (67%), as were the percentages reaching ED ≥1000 mg (62.7% vs 64%, respectively) and ≥2000 mg (37% for each group), demonstrating robustness and reproducibility of the originally published results among those receiving their first 12 months of therapy. The consistency in these results suggests that participants who started therapy

approximately 1 year later than those in the EPITOPE study can still benefit from the disease-modifying effects of allergen immunotherapy, as their immune systems remain especially responsive to immunomodulation during early childhood. During the first year of open-label VP250 treatment in the placebo-crossover group, 1 participant experienced a treatment-related event reported as anaphylaxis (coughing and excessive conjunctival tearing), which did not require epinephrine treatment or led to study discontinuation.

Among participants receiving a second year of VP250 treatment, there were no reported treatment-related anaphylaxis or systemic allergic events, treatment-related TEAEs that led to study withdrawal, and no serious treatment-related TEAEs. The frequency and severity of treatment-related local application-site reactions decreased from year 1 to year 2 of active treatment.

The retention rate was high (87%), with most EPITOPE participants opting to enroll in this OLE study before the unblinding of their treatment arm in EPITOPE. In addition, overall compliance rates during this study were also high (approximately 95% in both groups), and only 1 participant, originally randomized to placebo in the dose-ranging substudy, discontinued due to an AE. This suggests that VP250 is well tolerated, and daily use can be easily maintained through at least 2 years.

These results represent the first long-term data for toddlers aged 1 through 3 years (at study initiation) using VP250. These findings align with the long-term open-label efficacy and safety data of VP250 from the phase 3 PEOPLE study in 4- to 11-year-olds and the phase 2 OLFUS-VIPES study in 6- to 55-year-olds.[28,32] Final results of the EPITOPE OLE will be available at the completion of 3 years of treatment for all participants. Taken together, these data contribute to the evidence from more than 1300 peanut-allergic participants demonstrating that long-term VP250 treatment has the potential to provide additional benefits with a consistent safety profile. Furthermore, based on this growing body of evidence, the European Academy of Allergy and Clinical Immunology recently updated their guidelines to recommend EPIT with the patch for treating PA in children and adolescents, once approved by regulatory authorities.[33]

This study has limitations. First, the results presented here are from the OLE study, which typically involve a population enriched with participants who responded favorably to treatment during the initial 12-month placebo-controlled phase. However, this limitation is partially mitigated by the high proportion of participants who chose to enter the OLE study. Furthermore, at the time of entry to the OLE study, participants and investigators remained blinded to the initial treatment allocation in EPITOPE. Second, the COVID-19 pandemic coincided with the trial, potentially causing delays that pushed participants outside the protocol-specified timeframe for scheduled study visits. These delays may have also influenced some participants' decisions not to enroll in the OLE study, despite having completed EPITOPE.

CONCLUSIONS

Like other forms of allergen-specific immunotherapy, EPIT with the VIASKIN patch is designed to desensitize the immune system through repeated allergen exposure over time and typically over several years. The EPITOPE OLE study provides evidence that VP250 treatment for up to 24 months is well tolerated with a consistent safety profile and further increases peanut desensitization in children aged 1 through 3 years. The second year of treatment showed enhanced protection, with increased median ED and fewer treatment-related AEs. These results, demonstrating continued benefit beyond 1 year, align with prior VP250 studies in an older population as well as with long-term experience with subcutaneous immunotherapy for inhalant and venom allergies. EPITOPE placebo participants who received 12 months of open-label VP250 had nearly identical safety and efficacy results to the EPITOPE VP250 treatment arm, confirming the robustness and reproducibility of these findings. Overall, findings from the OLE study suggest that VP250, if approved, could be an effective and safe treatment option for PA in young children.

Acknowledgments

The authors wish to thank the patients, family members, and staff from all trial sites who participated in the study. Editorial support was provided by Red Nucleus, funded by DBV Technologies. VIASKIN is a trademark of DBV Technologies.

REFERENCES

1. Lieberman JA, Gupta RS, Knibb RC, Haselkorn T, Tilles S, Mack DP, et al. The global burden of illness of peanut allergy: a comprehensive literature review. Allergy 2021;76:1367-84.
2. Sicherer SH, Muñoz-Furlong A, Sampson HA. Prevalence of peanut and tree nut allergy in the United States determined by means of a random digit dial telephone survey: a 5-year follow-up study. J Allergy Clin Immunol 2003;112:1203-7.
3. Sicherer SH, Muñoz-Furlong A, Godbold JH, Sampson HA. US prevalence of self-reported peanut, tree nut, and sesame allergy: 11-year follow-up. J Allergy Clin Immunol 2010;125:1322-6.
4. 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.
5. Fleischer DM, Sicherer S, Greenhawt M, Campbell D, Chan E, Muraro A, et al. Consensus communication on early peanut introduction and the prevention of peanut allergy in high-risk infants. Ann Allergy Asthma Immunol 2015;115:87-90.
6. Parker KM, Dang TD, Wijesuriya R, Soriano VX, Lowe AJ, Dharmage SC, et al. Longitudinal peanut and Ara h 2 specific-IgE, -IgG_4, and -IgG_4/-IgE ratios are associated with the natural resolution of peanut allergy in childhood. Allergy 2024;79:1868-80.
7. Peters RL, Guarnieri I, Tang MLK, Lowe AJ, Dharmage SC, Perrett KP, et al. The natural history of peanut and egg allergy in children up to age 6 years in the HealthNuts population-based longitudinal study. J Allergy Clin Immunol 2022;150:657-65.e613.
8. Nowak-Wegrzyn A, Hass SL, Donelson SM, Robison D, Cameron A, Etschmaier M, et al. The Peanut Allergy Burden Study: impact on the quality of life of patients and caregivers. World Allergy Organ J 2021;14:100512.
9. Greenhawt M, Abrams EM, Chalil JM, Tran O, Green TD, Shaker MS. The impact of allergy specialty care on health care utilization among peanut allergy children in the United States. J Allergy Clin Immunol Pract 2022;10:3276-83.
10. Capucilli P, Wang KY, Spergel JM. Food reactions during avoidance: focus on peanut. Ann Allergy Asthma Immunol 2020;124:459-65.
11. Palforzia. The Netherlands: European Medicines Agency. Accessed March 6, 2025. https://www.ema.europa.eu/en/medicines/human/EPAR/palforzia
12. Palforzia [package insert]. Bridgewater, NJ: Aimmune Therapeutics; 2020.
13. Xolair [package insert]. San Francisco, CA: Genentech Inc; 2024.
14. 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.
15. Wood RA, Togias A, Sicherer SH, Shreffler WG, Kim EH, Jones SM, et al. Omalizumab for the treatment of multiple food allergies. N Engl J Med 2024;390:889-99.
16. Fiocchi A, Ebisawa M. Omalizumab is the Columbus egg for food allergies. Curr Opin Allergy Clin Immunol 2024;24:144-6.

17. Sampson HA, Bird JA, Fleischer D, Shreffler WG, Spergel JM. Who are the potential patients for omalizumab for food allergy? Ann Allergy Asthma Immunol 2024;132:569-71.
18. Togias A, Cooper SF, Acebal ML, Assa'ad A, Baker JR Jr, Beck LA, et al. Addendum guidelines for the prevention of peanut allergy in the United States: report of the National Institute of Allergy and Infectious Diseases—sponsored expert panel. J Allergy Clin Immunol 2017;139:29-44.
19. Roberts G, Bahnson HT, Du Toit G, O'Rourke C, Sever ML, Brittain E, et al. Defining the window of opportunity and target populations to prevent peanut allergy. J Allergy Clin Immunol 2023;151:1329-36.
20. Mack DP, Greenhawt M, Turner PJ, Wasserman RL, Hanna MA, Shaker M, et al. Information needs of patients considering oral immunotherapy for food allergy. Clin Exp Allergy 2022;52:1391-402.
21. Soriano VX, Peters RL, Moreno-Betancur M, Ponsonby AL, Gell G, Odoi A, et al. Association between earlier introduction of peanut and prevalence of peanut allergy in infants in Australia. JAMA 2022;328:48-56.
22. Du Toit G, Brown KR, Vereda A, Irani AM, Tilles S, Ratnayake A, et al. Oral immunotherapy for peanut allergy in children 1 to less than 4 years of age. NEJM Evid 2023;2:EVIDoa2300145.
23. Jones SM, Kim EH, Nadeau KC, Nowak-Wegrzyn A, Wood RA, Sampson HA, et al. 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. Lancet 2022;399:359-71.
24. Kim EH, Bird JA, Keet CA, Virkud YV, Herlihy L, Ye P, et al. Desensitization and remission after peanut sublingual immunotherapy in 1- to 4-year-old peanut-allergic children: a randomized, placebo-controlled trial. J Allergy Clin Immunol 2024;153:173-81.e10.
25. Kim EH, Yang L, Ye P, Guo R, Li Q, Kulis MD, et al. Long-term sublingual immunotherapy for peanut allergy in children: clinical and immunologic evidence of desensitization. J Allergy Clin Immunol 2019; 144:1320-1326.e1.
26. Fleischer DM, Bégin P, Chan ES, Cheema A, Gagnon R, Sussman G, et al. Efficacy of epicutaneous immunotherapy with Viaskin™ Peanut for 4 to 7-year-old peanut-allergic children in a phase 3 clinical trial (PEPITES). Presented at. Quebec, Canada: Canadian Society of Allergy and Clinical Immunology (CSACI) 77th Annual Scientific Meeting; September 23-25, 2006.
27. Greenhawt M, Sindher SB, Wang J, O'Sullivan M, du Toit G, Kim EH, et al. Phase 3 trial of epicutaneous immunotherapy in toddlers with peanut allergy. N Engl J Med 2023;388:1755-66.
28. Sampson HA, Shreffler WG, Yang WH, Sussman GL, Brown-Whitehorn TF, Nadeau KC, et al. Effect of varying doses of epicutaneous immunotherapy vs placebo on reaction to peanut protein exposure among patients with peanut sensitivity: a randomized clinical trial. JAMA 2017;318:1798-809.
29. Lee ECK, Trogen B, Brady K, Ford LS, Wang J. The natural history and risk factors for the development of food allergies in children and adults. Curr Allergy Asthma Rep 2024;24:121-31.
30. Hervé PL, Dioszeghy V, Matthews K, Bee KJ, Campbell DE, Sampson HA. Recent advances in epicutaneous immunotherapy and potential applications in food allergy. Front Allergy 2023;4:1290003.
31. Loprinzi Brauer CE, Motosue MS, Li JT, Hagan JB, Bellolio MF, Lee S, et al. Prospective validation of the NIAID/FAAN criteria for emergency department diagnosis of anaphylaxis. J Allergy Clin Immunol Pract 2016;4:1220-6.
32. Fleischer DM, Shreffler WG, Campbell DE, Green TD, Anvari S, Assa'ad A, et al. Long-term, open-label extension study of the efficacy and safety of epicutaneous immunotherapy for peanut allergy in children: PEOPLE 3-year results. J Allergy Clin Immunol 2020;146:863-74.
33. Santos AF, Riggioni C, Agache I, Akdis CA, Akdis M, Alvarez-Perea A, et al. EAACI guidelines on the management of IgE-mediated food allergy. Allergy 2025;80:14-36.

ONLINE REPOSITORY

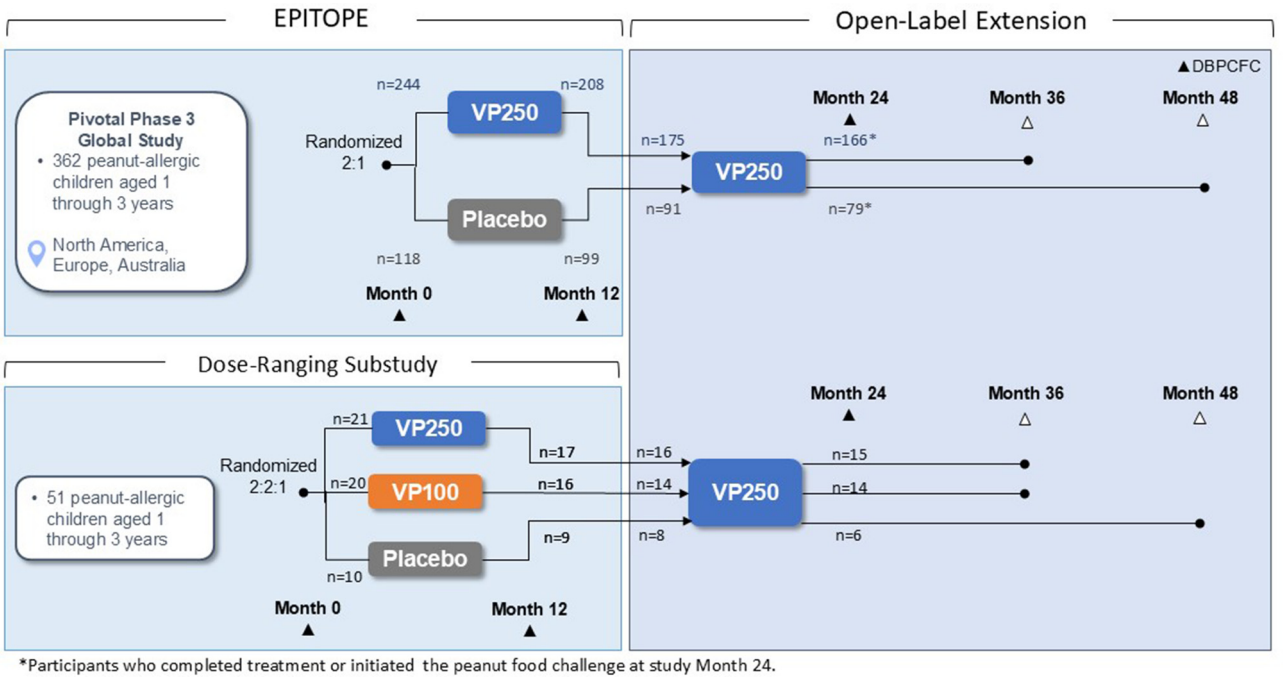

FIGURE E1. Study schema. EPITOPE was a phase 3 randomized double-blind, placebo-controlled study in children aged 1 through 3 years with confirmed peanut allergy. A total of 362 participants were randomized 2:1 to receive 12 months of EPIT with either VIASKIN peanut 250 μg (VP250) or placebo. A dose-ranging substudy was conducted before initiating EPITOPE in which 51 peanut-allergic children aged 1 through 3 years were randomized 2:2:1 to receive the VIASKIN patch for 12 months at a dose of 100 μg or 250 μg of peanut protein or placebo. Eligible participants were invited to enter the open-label extension to receive up to 36 months of treatment with VP250. Double-blind, placebo-controlled food challenges (DBPCFCs) were performed every 12 months.

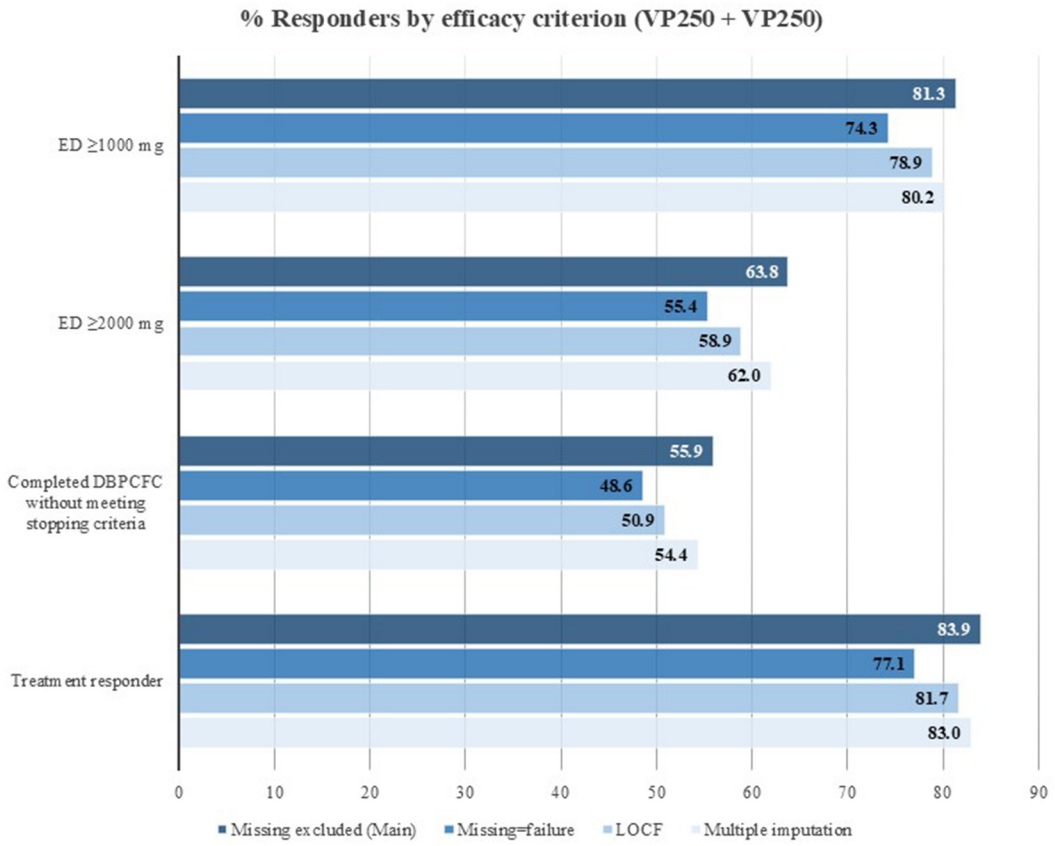

FIGURE E2. Percentage of responders by the efficacy criterion in the VP250+VP250 group. The percentage of responders for each efficacy endpoint is shown for the participants receiving 24 months of treatment with VP250. Prespecified sensitivity analyses of the efficacy endpoints were defined as follows: Missing=failure: participants with missing endpoint are considered as failure. Last observation carried forward (LOCF): participants with missing endpoint are imputed using the last observation carried forward where, if the month 24 endpoint is missing, then it will be imputed with the month 12 endpoint results, and if the month 12 endpoint is missing, then it will be imputed as failure (ie, baseline result). Multiple imputation: participants with missing endpoint are multiply imputed using a logistic regression model with prognostic factors (age, baseline IgE, baseline ED, and month 12 ED). *DBPCFC*, Double-blind, placebo-controlled food challenge; *ED*, eliciting dose; *VP250*, VIASKIN patch containing 250 μg of peanut protein.

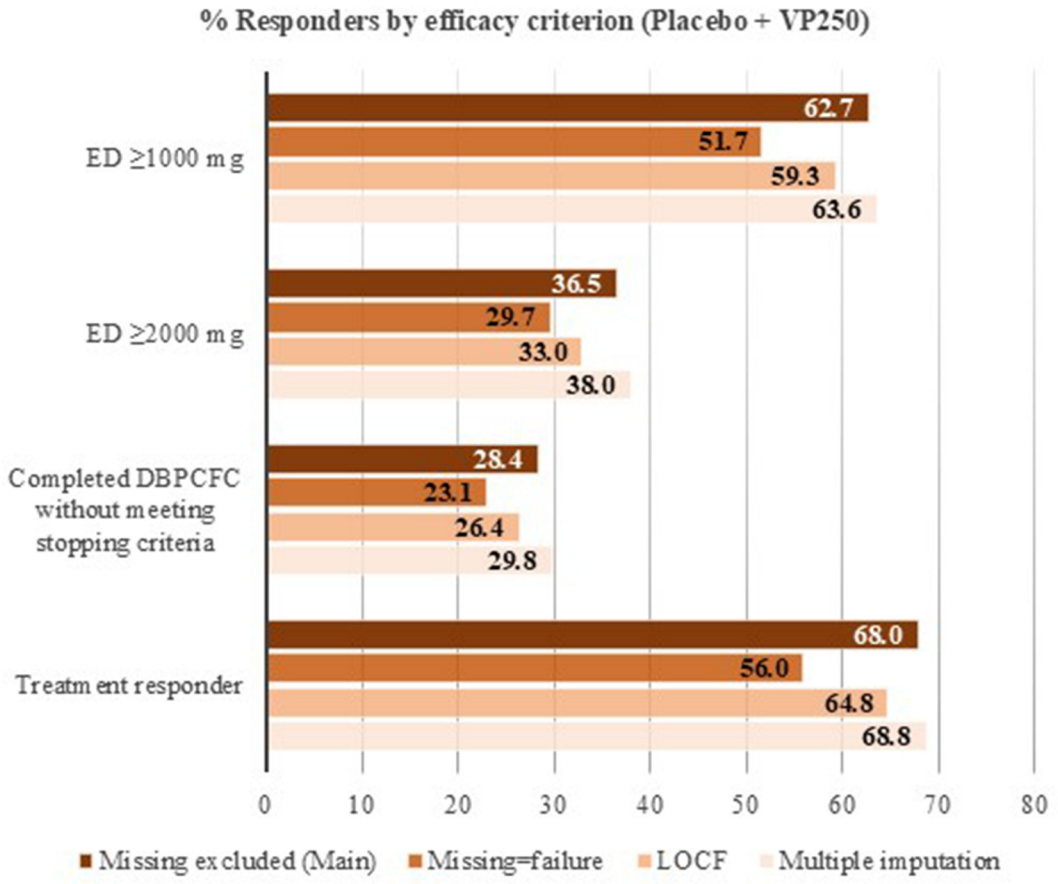

FIGURE E3. Percentage of responders by the efficacy criterion in the placebo+VP250 group. The percentage of responders for each efficacy endpoint is shown for the participants receiving 12 months of placebo in EPITOPE followed by 12 months of treatment with VP250 in the open-label extension. Prespecified sensitivity analyses of the efficacy endpoints were defined as follows: Missing=failure: participants with missing endpoint are considered as failure. Last observation carried forward (LOCF): participants with missing endpoint are imputed using the last observation carried forward where, if the month 24 endpoint is missing, then it will be imputed with the month 12 endpoint results, and if the month 12 endpoint is missing, then it will be imputed as failure (ie, baseline result). Multiple imputation: participants with missing endpoint are multiply imputed using a logistic regression model with prognostic factors (age, baseline IgE, baseline ED, and month 12 ED). *DBPCFC*, double-blind, placebo-controlled food challenge; *ED*, eliciting dose; *VP250*, VIASKIN patch containing 250 μg of peanut protein.

TABLE E1. EPITOPE baseline demographics and participant characteristics between participants enrolled in the OLE study versus not enrolled

	Enrolled in OLE (n = 266)	Not enrolled in OLE (n = 96)	Total (N = 362)	*P* value
Age (y)				.4513*
n	266	96	362	
Mean (SD)	2.5 (0.9)	2.4 (0.9)	2.5 (0.9)	
Median	2.5	2.4	2.5	
Q1, Q3	1.7, 3.2	1.7, 3.1	1.7, 3.2	
Range	1.0-3.9	1.0-3.9	1.0-3.9	
Sex, n (%)				.8038†
F	84 (31.6)	29 (30.2)	113 (31.2)	
M	182 (68.4)	67 (69.8)	249 (68.8)	
Race, n (%)				.1524†
Missing	9	5	14	
Asian	50 (19.5)	15 (16.5)	65 (18.7)	
Black or African American	0	2 (2.2)	2 (0.6)	
Native Hawaiian or other Pacific Islander	2 (0.8)	0	2 (0.6)	
Other	37 (14.4)	13 (14.3)	50 (14.4)	
White	168 (65.4)	61 (67.0)	229 (65.8)	
Baseline IgE peanut (kU_A/L)				.0018*
n	266	96	362	
Mean (SD)	58.3 (139.2)	77.1 (135.9)	63.3 (138.4)	
Median	11.4	22.6	14.2	
Q1, Q3	3.7, 52.9	7.9, 75.6	4.2, 61.8	
Range	0.7-1031.0	0.9-877.0	0.7-1031.0	
Baseline IgG_4 (mg/L)				.0035*
n	258	96	354	
Mean (SD)	1.6 (5.8)	1.9 (2.9)	1.7 (5.1)	
Median	0.3	0.7	0.4	
Q1, Q3	0.1, 1.0	0.2, 1.7	0.1, 1.1	
Range	0.1-76.7	0.1-14.2	0.1-76.7	
Baseline mean wheal diameter (mm)				.5388*
n	266	96	362	
Mean (SD)	10.6 (3.5)	10.4 (3.5)	10.6 (3.5)	
Median	10.0	9.3	10.0	
Q1, Q3	8.0, 12.5	8.0, 12.3	8.0, 12.5	
Range	5.0-27.5	5.0-28.0	5.0-28.0	
Baseline ED, n (%)				.2799‡
1	6 (2.3)	2 (2.1)	8 (2.2)	
3	16 (6.0)	4 (4.2)	20 (5.5)	
10	25 (9.4)	14 (14.6)	39 (10.8)	
30	31 (11.7)	13 (13.5)	44 (12.2)	
100	79 (29.7)	30 (31.3)	109 (30.1)	
300	109 (41.0)	33 (34.4)	142 (39.2)	
Ongoing MH of asthma, n (%)				.0034†
N	227 (85.3)	69 (71.9)	296 (81.8)	
Y	39 (14.7)	27 (28.1)	66 (18.2)	
Ongoing MH of eczema, n (%)				.5323†
N	55 (20.7)	17 (17.7)	72 (19.9)	
Y	211 (79.3)	79 (82.3)	290 (80.1)	
Ongoing MH of rhinitis, n (%)				.9777†
N	213 (80.1)	77 (80.2)	290 (80.1)	
Y	53 (19.9)	19 (19.8)	72 (19.9)	
Ongoing MH of food allergy other than peanut, n (%)				.5819†
N	86 (32.3)	34 (35.4)	120 (33.1)	
Y	180 (67.7)	62 (64.6)	242 (66.9)	

(continued)

TABLE E1. *(Continued)*

	Enrolled in OLE (n = 266)	Not enrolled in OLE (n = 96)	Total (N = 362)	*P* value
Responder primary analysis (missing = failure imputation), n (%)				<.0001[†]
N	102 (38.3)	64 (66.7)	166 (45.9)	
Y	164 (61.7)	32 (33.3)	196 (54.1)	

Report generated on June 12, 2024.

Percentages are calculated on nonmissing data.

ED, Eliciting dose; *MH*, medical history; *OLE*, open-label extension; *Q1*, first quartile; *Q3*, third quartile; *SD*, standard deviation.

[*]Kruskal-Wallis.

[†]χ^2.

[‡]Wilcoxon.

TABLE E2. Efficacy outcomes for all participants (EPITOPE and the dose-ranging substudy), by treatment arm

	VP100/VP250 + VP250 (N = 205), n (%)	Placebo + VP250 (N = 99), n (%)
Participants who started the M24 peanut FC	195 (95.1)	84 (84.8)
ED ≥1000 mg	n = 189 153 (81.0)	n = 81 51 (63.0)
ED ≥2000 mg	n = 181 112 (61.9)	n = 80 29 (36.3)
Completed DBPCFC without meeting stopping criteria	n = 181 96 (53.0)	n = 80 23 (28.8)
Treatment responder	n = 190 159 (83.7)	n = 81 55 (67.9)

DBPCFC, double-blind, placebo-controlled food challenge; *ED*, eliciting dose; *FC*, food challenge; *M*, month; *VP250*, VIASKIN patch containing 250 μg of peanut protein.

TABLE E3. Grading of local skin reactions, by year and treatment group

Worst grading, n (%)	VP250 + VP250 (N = 175)		Placebo + VP250 (N = 91)	
	Year 1 of treatment	Year 2 of treatment	Year 1 of treatment	Year 2 of treatment
Grade 0	3 (1.7)	18 (10.3)	20 (22.0)	5 (5.5)
Grade 1	61 (34.9)	108 (61.7)	58 (63.7)	44 (48.4)
Grade 2	89 (50.9)	47 (26.9)	12 (13.2)	37 (40.7)
Grade 3	22 (12.6)	2 (1.1)	1 (1.1)	5 (5.5)
Grade 4	0	0	0	0

VP250, VIASKIN patch containing 250 μg of peanut protein.

TABLE E4. Adverse events in participants who enrolled in the OLE study and were initially randomized to placebo, by year of treatment

	Placebo + VP250 (N = 91)	
Adverse event category, n (%)	Year 1 of treatment	Year 2 of treatment
TEAEs	91 (100)	90 (98.9)
Treatment-related TEAEs	87 (95.6)	87 (95.6)
Serious TEAEs	2 (2.2)	2 (2.2)
Treatment-related serious TEAEs	0	1 (1.1)
TEAEs leading to permanent study treatment discontinuation	0	0
Treatment-related local TEAEs	86 (94.5)	85 (93.4)
Severe treatment-related local TEAEs	8 (8.8)	15 (16.5)
Treatment-emergent local AESI	12 (13.2)	2 (2.2)
Anaphylactic reaction	3 (3.3)	6 (6.6)
Treatment-related anaphylactic reaction	0	1 (1.1)
TEAE leading to epinephrine use	7 (7.7)	7 (7.7)
Treatment-related TEAE leading to epinephrine use	0	0

AESI, Adverse event of special interest; *OLE*, open-label extension; *TEAE*, treatment-emergent adverse event; *VP250*, VIASKIN patch containing 250 μg of peanut protein.

TABLE E5. Adverse events in all participants (EPITOPE and dose-ranging substudy), by year and treatment group

	VP100/VP250 + VP250 (N = 205)		Placebo + VP250 (N = 99)	
Adverse event category, n (%)	**Year 1 of treatment**	**Year 2 of treatment**	**Year 1 of treatment**	**Year 2 of treatment**
TEAEs	205 (100)	200 (97.6)	99 (100)	98 (99.0)
Treatment-related TEAEs	205 (100)	183 (89.3)	94 (94.9)	95 (96.0)
Serious TEAEs	17 (8.3)	7 (3.4)	2 (2.0)	3 (3.0)
Treatment-related serious TEAEs	1 (0.5)	0	0	1 (1.0)
TEAEs leading to permanent study treatment discontinuation	0	0	0	1 (1.0)
Treatment-related local TEAEs	204 (99.5)	183 (89.3)	92 (92.9)	93 (93.9)
Severe treatment-related local TEAEs	37 (18.0)	9 (4.4)	8 (8.1)	16 (16.2)
Treatment-emergent local AESI	43 (21.0)	27 (13.2)	13 (13.1)	2 (2.0)
Anaphylactic reaction	15 (7.3)	15 (7.3)	3 (3.0)	7 (7.1)
Treatment-related anaphylactic reaction	4 (2.0)	0	0	1 (1.0)
TEAE leading to epinephrine use	19 (9.3)	12 (5.9)	7 (7.1)	7 (7.1)
Treatment-related TEAE leading to epinephrine use	2 (1.0)	0	0	0

AESI, Adverse event of special interest; *TEAE*, treatment-emergent adverse event; *VP250*, VIASKIN patch containing 250 μg of peanut protein.