Efficacy of Epicutaneous Immunotherapy With Viaskin™ Peanut for 4 to 7-Year-Old Peanut-Allergic Children in a Phase 3 Clinical Trial (PEPITES)

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RATIONALE

- Peanut allergy, one of the most common food allergies, can result in severe, potentially life-threatening reactions[1,2]
- Peanut allergy often develops early in life and is typically lifelong[3-6]
- Evidence is accumulating to suggest that allergic responses may be more modifiable in younger children than in older children.[6-9] As such, prioritizing treatments that target younger age groups is of importance
- Epicutaneous immunotherapy (EPIT) with Viaskin Peanut 250 µg, which is being studied in Phase 3 clinical trials, is a novel approach that aims to induce desensitization by delivering microgram quantities of peanut allergen to the skin[10-13]
- PEPITES, a 12-month Phase 3 clinical trial (NCT02636699), demonstrated that daily EPIT with Viaskin Peanut 250 µg (containing ~1/1000 of a peanut) was statistically superior to placebo in desensitizing peanut-allergic children aged 4 to 11 years based on double-blind, placebo-controlled food challenges (DBPCFCs) post-treatment[10]
- A post hoc analysis of PEPITES participants based on age at study entry was conducted to evaluate the effect of age on treatment response

OBJECTIVE

To characterize the efficacy and safety of daily EPIT with Viaskin Peanut 250 µg in peanut-allergic children aged 4 to 7 years at the time of entry into the PEPITES clinical trial

METHODS

- PEPITES was a randomized, double-blind, placebo-controlled clinical trial designed to assess the efficacy and safety of Viaskin Peanut 250 µg in 356 children aged 4 to 11 years with physician-diagnosed peanut allergy and a baseline eliciting dose (ED) to peanut protein of ≤300 mg **(Figure 1)**[10]
  - Subjects were randomized 2:1 to receive treatment with Viaskin Peanut 250 µg or placebo daily for 12 months
  - DBPCFCs were conducted according to PRACTALL guidelines at Month 0 (baseline) and Month 12 post-treatment using a standardized, blinded food matrix
  - DBPCFCs were discontinued when sufficient objective signs or symptoms met prespecified stopping criteria and required treatment
    - The peanut protein dose at which objective symptoms resulted in ending the food challenge was considered the subject's ED
  - Responder criteria based on EDs achieved at Month 12 are shown in **Table 1**
  - The primary measure of treatment effect was the difference in response rates between active and placebo treatment groups. The primary analysis applied a Wald test at a 2-sided 5% significance level to evaluate a null hypothesis of no difference, and the corresponding 2-sided 95% CI was calculated using Newcombe's method
  - Post hoc analyses examining efficacy and safety in subjects aged 4 to 7 years at study entry was performed using logistic regression with main effects for treatment and age as a continuous variable and their interaction. Once a treatment by age interaction was observed whereby efficacy was shown to decrease with age, the age ranges which optimized the treatment effect was then investigated

Figure 1. PEPITES Study Design

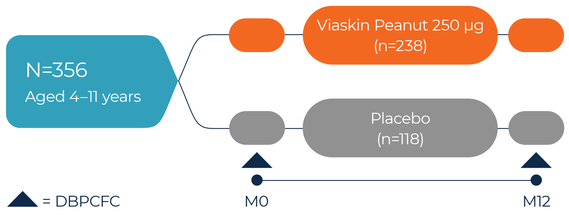


Table 1. Responder Criteria Based on EDs at Month 0 and Month 12

ED at Month 0	ED at Month 12 required for responder status
≤10 mg	≥300 mg
>10 to ≤300 mg	≥1000 mg

RESULTS

Study Population and Baseline Characteristics

- A total of 190 subjects comprised the 4 to 7-year-old subgroup: 125 received Viaskin Peanut 250 µg and 65 received placebo **(Table 2)**
- The distribution of baseline EDs in the 4 to 7-year-old Viaskin Peanut 250 µg and placebo recipients were similar, with a median ED of 100 mg in each group

Table 2. Demographics and Baseline Characteristics in the 4 to 7-Year-Old Population

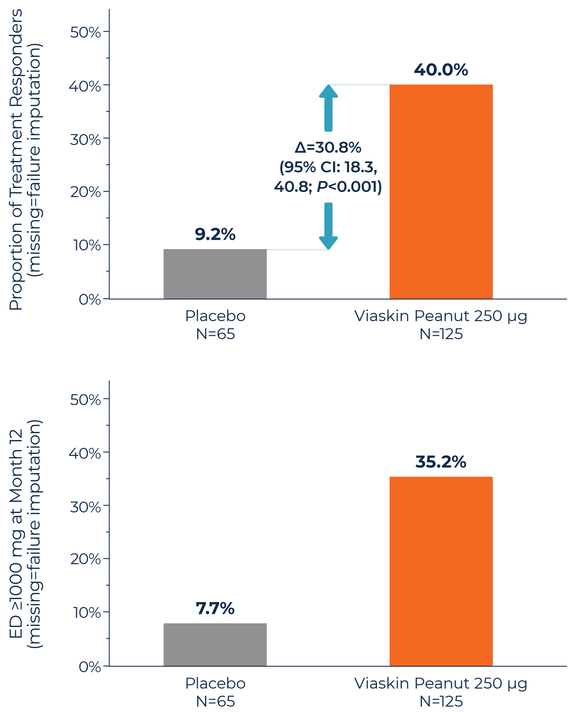
Category	Viaskin Peanut 250 µg (N =125)	Placebo (N =65)
Age (years)		
Median (Q1, Q3)	6 (5, 7)	6 (4, 7)
Gender, n (%)		
Female	45 (36.0%)	28 (43.1%)
Male	80 (64.0%)	37 (56.9%)
Race/Ethnic Origin, n (%)		
White	105 (84.0%)	50 (76.9%)
Asian	9 (7.2%)	4 (6.2%)
Black or African American	0 (0.0%)	2 (3.1%)
Other	11 (8.8%)	9 (13.8%)
Peanut-specific IgE, kU_A/L		
Median (Q1, Q3)	71.6 (17.1, 189.7)	99.6 (28.5, 247.3)
Peanut-specific IgG4, mg/L		
Median (Q1, Q3)	0.71 (0.38, 1.59)	0.77 (0.23, 1.53)
Peanut protein eliciting dose, mg		
Median (Q1, Q3)	100 (30, 300)	100 (30, 300)
Baseline eliciting dose, n (%)		
1 mg	0 (0.0%)	1 (1.5%)
3 mg	3 (2.4%)	2 (3.1%)
10 mg	18 (14.4%)	7 (10.8%)
30 mg	12 (9.6%)	12 (18.5%)
100 mg	52 (41.6%)	23 (35.4%)
300 mg	40 (32.0%)	20 (30.8%)
Medical history, n (%)		
Asthma	52 (41.6%)	23 (35.4%)
Eczema/atopic dermatitis	57 (45.6%)	35 (53.8%)
Allergic rhinitis	59 (47.2%)	33 (50.8%)
Food Allergy(ies) other than peanut	70 (56.0%)	34 (52.3%)

IgE=immunoglobulin E; IgG4=immunoglobulin G4; kU_A/L=kilounits of antibody per liter; Q1=quartile 1; Q3=quartile 3.

RESPONSE RATES

- In the total PEPITES population of 356 subjects aged 4–11 years, the responder rate for those in the Viaskin Peanut 250 µg arm (n=238) was 35.3% compared with 13.6% in the placebo arm (n=118)
  - The risk difference was 21.7% (95% CI: 12.4–29.8; *P*<0.001)
- By post hoc analysis, a larger treatment effect in subjects aged 4–7 years who received Viaskin Peanut 250 µg versus placebo was demonstrated **(Figure 2)**
  - 40.0% of subjects in the Viaskin Peanut 250 µg arm were responders compared with 9.2% in the placebo arm, with a risk difference of 30.8% (95% CI: 18.3–40.8; *P*<0.001)
  - In comparison, the difference in the proportion of treatment responders between Viaskin Peanut and placebo subjects aged 8–11 years was 11.2% (95% CI: -3.4–23.4)
- Furthermore, among subjects aged 4–7 years, 35.2% in the Viaskin Peanut 250 µg arm versus 7.7% in the placebo arm reached an ED of ≥1000 mg at Month 12 **(Figure 2)**

Figure 2. Response Rates by Response Criteria in Children Aged 4–7 Years



SAFETY

- The safety profile in the subgroup of children aged 4–7 years **(Table 3)** was consistent with that observed in the overall 4 to 11-year-old PEPITES population
  - The majority of subjects in both treatment arms experienced treatment-emergent adverse events (TEAEs) which were mainly mild to moderate in severity
- In the 4 to 7-year-old subgroup analysis, TEAEs considered related to treatment were reported in 60% of subjects in the Viaskin Peanut 250 µg arm and 40% in the placebo arm
- Serious adverse events (AEs) considered related to Viaskin Peanut 250 µg were reported in 2 subjects (1.6%) in the Viaskin Peanut 250 µg arm in the subgroup analysis, both of which were anaphylactic reactions

Table 3. Safety Profile According to Treatment Group in Children Aged 4–7 Years

	Viaskin Peanut 250 µg (n=125)		Placebo (n=65)	
Category (Any:)	n	(%)	n	(%)
TEAEs	120	(96)	58	(89.2)
Mild TEAEs	116	(92.8)	53	(81.5)
Moderate TEAEs	62	(49.6)	29	(44.6)
Severe TEAEs	6	(4.8)	2	(3.1)
Serious TEAEs	6	(4.8)	2	(3.1)
TEAEs considered related to IP	75	(60)	26	(40)
• TEAEs reported as related	65	(52)	21	(32.3)
• TEAEs reported as probably related	19	(15.2)	2	(3.1)
• TEAEs reported as possibly related	13	(10.4)	7	(10.8)
TEAEs considered unrelated to IP	116	(92.8)	57	(87.7)
• TEAEs reported as unlikely related	30	(24)	22	(33.8)
• TEAEs reported as unrelated	114	(91.2)	56	(86.2)
Serious TEAEs considered related to IP	2	(1.6)	0	0
TEAEs leading to permanent IP discontinuation	3	(2.4)	0	0
TEAEs leading to temporary IP discontinuation	18	(14.4)	6	(9.2)
TEAEs leading to death	0	0	0	0
Severe TEAEs considered related to IP	4	(3.2)	1	(1.5)
IP-induced local TEAEs	71	(56.8)	20	(30.8)
Severe IP-induced local TEAEs	4	(3.2)	1	(1.5)
Systemic allergic TEAE considered related to IP	6	(4.8)	0	0
TEAEs leading to an epinephrine intake	13	(10.4)	1	(1.5)
• TEAEs considered related to IP	5	(4)	0	0
• TEAEs considered unrelated to IP	8	(6.4)	1	(1.5)

IP=investigational product; medDRA=Medical Dictionary for Regulatory Activities; n=number of subjects experiencing at least 1 event.

Subjects were counted once per category. Serious AEs related to DBPCFCs were excluded. Viaskin Peanut 250 µg-induced local TEAEs are defined as TEAEs considered related to IP with a MedDRA High Level Term equal to "Application and instillation site reactions." Methodology of identification of systemic allergic AEs was based on the Standardized MedDRA Queries "Anaphylactic reaction."

CONCLUSIONS

- This post hoc analysis of the Phase 3 PEPITES clinical trial supports the concept that greater gains in desensitization may be achieved in younger vs older children, consistent with other studies supporting increased plasticity of the immune response earlier in childhood[7,8]
- A significant treatment effect was observed in subjects aged 4–7 years, with a difference in the proportion of responders between active and placebo of 30.8% (*P*<0.001); the lower bound of the 95% CI of this difference (18.3%), was above the 15% pre-specified criterion for a positive study as defined in PEPITES
  - This treatment effect in younger subjects was observed to be approximately 3 times greater than that seen in subjects aged 8–11 years
- Although the results reported here are subject to the limitations of post-hoc analyses, the findings warrant further investigation
- These findings are also consistent with recent topline results from the EPITOPE study, a Phase 3 study which examined safety and efficacy of Viaskin Peanut in 1 to 3-year-old peanut allergic children, and met its primary efficacy endpoint with 67% Viaskin Peanut 250 µg-treated participants meeting the responder criteria versus 33.5% placebo participants (risk difference=33.5%; 95% CI: 22.4–44.5, *P*<0.001)
- These combined data contribute to our understanding of the potential for epicutaneous immunotherapy for the treatment of peanut allergy

REFERENCES

1. Gupta RS, et al. *Pediatrics.* 2018;142(6):e20181235. **2.** Deschildre A, et al. *Clin Exp Allergy.* 2016;46(4):610-620. **3.** Sicherer SH, et al. *J Allergy Clin Immunol Pract.* 2020;8(6):1854-1864. **4.** Savage J, et al. *J Allergy Clin Immunol Pract.* 2016;4(2):196-204. **5.** Peters RL, et al. *J Allergy Clin Immunol.* Published online May 10, 2022. doi:10.1016/j.jaci.2022.04.008 **6.** Du Toit G, et al. *N Engl J Med.* 2015;372(9):803-813. **7.** Jones SM, et al. *Lancet.* 2022;399(10322):359-371. **8.** Vickery BP, et al. *J Allergy Clin Immunol.* 2017;139(1):173-181.e8. **9.** Chan ES, et al. *Ann Allergy Asthma Immunol.* 2020;124(5):479-486. **10.** Fleischer DM, et al. *JAMA.* 2019;321(10):946-955. **11.** Fleischer DM, et al. *J Allergy Clin Immunol.* 2020;146(4):863-874. **12.** Pongracic JA, et al. *J Allergy Clin Immunol Pract.* 2022;10(7):1864-1873 e10. **13.** Wang J, Sampson H. *Pediatr Allergy Immunol.* 2018;29(4):341-349.

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