Reactions due to Accidental Peanut Consumption During Epicutaneous Immunotherapy for Peanut Allergy in Toddlers

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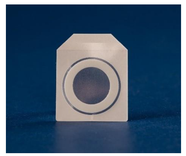
Rationale

- Despite following strict allergen avoidance, peanut-allergic children often experience allergic reactions due to accidental peanut consumption (APC)[1]
- One goal of food allergy immunotherapy is to reduce the likelihood of having an allergic reaction following an accidental exposure to the allergen[2]
- Viaskin™, a patch-based technology platform, is currently being investigated for the treatment of peanut allergy (**Figure 1**). This novel approach to epicutaneous immunotherapy (EPIT) involves the daily administration of a patch (VP250) containing 250 µg (~1/1000 of 1 peanut) to intact skin in order to induce desensitization
  - The safety and efficacy of 12 months of EPIT with VP250 in children have been previously investigated in phase 3 randomized clinical trials[3,4]
- Previous results of EPIT with VP250 in children aged 1-3 years in the EPITOPE study demonstrated reduced rates of allergic reactions due to APC over 1 year of treatment, compared with placebo[4]

Figure 1. VP250 Patch



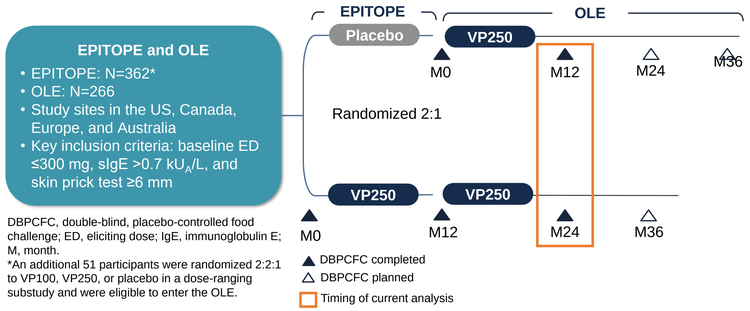
Objective

- To further characterize accidental reactions in peanut-allergic children aged 1-3 years, we examined APC rates through the first year of the EPITOPE open-label extension (OLE) period

Methods

- EPITOPE was a randomized, double-blind, placebo-controlled trial assessing the efficacy and safety of VP250 in peanut-allergic toddlers aged 1-3 years[4] (**Figure 2**)
  - 362 participants were randomized 2:1 to 12 months of VP250 or placebo. In addition, a dose-ranging substudy of EPITOPE randomized 51 participants 2:2:1 to VP250, Viaskin Peanut 100 µg (VP100), or placebo
  - All participants who completed Month 12 DCPCFC were eligible to enroll in the OLE to receive up to 3 years of VP250 treatment

Figure 2. EPITOPE and OLE Study Design



DBPCFC, double-blind, placebo-controlled food challenge; ED, eliciting dose; IgE, immunoglobulin E; M, month.
*An additional 51 participants were randomized 2:2:1 to VP100, VP250, or placebo in a dose-ranging substudy and were eligible to enter the OLE.

- Data on APCs occurring during EPITOPE and the OLE were collected prospectively
  - Families reported on known APCs, whether they resulted in an allergic reaction, as well as any related symptoms
- Rates of APCs and APCs resulting in an allergic reaction were analyzed by treatment groups (active vs placebo) and over time, up to Year 1 of the OLE (corresponding to 2 years of treatment)
- For comparisons between groups, Kruskal-Wallis tests were used for continuous data and chi-square tests for discrete data. A logit link generalized linear model with binomial distribution was used to assess the association between time on treatment and probability of an APC resulting in a reaction

Key Points

- These results demonstrate EPIT with VP250 may help reduce the risk of an allergic reaction following APC in young children, with increased time on treatment associated with a lower likelihood of experiencing a reaction upon APC
- No increase in APC events was observed during the OLE period, suggesting participants were not more likely to engage in risk-taking behavior on active treatment
- These results show that VP250 may help to offer real-world protection from reactions due to APC, with increased clinical benefit over time

Results

- Over 2 years, 62 participants reported an APC vs 351 participants who did not (**Table 1**)
  - 44/413 (11%) participants reported an APC during EPITOPE and 21/304 (7%) during Year 1 of the OLE (3 participants reported an APC during both EPITOPE and the OLE)
  - Participants with reported APC who did not have an accompanying allergic reaction had a lower baseline peanut-specific immunoglobulin E (IgE); however, no difference in baseline eliciting dose (ED) was observed across groups

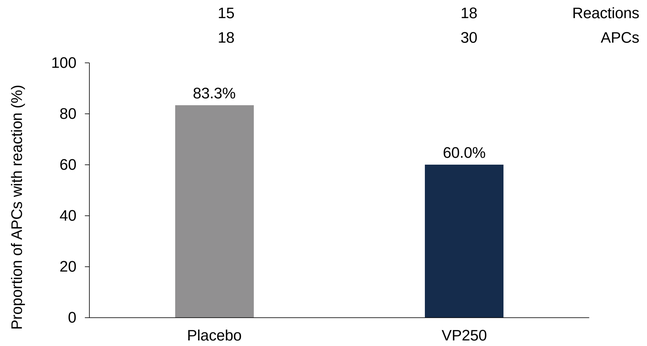
Table 1. Baseline Demographics and Patient Characteristics

	APC no reaction (N=20)	APC with reaction (N=42)	No APC (N=351)	*P* value
Age, y				0.0427[1]
Mean	2.2	2.8	2.5	
Median	2.0	3.1	2.5	
Q1, Q3	1.4, 3.3	2.0, 3.5	1.8, 3.3	
Sex, %				0.1382[2]
Female	5 (25.0)	8 (19.0)	117 (33.3)	
Male	15 (75.0)	34 (81.0)	234 (66.7)	
Baseline ED, %				0.1419[2]
1	2 (10.0)	0 (0.0)	6 (1.7)	
3	0 (0.0)	1 (2.4)	20 (5.7)	
10	2 (10.0)	8 (19.0)	33 (9.4)	
30	2 (10.0)	3 (7.1)	42 (12.0)	
100	7 (35.0)	15 (35.7)	104 (29.6)	
300	7 (35.0)	15 (35.7)	146 (41.6)	
Baseline mean wheal diameter, mm				0.0016[1]
Mean	8.8	9.7	10.7	
Median	8.0	8.5	10.0	
Q1, Q3	7.0, 11.3	7.0, 11.5	8.0, 12.5	
Baseline IgE peanut, kU$_A$/L				0.0034[1]
Median	3.4	17.1	15.9	
Q1, Q3	1.4, 15.0	3.7, 55.1	5.4, 67.3	

IgE, immunoglobulin E.
[1]Kruskal-Wallis test. [2]Chi-square test.

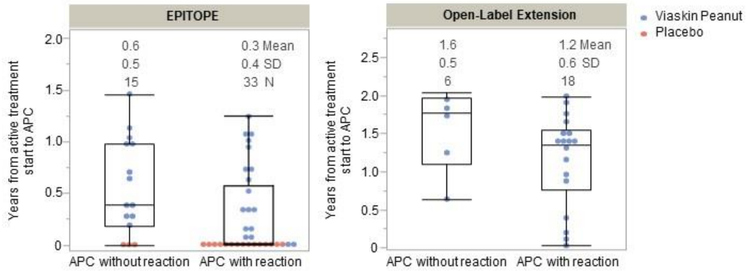
- In EPITOPE, proportions of participants with APCs between treatment groups were similar (15 placebo [12%] vs 29 active-treated [10%], Pearson chi-square test *P*=0.64)
- However, a lower proportion of APCs resulted in an allergic reaction among active-treated participants vs placebo (**Figure 3**); 60% of the APCs in active-treated participants were associated with a reaction (18/30; 29 participants, including 1 with two APCs both resulting in a reaction), whereas most APCs among placebo participants resulted in a reaction (15/18, 83.3%, 15 participants, including 2 participants with two APCs resulting in a reaction and 1 participant with two APCs both without a reaction)

Figure 3. Proportion of APCs Resulting in a Reaction During EPITOPE



- Results out to Year 1 of the OLE period demonstrated that increased time on treatment was associated with a reduced likelihood of APCs resulting in a reaction. **Figure 4** shows the distribution of time on active treatment between those who had a reaction vs those who did not. Incorporating this data in a generalized linear model (described in methods), it was determined that before treatment, the probability of an APC resulting in a reaction was 79% and reduced to 53% after 2 years of treatment

Figure 4. Impact of Duration of Active Treatment on Likelihood of a Reaction Following an APC



References: 1. Capucilli P et al. Food reactions during avoidance. *Ann Allergy Asthma Immunol.* 2020;124(5):459-465. 2. Greenhawt M et al. Understanding caregiver goals, benefits, and acceptable risks of peanut allergy therapies. *Ann Allergy Asthma Immunol.* 2018;121(5):575-579. 3. Fleischer DM et al. Effect of epicutaneous immunotherapy vs placebo on reaction to peanut protein ingestion among children with peanut allergy: the PEPITES randomized clinical trial, *JAMA*. 2019;321(10):946-955. 4. Greenhawt M et al. Phase 3 trial of epicutaneous immunotherapy in toddlers with peanut allergy. *N Engl J Med.* 2023;388(19):1755-1766.

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Viaskin™ is an investigational agent, and it has not yet been approved by the US FDA or any other regulatory authority.