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EPITOPE Study Results: Phase 3, Randomized, Double-blind, Placebo-controlled Study of Epicutaneous Immunotherapy in Peanut-allergic Toddlers

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Disclosures

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- Member, Joint Task Force on Allergy Practice Parameters
- Member of Nutricia, DBV, Novartis, Sanofi, Aquestive, Prota, Allergy Therapeutics, GSK, ALK-Abello, AstraZeneca
- Consultant, Aquestive
- Received honorarium from ImSci, MedLearning Group, RMSI, multiple state and local allergy societies, and the CSACI
- Member of the Medical Advisory team for the Allergy and Asthma Foundation of America and the International Association for Food Protein Enterocolitis (nonfinancial)
- Has received support from K08-HS024599 (Agency for Healthcare Research and Quality)
- Member of AAAAI Practice/Diagnostics/Therapeutics, Anaphylaxis, Adverse Reaction to Food, Vaccine committees
- Co-chair, AAAAI Primary Prevention of Food Allergy Working Group; Co-chair, AAAAI Oral Immunotherapy Office-based Practice Working Group
- Member, NIAID Expert Panel on early introduction of peanut to prevent peanut allergy
- Senior Associate Editor, *Annals of Allergy, Asthma, and Immunology*
- International Advisory Board, Lancet Child and Adolescent Health
- Editorial board: *Medscape Pediatrics*; *Infectious Diseases in Children, Pediatric Allergy and Immunology*
- Member, Scientific Advisory Council, National Peanut Board
- Member, EAACI Task Forces on Nutrition and Immunomodulation; Outcomes of Food Allergy Therapies
- Member, Core Outcome Measures for Food Allergy (COMFA) consortium, COST Action
- Member, Brighton Criteria Collaboration Case Definition for Anaphylaxis working group 2.0

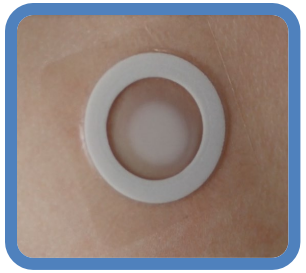
Study Rationale

Rationale

- There is currently no approved treatment for peanut allergy in children younger than 4 years, demonstrating a strong unmet need for an available treatment[1]
- Studies have shown early oral introduction of peanuts in children could reduce the risk of developing peanut allergy, suggesting the **immune system in infancy may be particularly responsive to immunomodulation**[2]

Epicutaneous immunotherapy (EPIT) with VP250 for peanut allergy[3,4]

- EPIT with investigational **VP250 is a novel patch-based approach** involving administration of microgram quantities of peanut allergen to intact skin **to induce desensitization**
- Single, daily patch applied to children's backs; first patch applied at study site, subsequent applications at home
- Each patch contains **250 µg peanut protein** (~1/1000 of 1 peanut kernel); **no up-dosing**
- **No restrictions based on illness or daily activities** required in clinical trial protocol



Objective

- **To assess the efficacy and safety of EPIT with VP250 among children 1 to <4 years of age with peanut allergy**

1. Kim EH, Burks AW. *Allergy*. 2020;75:1337-1346. 2. Du Toit G et al. *N Engl J Med*. 2015;372(9):803-813. 3. Tilles SA et al. *Ann Allergy Asthma Immunol*. 2018;121(2):145-149. 4. Sampson HA et al. *JAMA*. 2017;318:1798-1809.
Epicutaneous immunotherapy and Viaskin™ (VP250) are under clinical investigation and have not been approved for marketing by any health or regulatory authority.

EPITOPE Study Design: Multicenter, Randomized, Double-blind, Placebo-controlled Phase 3 Trial

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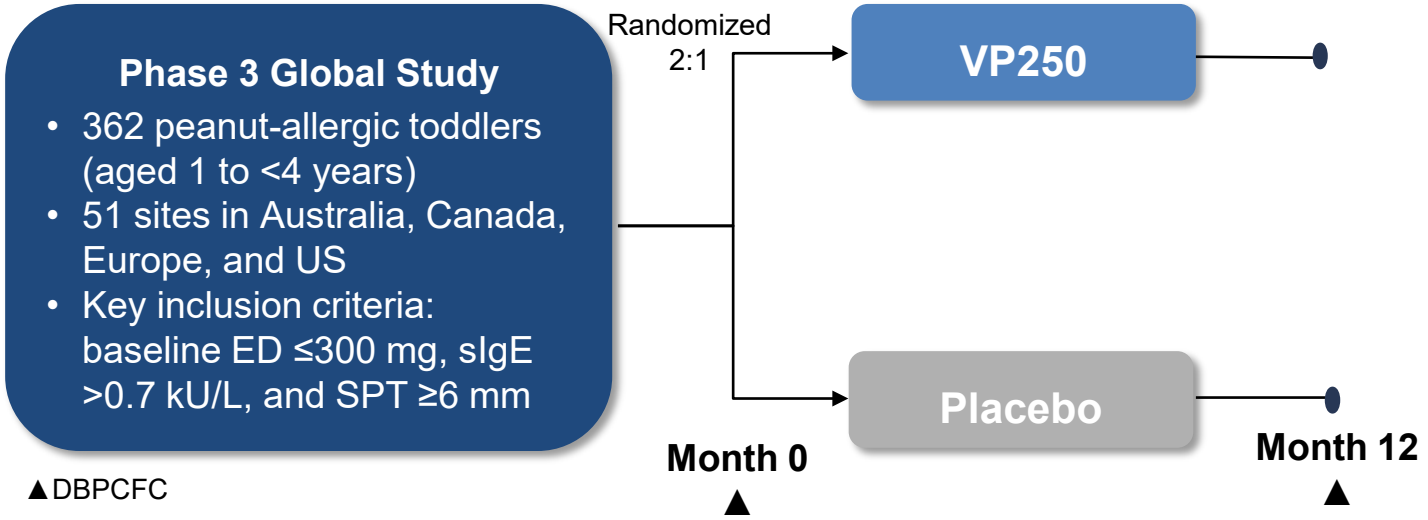
- Participants **randomized 2:1 to VP250 or placebo** daily for 12 months
- Month 0 and Month 12 DBPCFC conducted per PRACTALL guidelines[1]
  - Eliciting dose (ED) = dose at which signs/symptoms met the prespecified stopping criteria



Primary Efficacy Endpoint

- Percent difference in responders between VP250 and placebo, defined as M12 ED:
  - ≥1000 mg (if baseline ED >10 mg)

    or
  - ≥300 mg (if baseline ED ≤10 mg)

Additional Endpoints

- % reaching ED ≥1000 mg at M12
- % reaching CRD ≥3444 mg at M12
- Change in severity of symptoms elicited during DBPCFC from baseline to M12
- Safety as assessed by treatment-emergent adverse event rates, including anaphylaxis

CRD, cumulative reactive dose; DBPCFC, double-blind, placebo-controlled food challenge; sIgE, specific immunoglobulin E; SPT, skin prick test.

1. Sampson HA et al. *J Allergy Clin Immunol*. 2012;130(6):1260-1274.

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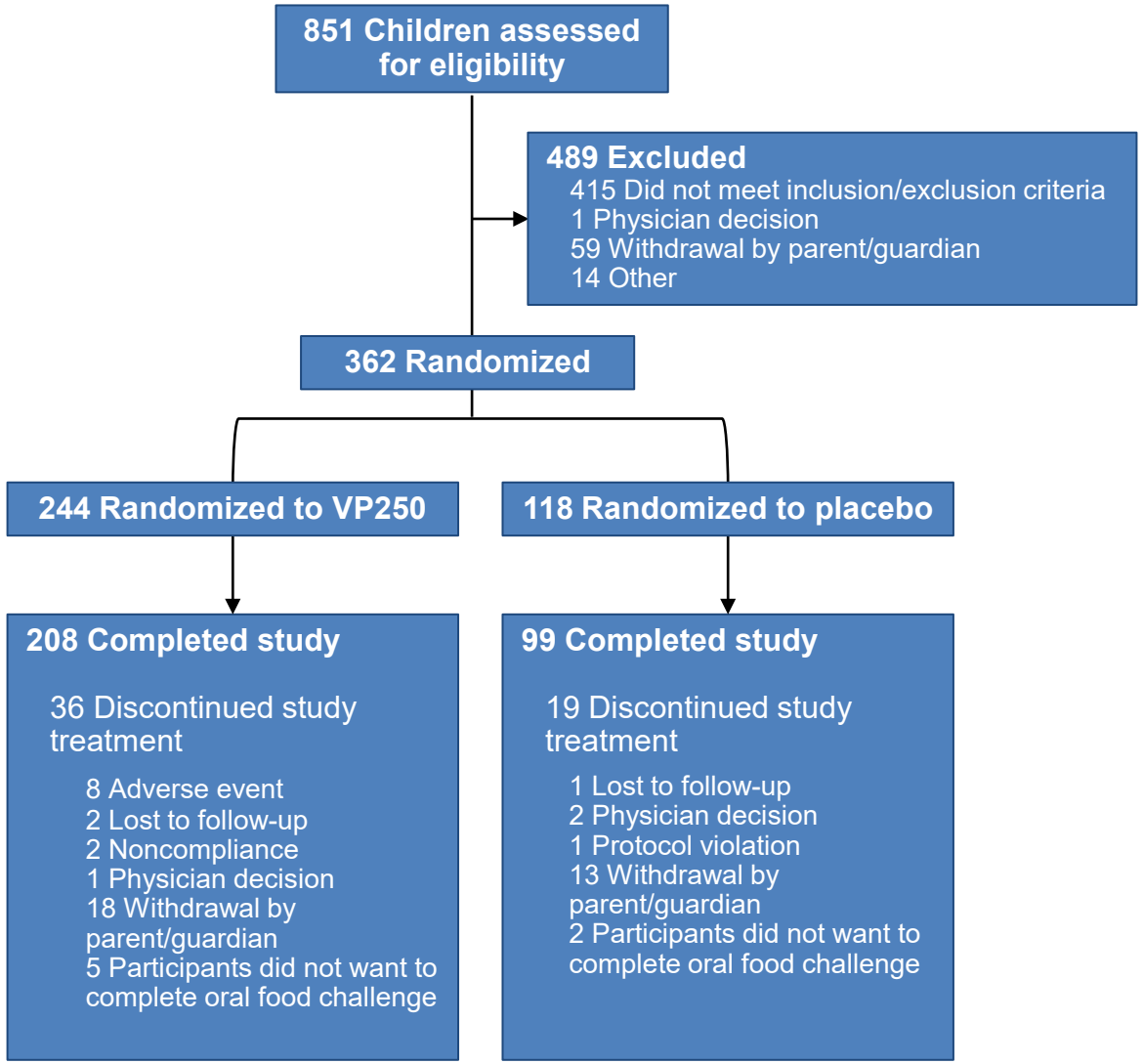
Participant Flow and Characteristics



Category	VP250 (N=244)	Placebo (N=118)
Age, years, median (Q1, Q3)	2.50 (1.75, 3.20)	2.40 (1.70, 3.10)
Age, category, n (%)		
1 year	83 (34.0)	43 (36.4)
2 years	76 (31.1)	38 (32.2)
3 years	85 (34.8)	37 (31.4)
Gender, n (%)		
Male	165 (67.6)	84 (71.2)
Female	79 (32.4)	34 (28.8)
Peanut-specific IgE, kU_A/L		
Median (Q1, Q3)	13.4 (4.04, 65.85)	14.75 (4.86, 52.11)
Range	0.8-971.0	0.7-1031.0
Peanut protein eliciting dose, mg		
Median (Q1, Q3)	100 (30, 300)	100 (30, 300)
Range	1-300	1-300
Medical history, n (%)		
Asthma	39 (16.0)	27 (22.9)
Eczema/atopic dermatitis	194 (79.5)	96 (81.4)
Allergic rhinitis	49 (20.1)	23 (19.5)
Food allergy(ies) other than peanut	161 (66.0)	81 (68.6)

- Baseline characteristics and demographics were **balanced between treatment groups**

IgE, immunoglobulin E; Q, quartile.
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Efficacy Results: Primary Endpoint

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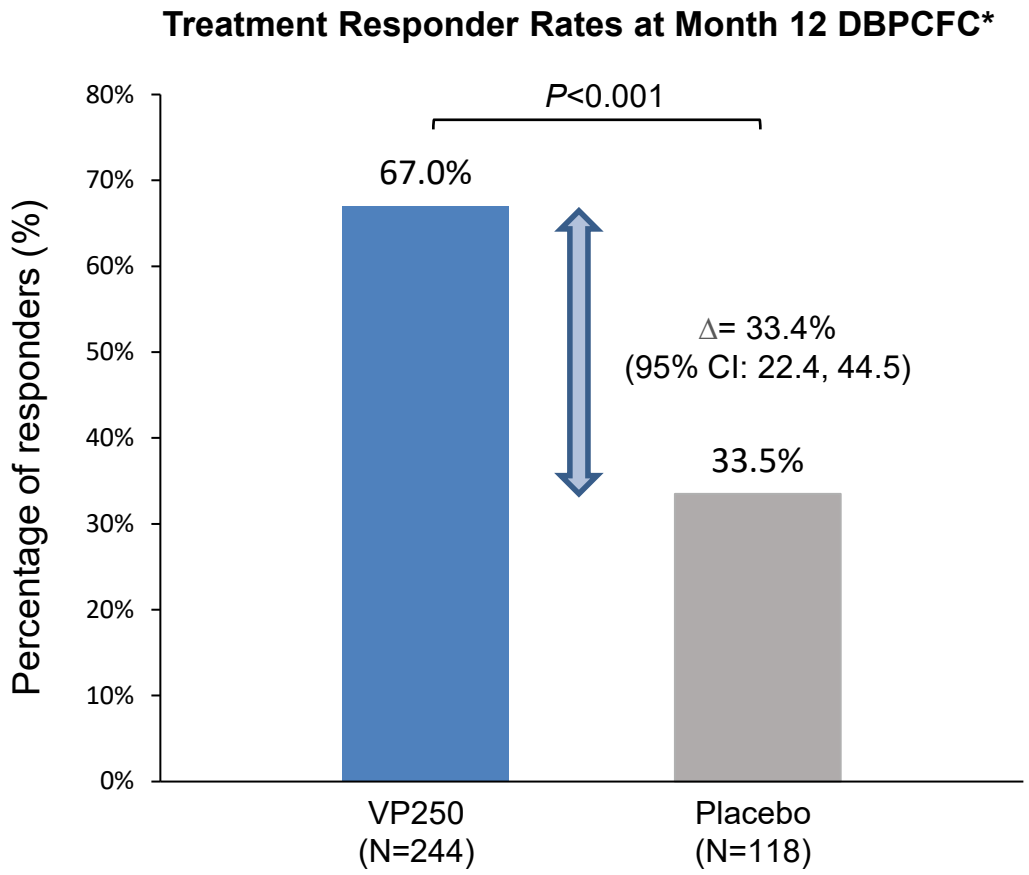
- At Month 12, a significantly larger percentage of participants achieved the **primary endpoint** in the **VP250 group vs placebo, 67.0% vs 33.5%,** respectively, with a **difference of 33.4%** (95% CI: 22.4, 44.5; *P*<0.001)



DBPCFC, double-blind, placebo-controlled food challenge; ED, eliciting dose.
*Primary analysis included all participants per the randomized assignment; assessed using a 2-sided Farrington-Manning 95% CI for the difference in response rates between the randomized groups. Treatment responder defined as M12 ED ≥1000 mg (if baseline ED >10 mg) or ≥300 mg (if baseline ED ≤10 mg).
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Primary Efficacy Endpoint: Prespecified Sensitivity Analyses

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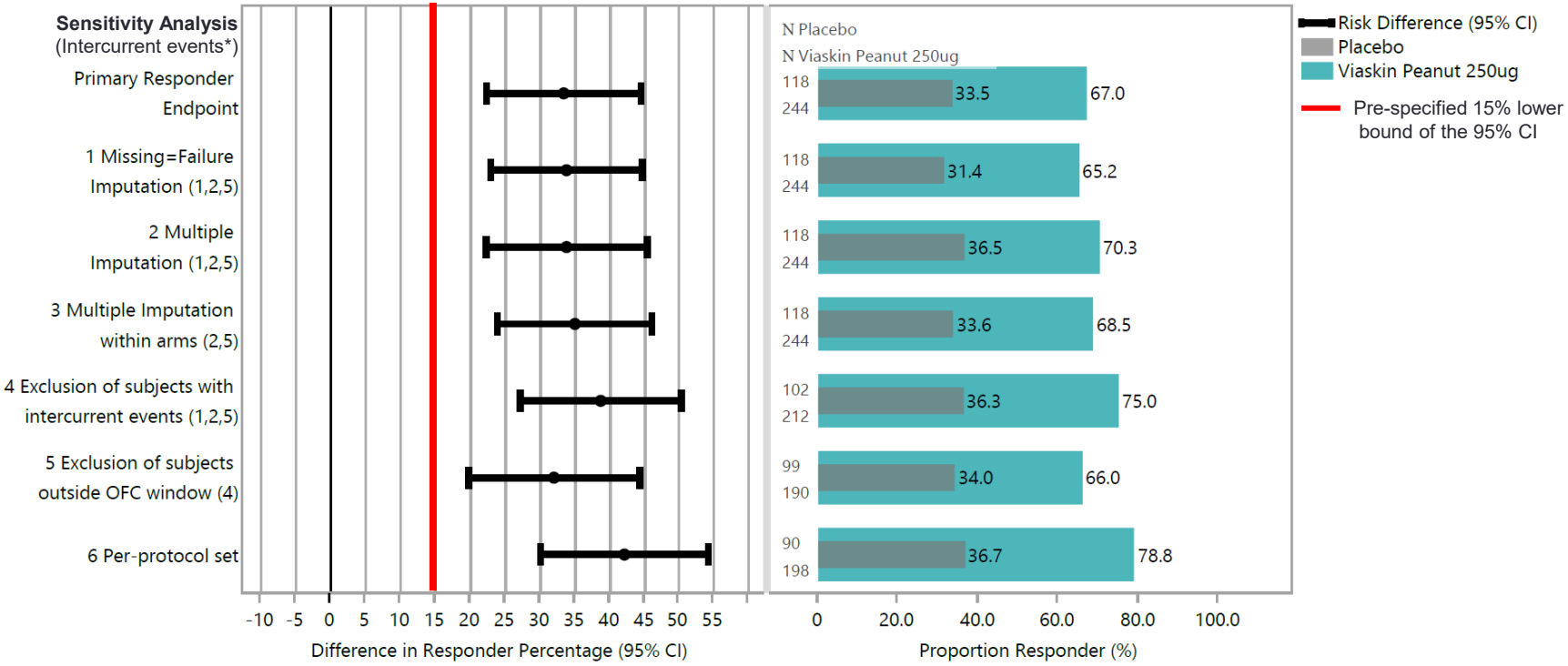
- All prespecified sensitivity analyses regarding the primary endpoint were statistically significant and demonstrated the **consistency of the treatment effect**



OFC, oral food challenge.
*Intercurrent events defined as: 1. early treatment discontinuation before 12 months; 2. participants refusing the peanut DBPCFC at Month 12; 3. peanut DBPCFC at Month 12 initiated but not finished; 4. DBPCFC at Month 12 falls outside the recommended time window; 5. discontinuation after 12 months with DBPCFC at Month 12 missing.
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Key Secondary Efficacy Endpoints: ED and CRD

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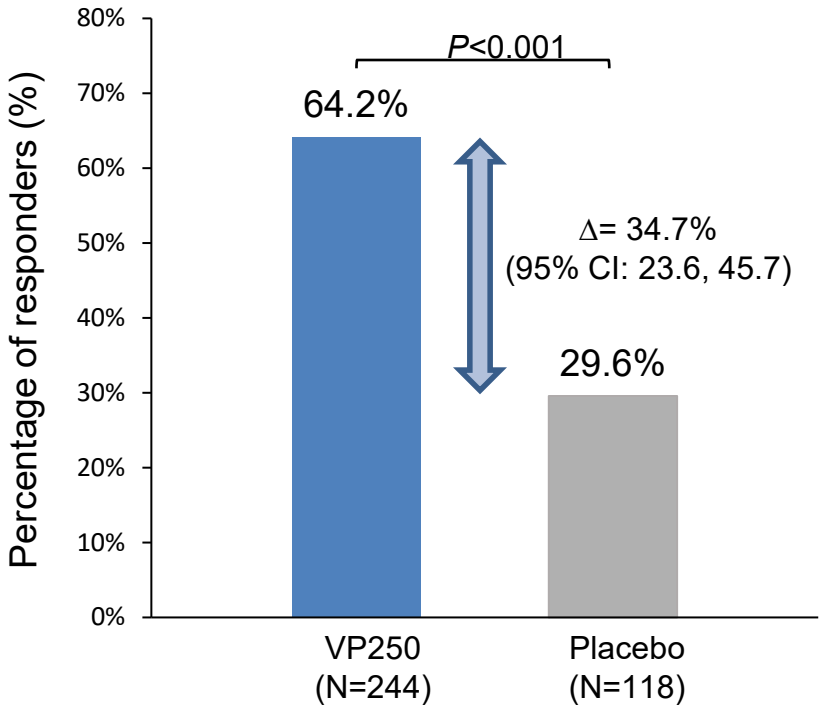
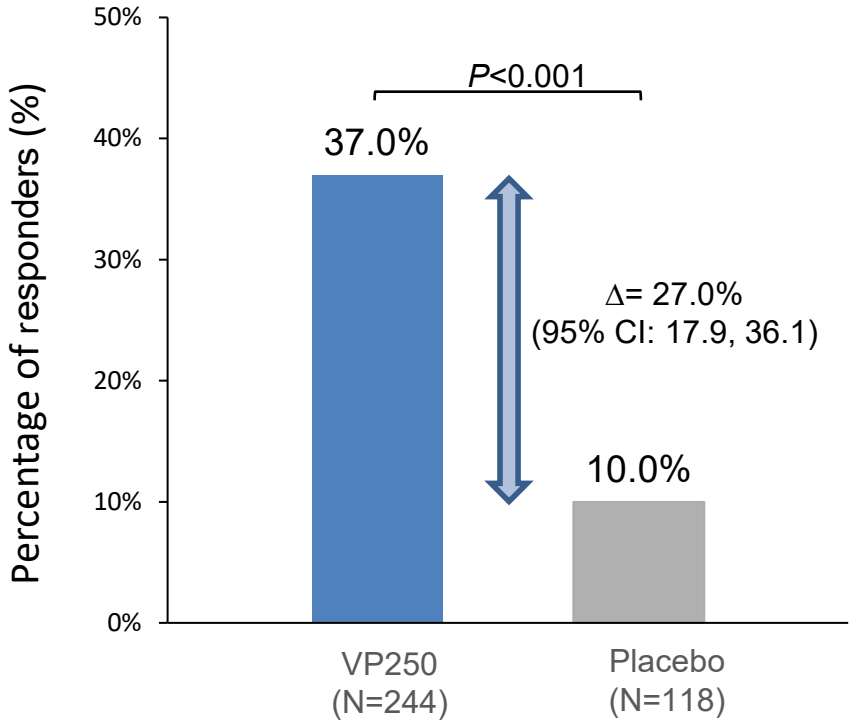
- At Month 12, regardless of baseline ED, a **statistically significantly larger percentage of participants in the VP250 vs placebo group achieved an ED ≥1000 mg or CRD ≥3444 mg**

ED ≥1000 mg at Month 12



CRD ≥3444 mg* at Month 12



CRD, cumulative reactive dose; ED, eliciting dose.
*At Month 12 DBPCFC, 1000 mg and 2000 mg doses added to DBPCFC for a maximum possible cumulative dose of 3444 mg. Participants with CRD ≥3444 mg include those who reached a CRD=3444 mg and participants who did not meet the stopping criteria at any dose during the M12 DBPCFC.
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Key Efficacy Endpoint: Reaction Severity[1,2]

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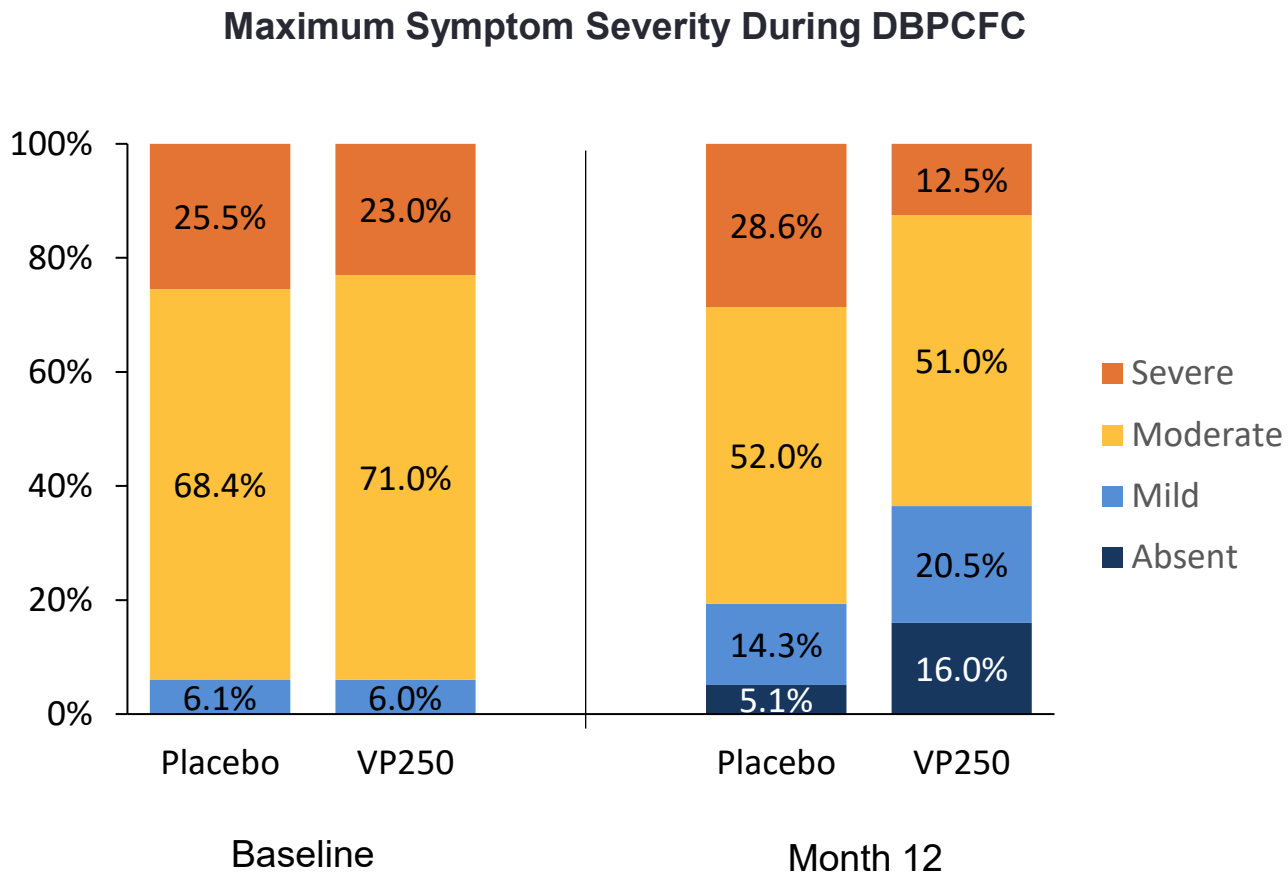
- Severity of reactions during DBPCFC was graded by the investigator according to PRACTALL[2] scoring as 0 (absent), 1 (mild), 2 (moderate) or 3 (severe); distribution of maximum severity at baseline and Month 12 was compared between treatment groups
- At baseline DBPCFC, the proportions of maximum reaction severity were balanced between groups
- **At Month 12**, the distribution of maximum symptom severity was **significantly shifted toward less severe symptoms in the VP250 group** relative to placebo (*P*<0.001)
- This **shift toward a reduction in reaction severity coincided with an increase in ED** and a greater proportion of responders in the VP250 vs placebo group



DBPCFC, double-blind, placebo-controlled food challenge; ED, eliciting dose.

1. Brown-Whitehorn T et al. Presented at ACAAI 2022. P183. 2. Sampson HA et al. *J Allergy Clin Immunol*. 2012;130(6):1260-1274.

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Safety Results

- Most participants in both the VP250 and placebo arms experienced TEAEs, which consisted **primarily of mild to moderate local skin reactions that decreased in frequency with time**
- **Serious adverse events (SAEs)** were reported by **8.6% in the VP250 group vs 2.5% in the placebo group**, of which 1 SAE in the VP250 group was considered treatment-related
- **Anaphylaxis considered related to treatment** was reported in 4 participants (**1.6%**), all in the VP250 arm
  - All events were mild or moderate in severity
  - Three (1.2%) participants were treated with a single dose of epinephrine, and 1 participant was treated with no epinephrine
- **Treatment compliance** was high and comparable between groups, with an overall mean rate of **97.0%**

TEAE, treatment-emergent adverse event.
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Safety Results *(cont)*

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	VP250 (N=244)		Placebo (N=118)	
TEAEs Related to Investigational Product	n	(%)	n	(%)
Any TEAE	244	100	112	94.9
Serious TEAE	1	0.4	0	0
Severe TEAE	57	23.4	11	9.3
Moderate TEAE	208	85.2	59	50.0
Mild TEAE	238	97.5	110	93.2
System organ class preferred term				
Administration-site conditions	243	99.6	111	94.1
Skin and subcutaneous disorders	74	30.3	25	21.2
Immune system disorders	7	2.9	0	0
Anaphylactic reaction	4	1.6	0	0
Non-anaphylactic hypersensitivity reaction	3	1.2	0	0
Eye disorders	5	2.0	0	0
Infections and infestations	3	2.0	0	0
Gastrointestinal disorders	6	2.5	0	0
Respiratory, thoracic, and mediastinal disorders	11	4.5	1	0.8
Psychiatric disorders	6	2.5	0	0
Blood and lymphatic disorders	1	0.4	1	0.8
Nervous system disorders	1	0.4	1	0.8
TEAEs leading to temporary discontinuation	31	12.7	2	1.7
TEAEs leading to permanent discontinuation	7	2.9	0	0
TEAEs leading to epinephrine use	3	1.2	0	0
TEAEs leading to systemic or inhaled corticosteroid use	6	2.5	1	0.8
TEAEs leading to topical corticosteroid use	233	95.5	70	59.3

- The most reported **treatment-related TEAEs** were application-site reactions, including **erythema, pruritus, and swelling**
- **Seven (2.9%)** participants in the **VP250 group** and none in the placebo group **discontinued due to treatment-related TEAEs**

TEAE, treatment-emergent adverse event; n, number of participants experiencing at least 1 event; N, number of participants in treatment group.
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Conclusions

- This pivotal, phase 3 trial of children 1 to <4 years of age with peanut allergy met its primary endpoint with **significantly more participants meeting responder criteria in the VP250 group vs placebo** (**67.0% vs 33.5%**, respectively; difference: 33.4%; 95% CI: 22.4, 44.5 [*P*<0.001])
- 12 months of daily EPIT with VP250 was associated with **significant increases in ED and CRD**, as well as **decreases in reaction severity**, compared to placebo
- The **safety profile was consistent with prior VP250 studies** and demonstrated that EPIT with VP250 was well tolerated with low rates (1.6%) of treatment-related anaphylaxis and low (2.9%) discontinuations due to treatment-related TEAEs
- This is the first study of peanut desensitization in children <4 years of age using a non–oral immunotherapy route; **results from this study suggest VP250 may be a potential treatment option for young children with peanut allergy**

CRD, cumulative reactive dose; TEAE, treatment-emergent adverse event.
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