POOLED SAFETY DATA FROM PHASE 3 STUDIES OF EPICUTANEOUS IMMUNOTHERAPY FOR PEANUT ALLERGY IN CHILDREN AGED 4–11 YEARS

#097

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RATIONALE

- Peanut allergy causes substantial concerns for patients, caregivers, and families due to the risk of accidental ingestion and potentially severe reactions[1-4]
- The emergence of immunotherapeutic approaches to managing peanut allergy provides the possibility of mitigating reactions to accidental ingestion; the safety of these therapies will be important when considering their overall benefit:risk profile[1,2]
- Epicutaneous immunotherapy with investigational Viaskin™ Peanut 250 µg, which has been 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[1-3,5]
- The results of phase 3 studies (PEPITES [NCT02636699]; PEOPLE [NCT03013517]; REALISE [NCT02916446]) have evaluated the overall safety, tolerability, and efficacy of Viaskin Peanut 250 µg[1-3]

OBJECTIVE

- To assess the pooled safety of Viaskin Peanut 250 µg in peanut-allergic children treated for up to 36 months in phase 3 clinical studies

METHODS

- Analyses were performed on databases from the PEPITES, PEOPLE, and REALISE phase 3 studies and included subjects treated for up to 36 months with Viaskin Peanut 250 µg
- PEPITES was a 12-month, randomized, double-blind, placebo-controlled (RDBPC), multicenter trial; PEOPLE was an open-label extension to PEPITES[1,2]
  - Subjects aged 4 to 11 years at screening with physician-diagnosed peanut allergy were randomized 2:1 to receive Viaskin Peanut 250 µg or placebo daily
  - At the end of the 12-month RDBPC period in PEPITES, subjects who completed the study were offered the option of enrolling in PEOPLE, which was designed to evaluate long-term efficacy and safety of Viaskin Peanut 250 µg for up to 5 years of active treatment
- REALISE assessed the safety of Viaskin Peanut 250 µg in peanut-allergic children aged 4 to 11 years under conditions that approximated anticipated real-world use (where diagnosis is commonly made based on history and confirmatory skin/serum testing, without a double-blind placebo-controlled food challenge)[3]
  - The REALISE trial consisted of 2 parts: a 6-month RDBPC treatment period followed by an open-label active treatment period with Viaskin Peanut 250 µg, for a total of up to 36 months of active treatment
  - REALISE placebo subjects who received Viaskin Peanut 250 µg after the 6-month RDBPC period were included in this pooled analysis
- Safety outcomes assessed in the pooled analysis were investigator-assessed treatment-emergent adverse events (TEAEs), serious TEAEs, local cutaneous reactions, and systemic allergic TEAEs considered related to Viaskin Peanut 250 µg
- Analyses included number of subject-years (SY) of treatment and rates of events per 100 SY
- For direct comparisons of safety in placebo- and Viaskin Peanut 250 µg–treated subjects, adverse events (AEs) during the first 6 months of the PEPITES trial and the RDBPC treatment period of REALISE were analyzed

RESULTS

Subjects

- A total of 749 subjects were included in the overall pooled safety analyses, including 630 subjects (1689.3 SY) treated with Viaskin Peanut 250 µg for up to 36 months
- During the 6-month RDBPC period, these 749 subjects were randomized as 532 subjects treated with Viaskin Peanut 250 µg and 217 with placebo
  - Baseline demographics were similar between treatment groups (**Table 1**)

Table 1. Baseline Demographics by Initial Treatment Group (at Time of Randomization)

		VIASKIN PEANUT 250 µg (n=532)	PLACEBO (n=217)
Age (years)	Mean (SD)	7.3 (2.17)	7.2 (2.29)
	Median (min, max)	7.0 (4, 11)	7.0 (4, 11)
	Q1, Q3	5.0, 9.0	5.0, 9.0
Sex	Male	313 (58.8)	134 (61.8)
	Female	219 (41.2)	83 (38.2)
Peanut-specific IgE (kU/L)	Mean (SD)	167.63 (194.92)	200.17 (249.234)
	Median (min, max)	86.75 (0.78, 1515.00)	98.20 (1.03, 1907.00)
	Q1, Q3	36.95, 240.50	40.20, 268.00
Peanut-specific IgG4 (mg/L)	Mean (SD)	1.24 (1.703)	1.48 (2.624)
	Median (min, max)	0.71 (0.07, 13.70)	0.740 (0.07, 26.90)
	Q1, Q3	0.29, 1.43	0.29, 1.56
SPT: Mean wheal diameter (mm)	Mean (SD)	12.2 (4.31)	12.5 (4.52)
	Median (min, max)	11.0 (5.0, 43.0)	11.5 (6.0, 33.5)
	Q1, Q3	9.0, 14.0	9.0, 15.0
SPT: Longest wheal diameter (mm)	Mean (SD)	15.1 (5.75)	15.3 (6.15)
	Median (min, max)	14.0 (7.0, 59.0)	14.0 (6.0, 44.0)
	Q1, Q3	11.0, 18.0	11.0, 19.0

Data presented are number (%) of subjects unless indicated otherwise.
IgE=immunoglobulin E; IgG4=immunoglobulin G4; SD=standard deviation; SPT=skin prick test.

Comparison of TEAEs in Viaskin Peanut 250 µg–Treated vs Placebo-Treated Subjects During RDBPC Treatment Period (Pooled, 6-Month Data From PEPITES and REALISE)

- Most TEAEs were mild to moderate in both groups (Viaskin Peanut 250 µg, 2282/2293 [99.5%]; placebo, 731/732 [99.9%]) (**Table 2**)
- 1.1% of Viaskin Peanut 250 µg subjects and 1.8% of placebo subjects experienced serious TEAEs
- Permanent discontinuations due to TEAEs were low in both groups (Viaskin Peanut 250 µg, 1.1%; placebo, 0%)

Table 2. Overview of TEAEs in Subjects Receiving Viaskin Peanut 250 µg or Placebo in Pooled PEPITES and REALISE Studies From Months 0–6 (RDBPC Treatment Period)

CATEGORY	VIASKIN PEANUT 250 µg (n=532) N (%); NUMBER OF EVENTS	PLACEBO (n=217) N (%); NUMBER OF EVENTS
TEAEs	472 (88.7); 2293	175 (80.6); 732
Mild TEAEs	443 (83.3); 1892	163 (75.1); 634
Moderate TEAEs	200 (37.6); 390	58 (26.7); 97
Severe TEAEs	10 (1.9); 11	1 (0.5); 1
Serious TEAEs	6 (1.1); 6	4 (1.8); 4
TEAEs considered related	172 (32.3); 322	31 (14.3); 46
Serious TEAEs considered related	4 (0.8); 4	0
TEAEs leading to permanent discontinuation	6 (1.1); 9	0
TEAEs leading to temporary discontinuation	62 (11.7); 92	13 (6.0); 19
TEAEs leading to death	0	0
Viaskin Peanut 250 µg–induced local TEAEs[a]	129 (24.2); 198	19 (8.8); 26

[a]Induced local TEAEs are defined as TEAEs considered related to treatment with a MedDRA High Level Term equal to "Application and instillation site reactions."
TEAEs were categorized as related when investigator assessed as "possibly related," "probably related," or "related," and categorized as unrelated when assessed as "unlikely" or "unrelated."
MedDRA=Medical Dictionary for Regulatory Activities; TEAE=treatment-emergent adverse event.

Overview of TEAEs in Pooled Phase 3 Studies

- **Table 3** provides an overview of TEAEs occurring in the pooled population of subjects treated with Viaskin Peanut 250 µg
- TEAEs occurred in 98.4% of Viaskin Peanut 250 µg–treated subjects, with 758.5 events per 100 SY
  - The rate of serious TEAEs was 2.2 per 100 SY, with 0.4 per 100 SY treatment-related serious TEAEs
  - Systemic allergic TEAEs occurred at a rate of 5.3 per 100 SY
- Anaphylactic reactions occurred at a rate of 3.7 events per 100 SY in Viaskin Peanut 250 µg–treated subjects

Table 3. Overview of TEAEs in Subjects Receiving Viaskin Peanut 250 µg in Pooled Phase 3 Studies

	VIASKIN PEANUT 250 µg n=630, NSY=1689.3		
	n[a] (%)	NUMBER OF EVENTS	RATE (events per 100 SY)[b]
TEAEs	620 (98.4)	12,813	758.5
Severe TEAEs	77 (12.2)	373	22.1
Serious TEAEs	30 (4.8)	38	2.2
TEAEs considered treatment related	577 (91.6)	4108	243.2
Serious TEAEs considered treatment related	5 (0.8)	6	0.4
TEAEs leading to permanent discontinuation	19 (3)	34	2
TEAEs leading to death	0	0	0
Systemic allergic TEAEs[c]	60 (9.5)	89	5.3

[a]Number of subjects with at least 1 event.
[b]Rate=100 × number events/NSY.
[c]Identified through the algorithm of the Anaphylactic Reaction SMQ.
TEAEs were categorized as related when investigator assessed as "possibly related," "probably related," or "related," and categorized as unrelated when assessed as "unlikely" or "unrelated."
MedDRA=Medical Dictionary for Regulatory Activities; NSY=number of subject-years; TEAE=treatment-emergent adverse event; SMQ=Standardized MedDRA Queries.

Treatment-Related TEAEs in Pooled Phase 3 Studies

- The most common treatment-related TEAEs in Viaskin Peanut 250 µg–treated subjects were administration site reactions, occurring in 561 (89%) subjects (224.6 per 100 SY) (**Table 4**)
- Treatment-related anaphylactic reactions occurred at a rate of 1.6 events per 100 SY in Viaskin Peanut 250 µg–treated subjects
- Treatment-related TEAEs during Viaskin Peanut 250 µg administration were lower in the third year of treatment than in Years 1 and 2

Table 4. Investigator-Assessed Treatment-Related Administration Site Conditions Occurring in ≥10% of Viaskin Peanut 250 µg–Treated Subjects in Pooled Phase 3 Studies

APPLICATION SITE CONDITIONS	VIASKIN PEANUT 250 µg n=630, NSY=1689.3		
	n[a] (%)	NUMBER OF EVENTS	RATE (events per 100 SY)[b]
Erythema	459 (72.9)	3792	224.5
Pruritus	398 (63.2)	1384	81.9
Swelling	213 (33.8)	527	31.2
Eczema	89 (14.1)	115	6.8
Papules	86 (13.7)	139	8.2
Urticaria	73 (11.6)	209	12.4

[a]Number of subjects with at least 1 event.
[b]Rate=100 × number events/NSY.
Adverse events were classified into System Organ Class and Preferred Term using Version 20.1 of MedDRA.
MedDRA=Medical Dictionary for Regulatory Activities; NSY=number of subject years.

CONCLUSIONS

- This analysis evaluated safety outcomes in a large pooled database derived from 3 multicenter phase 3 trials (PEPITES, PEOPLE, and REALISE), encompassing 630 subjects who received treatment with Viaskin Peanut 250 µg for up to 36 months
- These data demonstrate that treatment with Viaskin Peanut 250 µg for up to 36 months in peanut-allergic children was generally safe and well tolerated
  - The most common treatment-related TEAEs were local skin reactions
  - There was a low occurrence of systemic allergic TEAEs and anaphylactic reactions
- A well-tolerated treatment approach with a favorable benefit:risk profile could afford those with peanut allergy a valuable therapeutic option for managing this serious condition

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