Changes in Biomarkers During Epicutaneous Immunotherapy for Peanut Allergy in Toddlers

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Rationale

- The double-blind, placebo-controlled food challenge (DBPCFC) is currently the gold standard for the diagnosis of peanut allergy and monitoring patients undergoing immunotherapy[1]
- However, due to factors limiting availability and willingness to complete food challenges,[1] changes in biomarkers remain an important tool in food allergy management, and are often used as a monitoring tool as part of routine follow-up and as evidence of immune modulation[2]
- VIASKIN®, a patch-based technology platform, is currently being investigated for the treatment of peanut allergy. This novel approach to epicutaneous immunotherapy (EPIT) involves the administration of a peanut patch (VP250) containing 250 µg peanut protein to intact skin to induce desensitization[3-7]
- Phase 3 studies have demonstrated that 12 months of daily EPIT with VP250 was statistically superior to placebo in desensitizing children with peanut allergy[3,7]
  - EPITOPE (NCT03211247) included 362 toddlers aged 1 through 3 years and demonstrated responder rates of 67% in the VP250 arm vs 33.5% in the placebo arm (difference: 33.4%; 95% CI: 22.4, 44.5 [*P*<0.001])[7]
  - Several VP250 studies have also demonstrated biomarker changes (decreases in peanut-specific [ps] immunoglobulin [IgE] and skin prick test [SPT] wheal size and a corresponding decrease in ps-immunoglobulin G4 [IgG4]) during EPIT with VP250[7,8]
- It remains to be known whether 1 year of placebo treatment preceding VP250 affects biomarker response

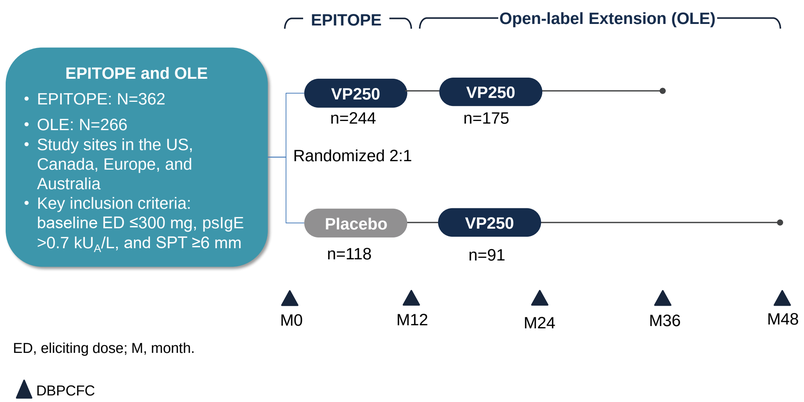
Objective

- To assess changes in psIgE, psIgG4, and SPT wheal size after 12 months of VP250 in participants in an open-label extension (OLE) study who were initially randomized to placebo for 12 months in EPITOPE

Methods

- Participants who completed the EPITOPE trial were eligible to enroll in the OLE study to receive up to 3 years of treatment with VP250 (**Figure 1**)

Figure 1. Study Design Diagram



ED, eliciting dose; M, month.

▲ DBPCFC

- psIgE, psIgG4, and SPT were measured at Month (M) 12, M15, M18, and M24 during EPITOPE and the OLE
- Results are provided for participants with available assessments at all timepoints

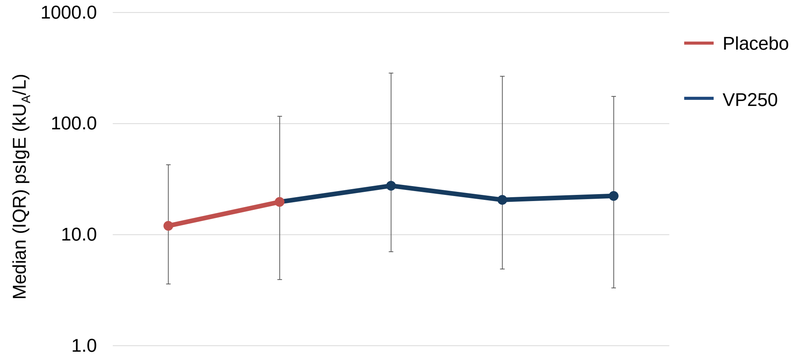
Key Points

- Following 1 year of placebo treatment, 1 year of EPIT with VP250 resulted in decreases in psIgE and SPT wheal size, as well as increases in psIgG4, beginning 3 months after VP250 treatment initiation, indicating immune modulation resulting from treatment
- These changes were similar to results seen in participants initially randomized to VP250 in EPITOPE[7] and are consistent with other allergen immunotherapies[9]

Results

- Of 118 EPITOPE placebo participants, 91 entered the OLE and received VP250
- While receiving placebo (n=47), median psIgE increased between EPITOPE baseline and M12
- After starting VP250 in the OLE, psIgE initially increased at M15, then decreased at M18 and M24 (**Figure 2**)

Figure 2. Trend of psIgE in the Placebo+VP250 Group

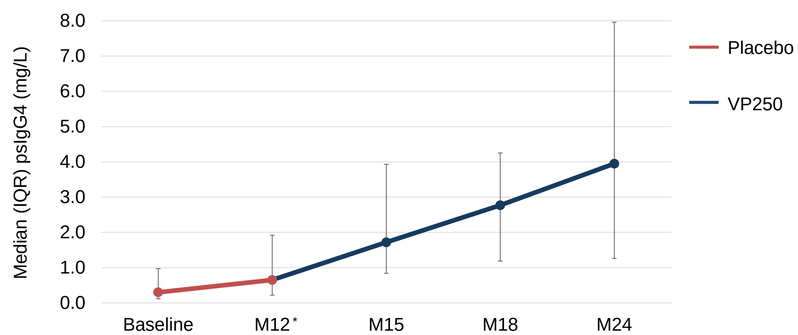


	Baseline	M12*	M15	M18	M24
Median	12.00	19.70	27.60	20.60	22.34
Min	0.74	0.19	0.16	0.16	0.10
Max	1031.00	705.00	1646.11	1950.00	1792.41

*Initiation of active treatment.
IQR, interquartile range; min, minimum; max, maximum.

- Median psIgG4 levels (n=48) increased slightly from baseline to M12 while receiving placebo. After starting active treatment during the OLE, greater increases in IgG4 were observed, which continued through M24 (**Figure 3**)

Figure 3. Trend of psIgG4 in the Placebo+VP250 Group

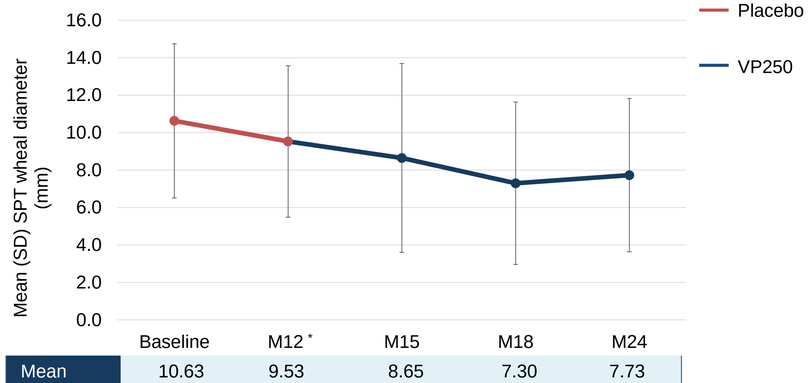


	Baseline	M12*	M15	M18	M24
Median	0.30	0.65	1.72	2.77	3.95
Min	0.07	0.07	0.14	0.18	0.07
Max	16.30	13.00	16.00	18.00	29.00

*Initiation of active treatment.
IQR, interquartile range; min, minimum; max, maximum.

- Mean SPT wheal size (n=61) remained relatively unchanged between baseline and M12 while receiving placebo, then decreased by M24 during the OLE (**Figure 4**)

Figure 4. Trend of SPT Wheal Size in the Placebo+VP250 Group



	Baseline	M12*	M15	M18	M24
Mean	10.63	9.53	8.65	7.30	7.73
SD	4.11	4.05	5.04	4.34	4.09

*Initiation of active treatment.
SD, standard deviation.

- Similar trends of decreases in psIgE and wheal size were observed after the first year of treatment with VP250 in EPITOPE, and the increases in psIgG4 remained (**Table 1**)

Table 1. Trend of psIgE, psIgG4, and SPT Wheal Size in VP250 EPITOPE Group After 1 Year of Treatment

Biomarker	Baseline	M12	Absolute Δ
Median psIgE (kU_A/L)	13.40	13.44	-0.71
Median psIgG4 (mg/L)	0.38	4.51	3.58
Mean SPT wheal diameter (mm)	10.54	7.09	-3.45

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VIASKIN® peanut patch is an investigational agent, and it has not yet been approved by the US FDA or any other regulatory authority.