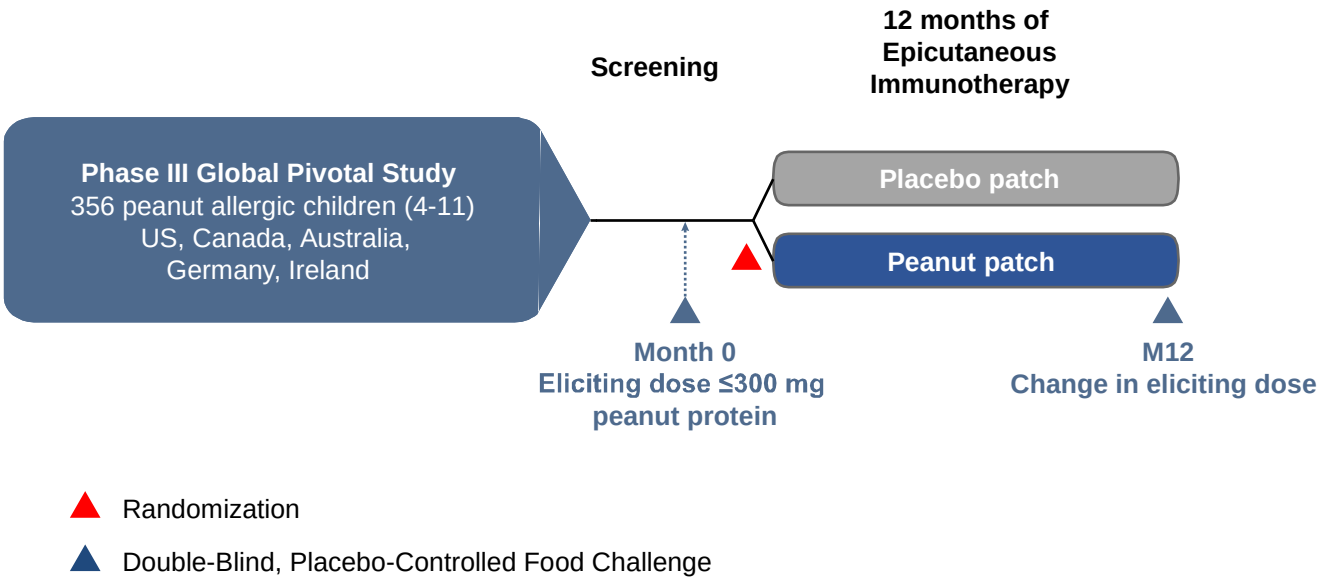
Supplementary Online Content

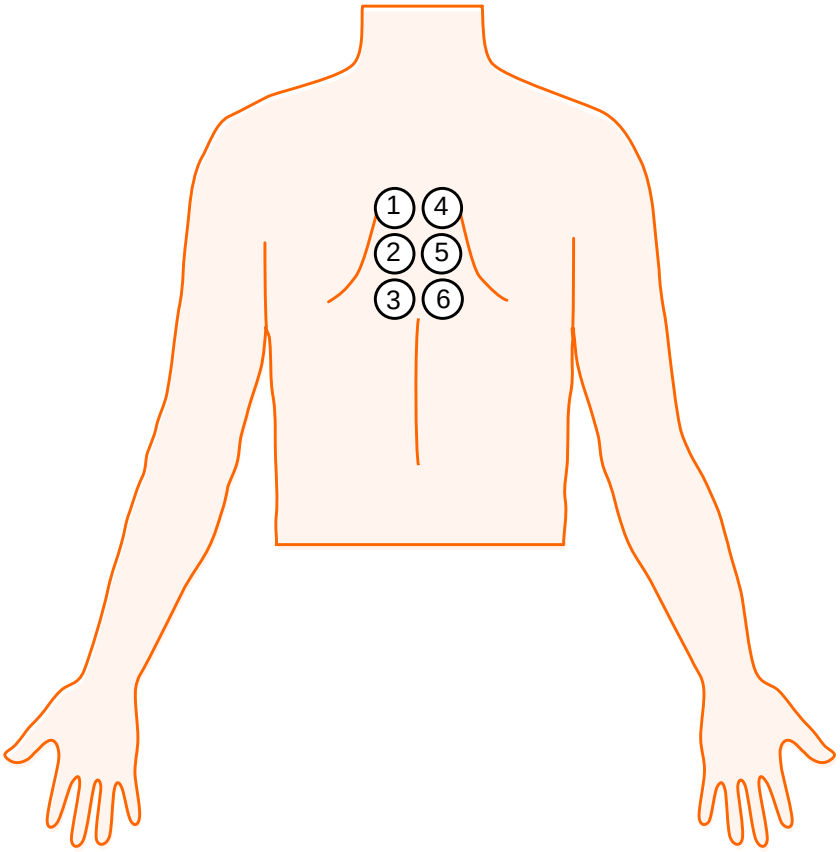
Fleischer DM, Greenhawt M, Sussman G, et al. Effect of epicutaneous immunotherapy vs placebo on reaction to peanut protein ingestion among children with peanut allergy: the PEPITES randomized clinical trial. *JAMA*. doi:10.1001/jama.2019.1113

This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1. Study Design



eFigure 2. Interscapular Patch Placement

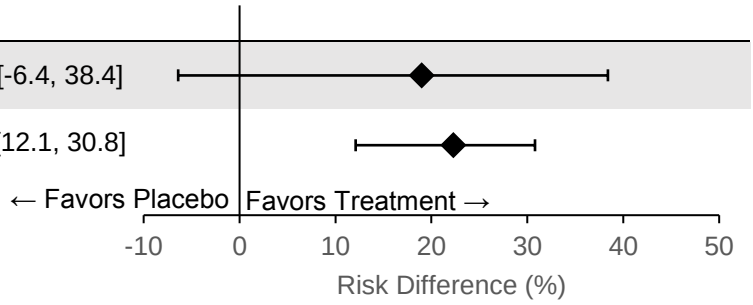


The location of patch application was the interscapular area of the back of the participants. There were 6 zones for applying the patch, 3 on each side of the spine. The first patch was applied on zone 1, the second on zone 2 (after removal of the first patch), and so forth, until all 6 zones had been used. After zone 6, dosing restarted with zone 1 and continued sequentially, as described.

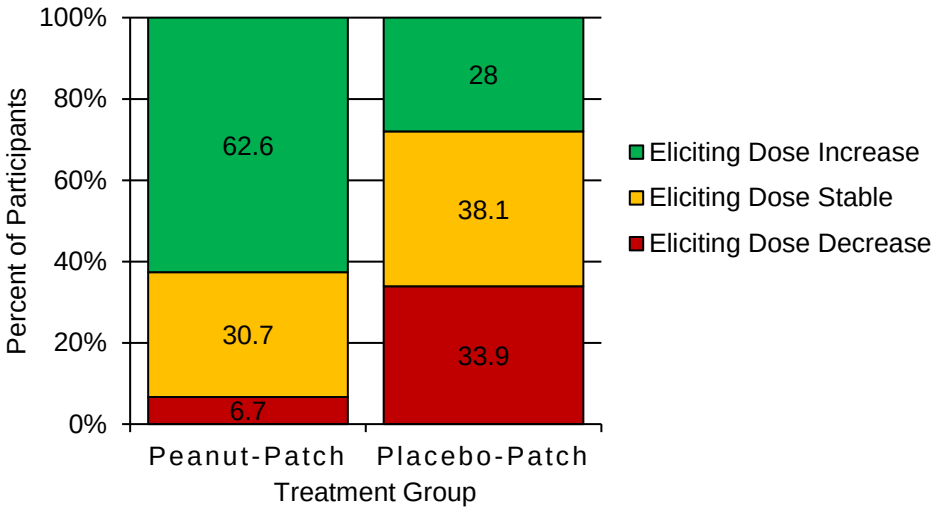
eFigure 3. (A) Differences in Response Rates Between the Peanut-Patch and Placebo-Patch Groups; (B) Distribution in Eliciting Dose Changes From Baseline at Month 12 (ITT Population)

A.

Analysis	Peanut-Patch % (n/N)	Placebo-Patch % (n/N)	Risk Difference (%)	CI
Low–eliciting dose subgroup	39.0 (16/41)	20.0 (4/20)	19.0	[-6.4, 38.4]
High–eliciting dose subgroup	34.5 (68/197)	12.2 (12/98)	22.3	[12.1, 30.8]



B.



Abbreviations: CI, 95% confidence interval.

Response Rates Within Baseline Eliciting Dose Subgroups

Response rates based on eliciting dose changes with peanut patch were numerically greater than with placebo patch in both subgroups: 39% in the low–eliciting dose subgroup (n=41) and 34.5% in the high–eliciting dose subgroup (n=197). The effect size in favor of peanut patch was comparable across subgroups (19% in the low–eliciting dose subgroup, 22.3% in the high–eliciting dose subgroup), but not statistically significant in the low–eliciting dose subgroup (eFigure 3A).

Eliciting Dose and Cumulative Reactive Dose

In a post-hoc analysis, 62.6% of participants in the peanut-patch group compared to 28% in the placebo-patch group experienced an increased eliciting dose at 12 months, and 53.1% of participants on active treatment increased their baseline eliciting dose from ⩽ 100mg to ⩾300mg, vs only 19% on placebo-patch. Conversely, 33.9% of participants in the placebo-patch group vs 6.7% in the peanut-patch group demonstrated an eliciting dose decrease (eFigure 3B). Median baseline cumulative reactive dose of peanut protein was 144mg (Q1, Q3: 44, 444) in both groups (eTable 3). After 12 months, the estimated median cumulative reactive dose difference between the peanut-patch and placebo-patch groups was 297mg.

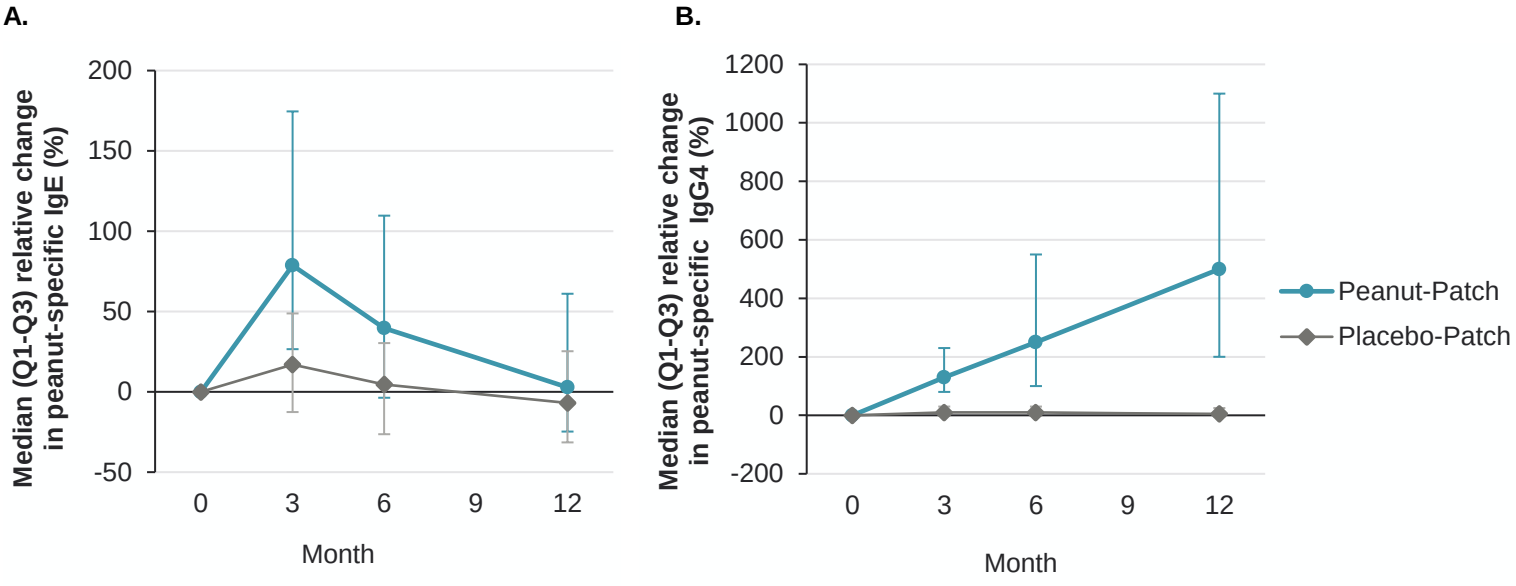
Immunologic Correlates

Median relative changes from baseline in peanut-specific immunologic markers over time for both groups are shown in eFigure 4. The median increase from baseline in peanut-specific IgE was greater in the peanut-patch vs placebo-patch group, respectively, at month 3 (70.1 kilounits of antibody per liter [kU_A/L] vs 9.8 kU_A/L) and month 6 (27.4 kU_A/L vs 1.32 kU_A/L). However, at month 12, peanut-specific IgE returned to near baseline in both groups (1.1 kU_A/L vs -1.1 kU_A/L). In contrast, mean peanut skin prick test wheal diameter decreased from baseline by month 3 (-3.03mm vs -1.03mm), month 6 (-3.5mm vs -1.21mm), and month 12 (-3.48mm vs -0.77mm), though in the peanut-patch group the decrease in the size of the skin test did not progress after month 6.

Levels of peanut-specific IgE to component proteins were also measured at the same time points as noted above. Trends were most prominent for Ara h 1. Ara h 1 sIgE levels in the peanut-patch group were markedly increased from baseline at month 3 (median change in active vs placebo, respectively: 16.62 kU_A/L vs 0.35 kU_A/L), as well as at month 6 (8.53 kU_A/L vs 0.02 kU_A/L) and at month 12 (1.47 kU_A/L vs -0.25 kU_A/L). Similar to total peanut IgE, Ara h 1 levels in the peanut-patch group peaked at month 3 and then regressed at month 6 and month 12, but the peanut-patch group remained highly discernable based on Ara h 1 values vs. placebo at all time points, and the decline was less notable than with total peanut IgE. The same trends were present for Ara h 2 and Ara h 3, but more minimally so compared to either Ara h 1 or total peanut IgE. No discernable change was noted for either Ara h 8 or Ara h 9.

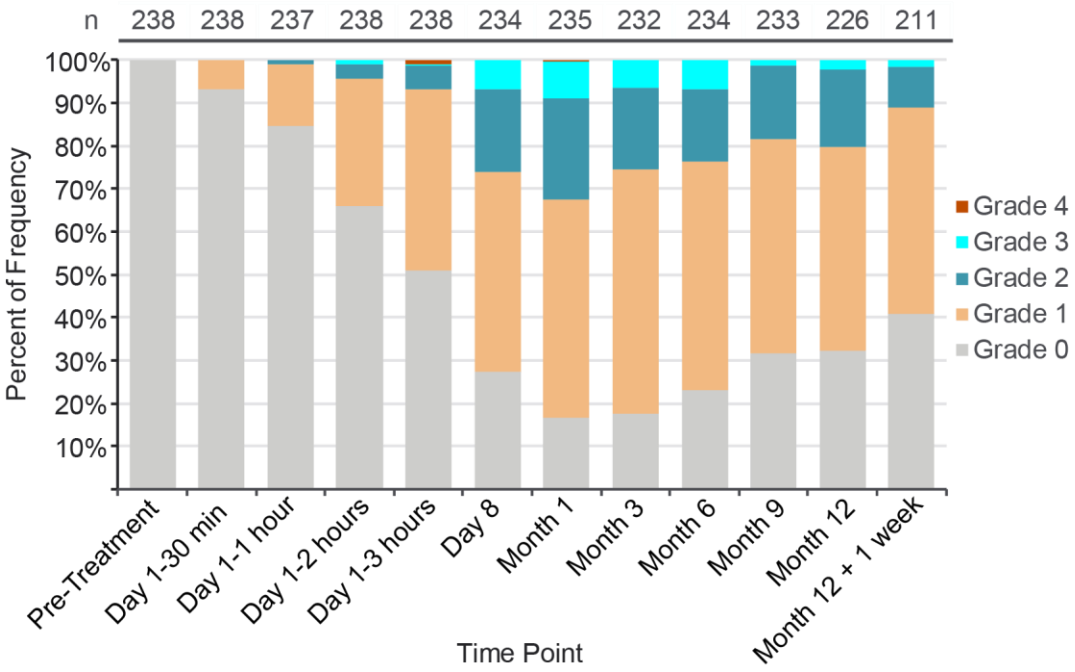
Median peanut-specific IgG4 increased over time in the peanut-patch group (change from baseline at month 3: 0.81 mg/L; month 6: 1.79 mg/L; month 12: 3.27 mg/L), while levels remained unchanged from baseline in the placebo-patch group. The change from baseline in peanut-specific IgG4 was greater at all time points with peanut patch vs placebo patch, and the groups were highly distinguished by this marker given a flat trend in the placebo arm. IgG4 to peanut component proteins mentioned above were also measured. For both Ara h 1 and Ara h 2 IgG4, an identical trend to total IgG4 was noted between peanut-patch and placebo groups at all time points, which readily distinguished the groups. This upward trend was highest for Ara h 2 IgG4, followed by total peanut IgG4, then Ara h 1 IgG4. Total peanut IgE to IgG4 ratio was also assessed, and showed a marked decrease in the peanut-patch group compared to baseline over the 12 months of treatment at all time points measured, as well as a marked decrease at all time points measured in the peanut-patch group compared to placebo at all time points, which also readily distinguished those on active therapy vs. placebo.

eFigure 4. Immunologic Correlates Over Time by Treatment Group



Abbreviations: IgE, immunoglobulin E; IgG4, immunoglobulin G4; Q1, first quartile; Q3, third quartile.

eFigure 5. Local Skin Reactions in the Peanut-Patch Group Over Time per Investigator's Assessment



Participants are still receiving treatment at month 12 + 1 week.
Reaction definitions: Grade 0: negative; Grade 1: only erythema, or erythema + infiltration; Grade 2: erythema, few papules; Grade 3: erythema, many or spreading papules; Grade 4: erythema, vesicles.

eTable 1. Symptom Scoring During Oral Food Challenge

Symptom	Scoring
Skin	
Erythematous rash	Percentage of area involved
Pruritus	0 = Absent 1 = Mild: occasional scratching 2 = Moderate: scratching continuously for >2 minutes at a time 3 = Severe: hard, continuous scratching, excoriations
Urticaria/Angioedema	0 = Absent 1 = Mild: <3 hives, or mild lip edema 2 = Moderate: <10 hives but >3, or significant lip or face edema 3 = Severe: generalized involvement
Rash	0 = Absent 1 = Mild: few areas of faint erythema 2 = Moderate: areas of erythema (>20% and <50%), macular and raised rash 3 = Severe: generalized marked erythema (>50%), extensive raised lesions (>25%)
Upper respiratory	
Sneezing/Itching	0 = Absent 1 = Mild: rare bursts 2 = Moderate: bursts <10, intermittent rubbing of nose/eyes/external ear canals 3 = Severe: continuous rubbing of nose/eyes, periocular swelling and/or long bursts of sneezing
Nasal congestion	0 = Absent 1 = Mild: some hindrance to breathing 2 = Moderate: nostrils feel blocked, breathing through mouth most of time 3 = Severe: nostrils occluded
Rhinorrhea	0 = Absent 1 = Mild: occasional sniffling 2 = Moderate: frequent sniffling, requires tissues 3 = Severe: nose runs freely despite sniffling and tissues
Laryngeal	0 = Absent 1 = Mild: throat clearing, occasional cough 2 = Moderate: hoarseness, frequent dry cough 3 = Severe: inspiratory stridor
Lower respiratory	
Wheezing	0 = Absent 1 = Mild: expiratory wheezing to auscultation 2 = Moderate: dyspnea, inspiratory and expiratory wheezing 3 = Severe: dyspnea, use of accessory muscles, audible wheezing
Gastrointestinal	
Subjective complaints	0 = Absent 1 = Mild: itchy mouth/throat, c/o nausea, abdominal pain, no change in activity 2 = Moderate: frequent c/o nausea or abdominal pain, decreased activity 3 = Severe: patient in bed; crying, notably distressed
Objective complaints	0 = Absent 1 = Mild: 1 episode of emesis or diarrhea 2 = Moderate: 2-3 episodes of emesis or diarrhea or 1 of each 3 = Severe: >3 episodes of emesis or diarrhea or 2 of each
Cardiovascular/Neurologic	
	0 = Normal: heart rate or BP for age/baseline 1 = Mild: color change, subjective response (weak, dizzy), or tachycardia, mental status change, mild hypotension (weak rapid pulse and/or 10-20% drop in BP from baseline) 2 = Moderate: drop in BP >20% from baseline, significant change in mental status, light-headedness, feeling of “impending doom” 3 = Severe: cardiovascular collapse, signs of impaired circulation, unconsciousness, bradycardia, cardiac arrest

Abbreviation: BP, blood pressure.

eTable 2. Pre-defined Hierarchical Order for Analysis of Efficacy Endpoints

Order	Efficacy endpoints (at M12)	Population or sub-group	Success criterion	Method / SAS Procedure
1	Difference in percentages of treatment responders	ITT Overall	95% CI lower bound ≥15%	2-sided Newcombe 95% CI (SAS FREQ procedure with RISKDIFF option)
2	Difference in percentages of treatment responders	ITT Screening ED subgroup 2 (>10mg)[a]	95% CI lower bound >0%	2-sided Newcombe 95% CI (SAS FREQ procedure with RISKDIFF option)
3	Difference in percentages of treatment responders	ITT Screening ED subgroup 1 (≤10mg)[b]	95% CI lower bound >0%	2-sided Newcombe 95% CI (SAS FREQ procedure with RISKDIFF option)
4	Cumulative reactive dose	ITT Overall	p ≤0.05	ANCOVA
5	Peanut protein ED	ITT Overall	p ≤0.05	ANCOVA
6	Difference in percentages of treatment responders	ITT Age group 6-11 years of age	95% CI lower bound >0%	2-sided Newcombe 95% CI (SAS FREQ procedure with RISKDIFF option)
7	Difference in percentages of treatment responders	ITT Age group 4-5 years of age	95% CI lower bound >0%	2-sided Newcombe 95% CI (SAS FREQ procedure with RISKDIFF option)
8	Difference in percentage of participants responsive to a cumulative dose ≥1,444 mg peanut protein	ITT Overall	95% CI lower bound >0%	2-sided Newcombe 95% CI (SAS FREQ procedure with RISKDIFF option)
9	Difference in percentage of participants unresponsive to a cumulative dose ≥1,444 mg peanut protein	ITT Overall	95% CI lower bound >0%	2-sided Newcombe 95% CI (SAS FREQ procedure with RISKDIFF option)
10	Cumulative reactive dose	ITT Screening ED subgroup 2[a]	p ≤0.05	ANCOVA
11	Peanut protein ED	ITT Screening ED subgroup 2[a]	p ≤0.05	ANCOVA
12	Cumulative reactive dose	ITT Screening ED subgroup 1[b]	p ≤0.05	ANCOVA
13	Peanut protein ED	ITT Screening ED subgroup 1[b]	p ≤0.05	ANCOVA
14	Difference in percentage of participants passing the challenge (percentage of participants unresponsive to the highest dose of peanut protein)	ITT Overall	95% CI lower bound >0%	2-sided Newcombe 95% CI (SAS FREQ procedure with RISKDIFF option)

Abbreviations: CI=Confidence Interval; ANCOVA = Analysis of covariance; ED = Eliciting dose; ITT = Intention-to-treat, comprised of all participants who were randomized.

[a] Screening ED subgroup 2 = high-eliciting dose subgroup: participants who had a baseline eliciting dose of >10mg-300mg peanut protein

[b] Screening ED subgroup 1 = low-eliciting dose subgroup: participants who had a baseline eliciting dose of ⩽10mg of peanut protein

eTable 3. Post Hoc Analysis Using Site Treated as a Random Effect

	Mixed Model (Site as Random Effect)	Independent Model (Unadjusted for Site)
Model	**Difference of treatment group Least Square means Estimate [Wald 95% CI]**	**Difference of treatment group Least Square means Estimate [Wald 95% CI]**
Distribution=bin, link=id	did not converge	21.7 [13.1 - 30.4]
Distribution=normal, link=id	21.5 [11.8 - 31.2]	21.7 [12.1 - 31.4]
Distribution=bin, link=logit	1.24 [0.65 - 1.84]	1.25 [0.66 - 1.84]
Distribution=normal, link=logit	1.20 [0.52 - 1.88]	1.25 [0.53 - 1.96]

eTable 4. Cumulative Reactive Dose (CRD)[a] of Peanut Protein by Treatment Group (ITT Population)

CRD of Peanut Protein (mg)	Peanut Patch (n = 238)	Placebo Patch (n = 118)	Difference in Median CRD (mg)[b]
Baseline			Not calculated
Mean (SD)	211.7 (172.3)	212.5 (186.6)	
Median (Q1, Q3)	144 (44, 444)	144 (44, 444)	
Range	1–547	1–744	
Month 12			297
Mean (SD)	905.7 (1076.6)	361.0 (655.8)	
Median (Q1, Q3)	444 (144, 1444)	144.0 (44, 444)	
Range	1–3444	1–3444	

Abbreviations: ITT, intention-to-treat, comprised of all participants who were randomized; Q1, first quartile; Q3, third quartile; SD, standard deviation.
[a]The cumulative reactive dose is the sum of all doses administered during a double-blind, placebo-controlled food challenge.
[b]Hodges and Lehmann estimate of the difference in median CRDs at month 12 between treatment groups.

eTable 5. Treatment Emergent Adverse Event Rates by System Organ Class and Preferred Term, by Treatment Group (Safety Population) with Exposure Adjusted Event Rate

	Peanut Patch (n=238)				Placebo Patch (n=118)			
Category	**No.**	**(%)**	**Number of Events**	**Exposure adjusted event rate[a]**	**No.**	**(%)**	**Number of Events**	**Exposure adjusted event rate[a]**
Any:								
TEAEs	227	(95.4)	2160	9.16	105	(89)	810	7.031
Mild TEAEs[b]	220	(92.4)	1683	7.137	97	(82.2)	677	5.877
Moderate TEAEs[c]	127	(53.4)	440	1.866	53	(44.9)	131	1.137
Severe TEAEs[d]	14	(5.9)	37	0.157	2	(1.7)	2	0.017
Serious TEAEs[e]	10	(4.2)	12	0.051	6	(5.1)	6	0.052
TEAEs considered related to patch[f]	142	(59.7)	569	2.413	41	(34.7)	157	1.363
TEAEs reported as related	125	(52.5)	483	2.048	33	(28)	138	1.198
TEAEs reported as probably related	27	(11.3)	41	0.174	3	(2.5)	4	0.035
TEAEs reported as possibly related	22	(9.2)	45	0.191	11	(9.3)	15	0.13
TEAEs considered unrelated to patch	220	(92.4)	1591	6.747	102	(86.4)	653	5.668
TEAEs reported as unlikely related	73	(30.7)	234	0.992	43	(36.4)	147	1.276
TEAEs reported as unrelated	216	(90.8)	1357	5.755	100	(84.7)	506	4.392
Serious TEAEs considered related to patch[f]	3	(1.3)	4	0.017	0	0	0	0
TEAEs leading to permanent patch discontinuation	4	(1.7)	4	0.017	0	0	0	0
TEAEs leading to temporary patch discontinuation	32	(13.4)	55	0.233	11	(9.3)	16	0.139
TEAEs leading to death	0	0	0	0	0	0	0	0
Severe TEAEs considered related to patch[f]	8	(3.4)	30	0.127	1	(0.8)	1	0.009
Patch-induced local TEAEs	137	(57.6)	508	2.154	32	(27.1)	138	1.198
Systemic allergic TEAE considered related to patch[f]	9	(3.8)	11	0.047	2	(1.7)	2	0.017
Severe patch-induced local TEAEs	8	(3.4)	29	0.123	1	(0.8)	1	0.009
TEAEs leading to an epinephrine intake	22	(9.2)	27	0.115	4	(3.4)	5	0.043
TEAEs considered related to patch[f]	7	(2.9)	7	0.03	1	(0.8)	1	0.009
TEAEs considered unrelated to patch	15	(6.3)	20	0.085	4	(3.4)	4	0.035

Abbreviation: n, number of participants in treatment group; TEAE, treatment-emergent adverse event.

[a]Exposure adjusted event rate based on the number of events divided by the total exposure of participants (235.8 patient-year for Peanut-Patch Group and 115.2 for Placebo Group)

[b]Mild: the adverse event was transient and easily tolerated by the participant.

[c]Moderate: the adverse event caused discomfort and interference with the participant's general condition.

[d]Severe: the adverse event caused considerable interference with the participant's general condition and may have been incapacitating.

[e]Serious: any untoward medical occurrence that at any dose results in death;is life-threatening, meaning that the participant is at risk of death at the time of the event but does not mean that the event hypothetically might have caused death if it were more severe; requires hospitalization (overnight or longer) or prolongation of existing hospitalization; results in persistent or significant disability or incapacity; is a congenital anomaly or birth defect; is an important medical event that may not be immediately life-threatening or result in death or hospitalization but that may jeopardize the participant or require intervention to prevent one of the above outcomes. Examples of such events are intensive treatment in an emergency room or at home for

allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalization; or development of drug dependency or drug abuse. Medical and scientific judgment should be exercised in deciding whether a case is serious and whether expedited reporting is appropriate.
[f]Considered related to study treatment when reported as possibly related, probably related or related. Considered unrelated to peanut-patch when reported as unlikely related or unrelated.

eTable 6. Summary of Treatment Emergent Adverse Events Considered Related to the Patch by Treatment Group

	Peanut Patch 250µg (n=238)				Placebo Patch (n=118)			
System Organ Class Preferred Term	**No.**	**(%)**	**Number of Events**	**Exposure adjusted Event Rate[b]**	**No.**	**(%)**	**Number of Events**	**Exposure adjusted Event Rate[b]**
Any TEAE considered related to Patch[a]	142	(59.7)	569	2.413	41	(34.7)	157	1.363
General disorders and administration site conditions	137	(57.6)	510	2.163	32	(27.1)	138	1.198
Administration site conditions	137	(57.6)	508	2.154	32	(27.1)	138	1.198
Pruritus[c]	82	(34.5)	152	0.645	14	(11.9)	30	0.26
Erythema[c]	67	(28.2)	118	0.5	20	(16.9)	54	0.469
Swelling[c]	38	(16)	86	0.365	2	(1.7)	18	0.156
Eczema	25	(10.5)	29	0.123	6	(5.1)	18	0.156
Reaction	21	(8.8)	29	0.123	2	(1.7)	5	0.043
Urticaria	15	(6.3)	23	0.098	0	0	0	0
Dermatitis	10	(4.2)	27	0.115	0	0	0	0
Irritation	8	(3.4)	10	0.042	2	(1.7)	3	0.026
Rash	6	(2.5)	6	0.025	0	0	0	0
Edema	5	(2.1)	7	0.03	1	(0.8)	5	0.043
Vesicles	2	(0.8)	4	0.017	1	(0.8)	1	0.009
Dryness	2	(0.8)	11	0.047	0	0	0	0
Discomfort	1	(0.4)	1	0.004	1	(0.8)	1	0.009
Pain	1	(0.4)	1	0.004	1	(0.8)	1	0.009
Papules	1	(0.4)	1	0.004	1	(0.8)	1	0.009
Discharge	1	(0.4)	1	0.004	0	0	0	0
Discoloration	1	(0.4)	1	0.004	0	0	0	0
Erosion	1	(0.4)	1	0.004	0	0	0	0
Inflammation	0	0	0	0	1	(0.8)	1	0.009
General disorders	2	(0.8)	2	0.008	0	0	0	0
Fatigue	2	(0.8)	2	0.008	0	0	0	0
Skin and subcutaneous tissue disorders	13	(5.5)	17	0.072	10	(8.5)	14	0.122
Urticaria	5	(2.1)	8	0.034	2	(1.7)	3	0.026
Eczema	2	(0.8)	2	0.008	3	(2.5)	5	0.043
Dermatitis atopic	1	(0.4)	1	0.004	1	(0.8)	1	0.009
Erythema	1	(0.4)	1	0.004	1	(0.8)	2	0.017
Papule	1	(0.4)	1	0.004	1	(0.8)	1	0.009
Generalized erythema	1	(0.4)	1	0.004	0	0	0	0
Pruritus generalized	1	(0.4)	1	0.004	0	0	0	0
Rash	1	(0.4)	1	0.004	0	0	0	0
Rash generalized	1	(0.4)	1	0.004	0	0	0	0
Pruritus	0	0	0	0	1	(0.8)	1	0.009
Skin reaction	0	0	0	0	1	(0.8)	1	0.009
Immune system disorders	12	(5)	15	0.064	1	(0.8)	1	0.009
Anaphylactic reaction	8	(3.4)	10	0.042	1	(0.8)	1	0.009
Non-anaphylactic hypersensitivity reaction	4	(1.7)	5	0.021	0	0	0	0
Eye disorders	8	(3.4)	9	0.038	1	(0.8)	1	0.009

	Peanut Patch 250µg (n=238)				Placebo Patch (n=118)			
System Organ Class Preferred Term	**No.**	**(%)**	**Number of Events**	**Exposure adjusted Event Rate[b]**	**No.**	**(%)**	**Number of Events**	**Exposure adjusted Event Rate[b]**
Conjunctivitis allergic	4	(1.7)	4	0.017	1	(0.8)	1	0.009
Eye pruritus	2	(0.8)	2	0.008	0	0	0	0
Eye swelling	2	(0.8)	2	0.008	0	0	0	0
Periorbital edema	1	(0.4)	1	0.004	0	0	0	0
Infections and infestations	6	(2.5)	9	0.038	0	0	0	0
Application site folliculitis	2	(0.8)	2	0.008	0	0	0	0
Conjunctivitis	2	(0.8)	3	0.013	0	0	0	0
Application site infection	1	(0.4)	2	0.008	0	0	0	0
Eczema infected	1	(0.4)	2	0.008	0	0	0	0
Respiratory, thoracic and mediastinal disorders	3	(1.3)	7	0.03	2	(1.7)	2	0.017
Nasal congestion	1	(0.4)	1	0.004	0	0	0	0
Pharyngeal edema	1	(0.4)	1	0.004	0	0	0	0
Rhinitis allergic	1	(0.4)	2	0.008	0	0	0	0
Throat irritation	1	(0.4)	3	0.013	0	0	0	0
Dyspnea	0	0	0	0	1	(0.8)	1	0.009
Wheezing	0	0	0	0	1	(0.8)	1	0.009
Psychiatric disorders	1	(0.4)	1	0.004	1	(0.8)	1	0.009
Insomnia	1	(0.4)	1	0.004	0	0	0	0
Anxiety	0	0	0	0	1	(0.8)	1	0.009
Vascular disorders	1	(0.4)	1	0.004	0	0	0	0
Flushing	1	(0.4)	1	0.004	0	0	0	0
Serious TEAE considered related to patch	3	(1.3)	4	0.017	0	0	0	0
Severe TEAE considered related to patch	8	(3.4)	30	0.127	1	(0.8)	1	0.009
Moderate TEAE considered related to patch	51	(21.4)	161	0.683	5	(4.2)	14	0.122
Mild TEAE considered related to patch	121	(50.8)	378	1.603	40	(33.9)	142	1.233
TEAEs considered related to patch leading to temporary discontinuation	16	(6.7)	26	0.110	2	(1.7)	3	0.026
TEAEs considered related to patch leading to permanent discontinuation	4	(1.7)	4	0.017	0	0	0	0

Abbreviations: n, number of participants in treatment group; TEAE, treatment-emergent adverse event.

[a] Adverse Events reported as Possibly related, Probably related or Related are considered as Related. Adverse Events reported as Unlikely related or Unrelated are considered as Unrelated.

[b] Exposure adjusted event rate based on the number of events divided by the total exposure of participants (235.8 patient-year for Peanut-Patch Group and 115.2 for Placebo Group)

[c] Swelling, Pruritus and Erythema (swelling, itching and redness) were to be reported as an adverse event after the first 6 months and in participant diaries on a daily basis during the first 6 months.

The following categories had no related reported TEAE's: nervous system disorders; injury, poison, and procedural complications; musculoskeletal and connective tissue disorders; ear and labyrinth disorders; neoplasms; metabolism and nutrition disorders; blood and lymphatic disorders; congenital, familial, and genetic disorders; hepatobiliary disorders; renal and urinary disorders; reproductive system and breast disorders; surgical and medical procedures; social circumstances.

eTable 7. Summary of Possibly Related, Probably Related, or Related Anaphylaxis Events Occurring in Peanut-Patch Participants

Patient No.	Treatment Relationship	Symptoms[a]	Study Day	Time of onset after last patch application[a]	Severity	SAE	Serious (Yes/No) /seriousness criteria	Epinephrine Administered	Additional Treatment	Contin-ued Study	Disposition Regarding Patch[a]
1	Probable	Urticaria, Cough, Vomiting, Lip Swelling	5	10 hours 15 min	Mild	No	No	Yes (1 dose)	Diphenhy-dramine	No	Patch permanently withdrawn the day of AE. Next visit, 4 days later, with parental consent withdrawal due to AE.
2	Possible	Urticaria, Itchy Throat, Dyspnea	16	1 hour 50 min	Moderate	Yes	Yes / Hospitalization less than 24 hours	Yes (1 dose)	Dimetindene, Betamethasone, IVF	Yes (to Day 349)	Temporary withdrawn for 11 days
2	Probable	Urticaria, Dyspnea	83	2 hours and 45 min	Moderate	No	No	No	Dimetindene, Salbutamol, Betamethasone	Yes (to Day 349)	Temporary withdrawn for 9 days
2	Possible	Urticaria, Itchy Throat, Wheeze	349	4 hours and 20 min	Moderate	Yes	Yes / Hospitalization less than 24 hours	No	Dimetindene, Salbutamol, Prednisone, Betamethasone	No	Temporarily interrupted for 2 days, restart few hours a day for 5 weeks and drop out due to AE
3	Possible	Urticaria, Angioedema, Cough, Wheeze, Dyspnea, Conjunctivitis	9	30 min	Moderate	Yes	Yes / Hospitalization less than 24 hours	Yes (1 dose)	Cetirizine, Salbutamol, Prednisolone	No	Drop out due to AE the same day

Patient No.	Treatment Relationship	Symptoms[a]	Study Day	Time of onset after last patch application[a]	Severity	SAE	Serious (Yes/No) /seriousness criteria	Epinephrine Administered	Additional Treatment	Contin -ued Study	Disposition Regarding Patch[a]
4	Possible	Urticaria, Angioedema, Cough, Wheeze, Dyspnea, Conjunctivitis	17	1 hour	Moderate	No	No	No	Cetirizine, Salbutamol, Prednisolone, Budesonide	Yes	Temporarily withdrawn for 1 month because the site wanted the participant to restart peanut-patch at the site, the family lived far away, and the restart plan was delayed by an underlying febrile illness.
5	Probable	Urticaria, Cough	20	1 hour	Moderate	Yes	Yes / Medically significant	Yes (1 dose)	Diphenhy-dramine, Albuterol, Dexamethasone	Yes	Temporarily interrupted for 1 day
6	Possible	Urticaria, Pruritus, Vomiting	162	18 hours	Moderate	No	No	Yes (1 dose)	Diphenhy-dramine, Cetirizine	Yes	Patch maintained, no interruption
7	Related	Wheezing Nausea, Mouth Tingling, Sweating, Flushing, Lethargy	17	Immediately after 2nd patch same day	Moderate	No	No	Yes (1 dose)	Diphenhy-dramine, Salbutamol, Prednisolone	Yes	Temporarily interrupted for 24 hours
8	Possible	Vomiting, Conjunctivitis , Nasal Congestion	107	Around 21 hours	Mild	No	No	No	Paracetamol, Ondansetron	Yes	Temporarily interrupted for 2 days

Abbreviations: AE, adverse event; ER, emergency room; IVF, intravenous fluids; SAE, serious adverse event.
[a]Data retrieved based on Case Medical Narratives.