



Clinical trial results:

A double-blind, placebo-controlled, randomized phase III trial to assess the safety and efficacy of Viaskin® Peanut in peanut-allergic young children 1-3 years of age (EPITOPE study)

Summary

EudraCT number	2016-003679-23
Trial protocol	IE FR DE NL
Global end of trial date	27 April 2022

Results information

Result version number	v1 (current)
This version publication date	07 March 2024
First version publication date	07 March 2024

Trial information

Trial identification

Sponsor protocol code	EPITOPE-V712-304
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03211247
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	DBV Technologies
Sponsor organisation address	177-181 avenue Pierre Brossolette, Montrouge, France, 92120
Public contact	Chief Medical Officer, DBV Technologies, +33 155 42 78 78, clinicaltrials@dbv-technologies.com
Scientific contact	Chief Medical Officer, DBV Technologies, +33 155 42 78 78, clinicaltrials@dbv-technologies.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001481-PIP01-13
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 April 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	27 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to assess the efficacy and safety of DBV712 250 micrograms (mcg) to induce desensitization to peanut in peanut-allergic participants 1 to 3 years of age after a 12-month treatment period with epicutaneous immunotherapy (EPIT).

Protection of trial subjects:

This study was conducted in accordance with the Note for Guidance on GCP International Council for Harmonization Harmonized Tripartite Guideline E6 R1/Integrated Addendum E6; R2 United States Food and Drug Administration (FDA) Code of Federal Regulations (Title 21 Parts 50, 56, 312), requirements for the conduct of clinical studies as provided in the European Union Directive 2001/20/EC; the general guidelines indicated in the Declaration of Helsinki; and all applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 July 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Ireland: 15
Country: Number of subjects enrolled	Australia: 59
Country: Number of subjects enrolled	United Kingdom: 32
Country: Number of subjects enrolled	Canada: 27
Country: Number of subjects enrolled	United States: 207
Worldwide total number of subjects	362
EEA total number of subjects	37

Notes:

Subjects enrolled per age group

In utero	0
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Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	126
Children (2-11 years)	236
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase III, study was conducted in participants aged 1 to 3 years with peanut-allergy at 51 centers. The duration of study was approximately 62 weeks (6-week: screening period; 12-month treatment period; and 4-week follow-up period).

Pre-assignment

Screening details:

A total of 362 participants were randomized in a 2:1 ratio to receive Viaskin™ Peanut (DBV712) 250 mcg or placebo.

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Viaskin Peanut 250 mcg

Arm description:

Participants applied 1 new Viaskin Peanut 250 mcg patch on intact skin for 24 hours daily for up to 12 months. Each patch contained 250 mcg peanut protein extract for epicutaneous administration. The application duration was progressively increased to a duration of 24 ±4 hours daily over a 4-week period (2 hours during the first week, 4 hours during the second week, 8 hours during the third week, 12 hours during the fourth week onwards, and 24 ± 4 hours every day fifth week onwards).

Arm type	Experimental
Investigational medicinal product name	Viaskin Peanut
Investigational medicinal product code	
Other name	DBV712
Pharmaceutical forms	Cutaneous patch
Routes of administration	Epicutaneous use

Dosage and administration details:

The Viaskin peanut patch contained a dry deposit of a formulation of peanut protein extract. The drug substance is an unmodified, lyophilized peanut extract produced from the extraction and freeze drying of defatted peanut flour. Application of the DBV712 patch at a similar time for each daily application (morning or evening) was recommended.

Arm title	Placebo
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Arm description:

Participants applied 1 new placebo patch on intact skin for 24 hours daily for up to 12 months. The application duration was progressively increased to a duration of 24 ±4 hours daily over a 4-week period (2 hours during the first week, 4 hours during the second week, 8 hours during the third week, 12 hours during the fourth week onwards, and 24 ± 4 hours every day fifth week onwards).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous patch
Routes of administration	Epicutaneous use

Dosage and administration details:

The placebo treatment consists of a matching cutaneous patch and dry deposit formulation. Application of the placebo patch at a similar time for each daily application (morning or evening) was recommended.

Number of subjects in period 1	Viaskin Peanut 250 mcg	Placebo
Started	244	118
Completed	208	99
Not completed	36	19
Physician decision	1	2
Participant withdrawal by Parent or Caregiver	18	13
Adverse event, non-fatal	8	-
Noncompliance with study drug	2	-
Participant did not complete oral food challenge	5	2
Lost to follow-up	2	1
Protocol deviation	-	1

Baseline characteristics

Reporting groups

Reporting group title	Viaskin Peanut 250 mcg
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Reporting group description:

Participants applied 1 new Viaskin Peanut 250 mcg patch on intact skin for 24 hours daily for up to 12 months. Each patch contained 250 mcg peanut protein extract for epicutaneous administration. The application duration was progressively increased to a duration of 24 ±4 hours daily over a 4-week period (2 hours during the first week, 4 hours during the second week, 8 hours during the third week, 12 hours during the fourth week onwards, and 24 ± 4 hours every day fifth week onwards).

Reporting group title	Placebo
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Reporting group description:

Participants applied 1 new placebo patch on intact skin for 24 hours daily for up to 12 months. The application duration was progressively increased to a duration of 24 ±4 hours daily over a 4-week period (2 hours during the first week, 4 hours during the second week, 8 hours during the third week, 12 hours during the fourth week onwards, and 24 ± 4 hours every day fifth week onwards).

Reporting group values	Viaskin Peanut 250 mcg	Placebo	Total
Number of subjects	244	118	362
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	2.52 ± 0.872	2.43 ± 0.868	-
Gender categorical Units: Subjects			
Female	79	34	113
Male	165	84	249
Race Units: Subjects			
White	159	70	229
Black or African American	1	1	2
Asian	41	24	65
Other	35	17	52
Not collected	8	6	14

End points

End points reporting groups

Reporting group title	Viaskin Peanut 250 mcg
Reporting group description: Participants applied 1 new Viaskin Peanut 250 mcg patch on intact skin for 24 hours daily for up to 12 months. Each patch contained 250 mcg peanut protein extract for epicutaneous administration. The application duration was progressively increased to a duration of 24 ±4 hours daily over a 4-week period (2 hours during the first week, 4 hours during the second week, 8 hours during the third week, 12 hours during the fourth week onwards, and 24 ± 4 hours every day fifth week onwards).	
Reporting group title	Placebo
Reporting group description: Participants applied 1 new placebo patch on intact skin for 24 hours daily for up to 12 months. The application duration was progressively increased to a duration of 24 ±4 hours daily over a 4-week period (2 hours during the first week, 4 hours during the second week, 8 hours during the third week, 12 hours during the fourth week onwards, and 24 ± 4 hours every day fifth week onwards).	

Primary: Percentage of Treatment Responders at Month 12

End point title	Percentage of Treatment Responders at Month 12
End point description: A participant was defined as a treatment responder if the initial eliciting dose (ED) was > 10 milligram (mg) peanut protein and the ED was ≥1000 mg peanut protein at the post-treatment double-blind placebo-controlled food challenge (DBPCFC) at Month 12 OR the initial ED at baseline was ≤10 mg peanut protein and the ED was ≥300 mg peanut protein at the post-treatment DBPCFC at Month 12. The FAS comprised of all participants who were randomized in the study.	
End point type	Primary
End point timeframe: Month 12	

End point values	Viaskin Peanut 250 mcg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244	118		
Units: percentage of participants				
number (confidence interval 95%)	67.0 (60.93 to 73.01)	33.5 (24.84 to 42.24)		

Statistical analyses

Statistical analysis title	Difference between Viaskin 250 mcg and Placebo
Statistical analysis description: Difference between the percentage of treatment responders in Viaskin 250 mcg compared to placebo.	
Comparison groups	Viaskin Peanut 250 mcg v Placebo

Number of subjects included in analysis	362
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Wald test
Parameter estimate	Proportion difference
Point estimate	33.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.36
upper limit	44.49

Secondary: Cumulative Reactive Dose (CRD) of Peanut Protein at Month 12 Using Analysis of Covariance (ANCOVA) Model

End point title	Cumulative Reactive Dose (CRD) of Peanut Protein at Month 12 Using Analysis of Covariance (ANCOVA) Model
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End point description:

The peanut protein CRD was defined as the sum of all peanut protein doses taken by the participant during the DBPCFC, calculated as follows:
If the ED reported by the investigator in the electronic case report form (eCRF) is missing, then the CRD is missing; If the ED reported by the investigator in the eCRF was not missing then the CRD was calculated as the sum of all doses given, including also the partial doses. The CRD in each treatment group at Month 12 was compared using ANCOVA model. The FAS comprised of all participants who were randomized in the study.

End point type	Secondary
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End point timeframe:

Month 12

End point values	Viaskin Peanut 250 mcg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244	118		
Units: milligram (mg)				
geometric mean (confidence interval 95%)	1010.31 (842.18 to 1212.01)	322.57 (248.37 to 418.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CRD of Peanut Protein to Month 12

End point title	Change From Baseline in CRD of Peanut Protein to Month 12
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End point description:

The peanut protein CRD was defined as the sum of all peanut protein doses taken by the participant during the DBPCFC, calculated as follows:

If the ED reported by the investigator in the eCRF is missing, then the CRD is missing; If the ED reported by the investigator in the eCRF was not missing then the CRD was calculated as the sum of all doses given, including also the partial doses. The FAS comprised of all participants who were randomized in the study.

End point type	Secondary
End point timeframe:	
Baseline (Day 1) and Month 12	

End point values	Viaskin Peanut 250 mcg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244	118		
Units: mg				
median (inter-quartile range (Q1-Q3))	1300.0 (140.0 to 3000.0)	0.0 (0.0 to 1000.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: ED of Peanut Protein at Month 12 Using ANCOVA Model

End point title	ED of Peanut Protein at Month 12 Using ANCOVA Model			
End point description:				
The peanut protein ED was the individual dose of peanut protein administered to participants during the food challenge procedure, which triggered objective allergic reactions, leading to stopping the challenge. The ED in each treatment group at Month 12 was compared using ANCOVA model. The FAS comprised of all participants who were randomized in the study.				
End point type	Secondary			
End point timeframe:				
Month 12				

End point values	Viaskin Peanut 250 mcg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244	118		
Units: mg				
geometric mean (confidence interval 95%)	659.36 (553.84 to 784.99)	223.12 (173.40 to 287.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in ED of Peanut Protein to Month 12

End point title	Change From Baseline in ED of Peanut Protein to Month 12
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End point description:

The peanut protein ED was the individual dose of peanut protein administered to participants during the food challenge procedure, which triggered objective allergic reactions, leading to stopping the challenge. The FAS comprised of all participants who were randomized in the study.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) and Month 12

End point values	Viaskin Peanut 250 mcg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244	118		
Units: mg				
median (inter-quartile range (Q1-Q3))	900.0 (90.0 to 1700.0)	0.0 (0.0 to 700.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Severity of Objective Symptoms at Baseline and Month 12 During Double-Blind Placebo-Controlled Food Challenge

End point title	Percentage of Participants With Severity of Objective Symptoms at Baseline and Month 12 During Double-Blind Placebo-Controlled Food Challenge
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End point description:

The objective symptoms collected during the DBPCFC included skin (erythematous rash, pruritus, urticaria/angioedema, rash), upper respiratory (sneezing/itching, nasal congestion, rhinorrhea, laryngeal), lower respiratory (wheezing), gastrointestinal (diarrhea, vomiting, cardiovascular), and eyes (conjunctivitis, any other objective symptoms). With the exception of erythematous rash (recorded as Yes/No), each symptom was graded as: 0=" absent", 1=" mild", 2=" moderate" or 3=" severe". For erythematous rash, the percent area involved was collected. Percentages were calculated based on the number of participants in each time point. The FAS comprised of all participants who were randomized in the study. Only data from the participants analyzed were reported.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) and Month 12

End point values	Viaskin Peanut 250 mcg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244	118		
Units: percentage of participants				
number (not applicable)				
Baseline: Absent (n=244, 118)	0	0		

Baseline: Mild (n=244, 118)	7.0	7.6		
Baseline: Moderate (n=244, 118)	68.4	67.8		
Baseline: Severe (n=244, 118)	24.6	24.6		
Month 12: Absent (n=200, 98)	16.0	6.1		
Month 12: Mild (n=200, 98)	20.5	14.3		
Month 12: Moderate (n=200, 98)	51.0	51.0		
Month 12: Severe (n=200, 98)	12.5	28.6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The TEAEs were collected from Day 1 up to Month 12

Adverse event reporting additional description:

The SAF comprised of all participants from the FAS who received at least 1 dose of IMP.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	Viaskin Peanut 250 mcg
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Reporting group description:

Participants applied 1 new Viaskin Peanut 250 mcg patch on intact skin for 24 hours daily for up to 12 months. Each patch contained 250 mcg peanut protein extract for epicutaneous administration. The application duration was progressively increased to a duration of 24 ±4 hours daily over a 4-week period (2 hours during the first week, 4 hours during the second week, 8 hours during the third week, 12 hours during the fourth week onwards, and 24 ± 4 hours every day fifth week onwards).

Reporting group title	Placebo
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Reporting group description:

Participants applied 1 new placebo patch on intact skin for 24 hours daily for up to 12 months. The application duration was progressively increased to a duration of 24 ±4 hours daily over a 4-week period (2 hours during the first week, 4 hours during the second week, 8 hours during the third week, 12 hours during the fourth week onwards, and 24 ± 4 hours every day fifth week onwards).

Serious adverse events	Viaskin Peanut 250 mcg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 244 (8.61%)	3 / 118 (2.54%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Medication error			
subjects affected / exposed	2 / 244 (0.82%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 244 (0.41%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Aplasia pure red cell			

subjects affected / exposed	1 / 244 (0.41%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction to food			
subjects affected / exposed	0 / 244 (0.00%)	2 / 118 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylaxis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food allergy			
subjects affected / exposed	1 / 244 (0.41%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Periorbital oedema			
subjects affected / exposed	1 / 244 (0.41%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchial hyperreactivity			
subjects affected / exposed	2 / 244 (0.82%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wheezing			
subjects affected / exposed	6 / 244 (2.46%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 8	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			

subjects affected / exposed	1 / 244 (0.41%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 244 (0.41%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metapneumovirus infection			
subjects affected / exposed	1 / 244 (0.41%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 244 (0.41%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 244 (0.41%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Viaskin Peanut 250 mcg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	244 / 244 (100.00%)	117 / 118 (99.15%)	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	10 / 244 (4.10%)	12 / 118 (10.17%)	
occurrences (all)	12	18	
General disorders and administration site conditions			
Application site discolouration			
subjects affected / exposed	15 / 244 (6.15%)	0 / 118 (0.00%)	
occurrences (all)	16	0	
Application site eczema			
subjects affected / exposed	34 / 244 (13.93%)	10 / 118 (8.47%)	
occurrences (all)	66	12	
Application site erosion			
subjects affected / exposed	32 / 244 (13.11%)	5 / 118 (4.24%)	
occurrences (all)	44	6	
Application site erythema			
subjects affected / exposed	239 / 244 (97.95%)	107 / 118 (90.68%)	
occurrences (all)	2182	760	
Application site oedema			
subjects affected / exposed	58 / 244 (23.77%)	21 / 118 (17.80%)	
occurrences (all)	504	105	
Application site papules			
subjects affected / exposed	41 / 244 (16.80%)	9 / 118 (7.63%)	
occurrences (all)	63	10	
Application site pruritus			
subjects affected / exposed	231 / 244 (94.67%)	72 / 118 (61.02%)	
occurrences (all)	2925	523	
Application site swelling			
subjects affected / exposed	177 / 244 (72.54%)	46 / 118 (38.98%)	
occurrences (all)	2044	278	
Application site urticaria			
subjects affected / exposed	68 / 244 (27.87%)	3 / 118 (2.54%)	
occurrences (all)	152	3	

Application site vesicles subjects affected / exposed occurrences (all)	43 / 244 (17.62%) 179	11 / 118 (9.32%) 21	
Pyrexia subjects affected / exposed occurrences (all)	84 / 244 (34.43%) 150	50 / 118 (42.37%) 83	
Immune system disorders			
Anaphylactic reaction subjects affected / exposed occurrences (all)	18 / 244 (7.38%) 24	2 / 118 (1.69%) 2	
Food allergy subjects affected / exposed occurrences (all)	33 / 244 (13.52%) 64	13 / 118 (11.02%) 20	
Hypersensitivity subjects affected / exposed occurrences (all)	24 / 244 (9.84%) 30	11 / 118 (9.32%) 22	
Seasonal allergy subjects affected / exposed occurrences (all)	28 / 244 (11.48%) 50	3 / 118 (2.54%) 4	
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	22 / 244 (9.02%) 48	11 / 118 (9.32%) 21	
Teething subjects affected / exposed occurrences (all)	12 / 244 (4.92%) 32	7 / 118 (5.93%) 12	
Vomiting subjects affected / exposed occurrences (all)	56 / 244 (22.95%) 87	21 / 118 (17.80%) 34	
Respiratory, thoracic and mediastinal disorders			
Asthma subjects affected / exposed occurrences (all)	22 / 244 (9.02%) 35	9 / 118 (7.63%) 30	
Cough subjects affected / exposed occurrences (all)	48 / 244 (19.67%) 91	24 / 118 (20.34%) 42	

Nasal congestion subjects affected / exposed occurrences (all)	15 / 244 (6.15%) 21	9 / 118 (7.63%) 14	
Rhinitis allergic subjects affected / exposed occurrences (all)	22 / 244 (9.02%) 28	10 / 118 (8.47%) 17	
Rhinorrhoea subjects affected / exposed occurrences (all)	36 / 244 (14.75%) 66	23 / 118 (19.49%) 35	
Wheezing subjects affected / exposed occurrences (all)	21 / 244 (8.61%) 39	6 / 118 (5.08%) 15	
Skin and subcutaneous tissue disorders			
Dermatitis diaper subjects affected / exposed occurrences (all)	9 / 244 (3.69%) 15	6 / 118 (5.08%) 7	
Eczema subjects affected / exposed occurrences (all)	59 / 244 (24.18%) 125	30 / 118 (25.42%) 67	
Erythema subjects affected / exposed occurrences (all)	36 / 244 (14.75%) 49	15 / 118 (12.71%) 27	
Pruritus subjects affected / exposed occurrences (all)	23 / 244 (9.43%) 39	13 / 118 (11.02%) 13	
Rash subjects affected / exposed occurrences (all)	37 / 244 (15.16%) 55	14 / 118 (11.86%) 24	
Urticaria subjects affected / exposed occurrences (all)	85 / 244 (34.84%) 244	44 / 118 (37.29%) 96	
Infections and infestations			
Conjunctivitis subjects affected / exposed occurrences (all)	14 / 244 (5.74%) 15	1 / 118 (0.85%) 1	
Croup infectious			

subjects affected / exposed	12 / 244 (4.92%)	12 / 118 (10.17%)
occurrences (all)	13	15
Ear infection		
subjects affected / exposed	23 / 244 (9.43%)	15 / 118 (12.71%)
occurrences (all)	42	28
Gastroenteritis		
subjects affected / exposed	31 / 244 (12.70%)	13 / 118 (11.02%)
occurrences (all)	41	17
Gastroenteritis viral		
subjects affected / exposed	22 / 244 (9.02%)	3 / 118 (2.54%)
occurrences (all)	23	7
Influenza		
subjects affected / exposed	14 / 244 (5.74%)	5 / 118 (4.24%)
occurrences (all)	14	6
Nasopharyngitis		
subjects affected / exposed	53 / 244 (21.72%)	18 / 118 (15.25%)
occurrences (all)	102	35
Otitis media		
subjects affected / exposed	21 / 244 (8.61%)	4 / 118 (3.39%)
occurrences (all)	33	8
Otitis media acute		
subjects affected / exposed	1 / 244 (0.41%)	6 / 118 (5.08%)
occurrences (all)	1	7
Pneumonia		
subjects affected / exposed	6 / 244 (2.46%)	6 / 118 (5.08%)
occurrences (all)	6	7
Respiratory tract infection viral		
subjects affected / exposed	29 / 244 (11.89%)	8 / 118 (6.78%)
occurrences (all)	54	21
Upper respiratory tract infection		
subjects affected / exposed	102 / 244 (41.80%)	43 / 118 (36.44%)
occurrences (all)	239	129
Viral infection		
subjects affected / exposed	47 / 244 (19.26%)	19 / 118 (16.10%)
occurrences (all)	76	25
Viral upper respiratory tract infection		

subjects affected / exposed	30 / 244 (12.30%)	13 / 118 (11.02%)	
occurrences (all)	46	21	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 May 2017	The sample size of the study was revised to reflect changes in the statistical methods for primary efficacy analysis following FDA's recommendations. The total number of participants needed was increased from 241 to 331 participants. The statistical methods for primary efficacy analysis, including the sensitivity analyses on the primary endpoint, the subgroup analyses, and the secondary efficacy analyses, were revised to take into account FDA's recommendations.
11 September 2017	Administrative changes and minor typographical and grammar changes were incorporated. Definition for DBPCFC was updated. The definition of treatment response was adapted, with the terms "objective symptoms leading to DBPCFC stop" being replaced by "symptoms leading to DBPCFC stop". The evaluation of the change in severity of objective symptoms elicited during DBPCFCs was enlarged to that of symptoms elicited during the DBPCFCs. Inclusion criterion definition updated and exclusion criterion replaced. Description of the DBPCFC procedure updated for additional clarification. The description of the severity score based on the grades of objective symptoms elicited during the DBPCFCs was enlarged to that of symptoms elicited during the DBPCFCs. Part IV of the Oral Food Challenge Symptom Score Sheet was modified.
09 November 2017	Packaging, labelling and storage conditions of Viaskin peanut were updated. An erroneous study timepoint for the Investigator assessment of patch adhesion was also corrected, and an administrative change was introduced.
18 June 2018	Minor clarification in study design was added. Sample size was increased. Modification of reporting of pre-specified local skin reactions at patch application sites by the parents/guardians: extension to the whole treatment duration for participants. Quality of life questionnaire was added. Modification of patch adhesion assessment by parents/guardians : extension to the whole treatment duration for participants. Further clarified the exclusion criterion related to concomitant treatment for asthma and precision of exclusion criterion related to prior oral immunotherapy. Three endpoints from secondary endpoints were moved to other efficacy endpoints. The definition of AEs of special interest was updated. Immunological markers assessment was updated. Exploratory variables regarding gene mutation analysis were removed. Quality of life analysis and exploratory blood assessment were added. The statistical methods section was modified. Administrative changes, and clarifications regarding study personnel were incorporated. Minor precision in the title of Appendix 6 was incorporated. Appendix 8, 9 and 10 details were added. Administrative changes and typographical corrections updated.
28 August 2018	Sample size was updated. The acceptability criterion for epicutaneous system adhesion was removed. The hierarchical order for the analysis of efficacy endpoints were shortened. All statistical analytical details (other than primary efficacy analysis) were removed from the protocol and planned to be detailed in the statistical analysis plan. Modification of epicutaneous system adhesion assessments by parents/caregivers. Addition of solicited AEs during the study for both local (application site reactions) and systemic allergic AEs of the study, per FDA's request. The intent-to-treat (ITT) Population was replaced by a modified intent-to-treat (mITT) population.
15 November 2019	Study duration for each participant was increased by 2 weeks. Subgroup analyses on secondary efficacy endpoints were removed. The hierarchical order of efficacy analyses was updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported