



Clinical trial results:

A Double-blind, Placebo-controlled, Randomized Phase III Pivotal Trial to Assess the Efficacy and Safety of Peanut Epicutaneous Immunotherapy with Viaskin® Peanut in Peanut-allergic Children (PEPITES Study)

Summary

EudraCT number	2015-002461-37
Trial protocol	IE DE
Global end of trial date	18 August 2017

Results information

Result version number	v1 (current)
This version publication date	15 September 2021
First version publication date	15 September 2021

Trial information

Trial identification

Sponsor protocol code	V712-301
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02636699
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 1-55-42-78-78, clinicaltrials@dbv-technologies.com
Scientific contact	Chief Medical Officer, DBV Technologies, 33 1-55-42-78-78, 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)	EMA-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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 August 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	18 August 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy and safety of DBV712 (Viaskin® Peanut) to induce desensitization to peanut in peanut-allergic participants aged 4 to 11 years old after a 12-month treatment period by epicutaneous immunotherapy.

Protection of trial subjects:

This study was designed and conducted in accordance with the International Council for Harmonisation Good Clinical Practice, as required by the major Regulatory Authorities, and in accordance with the ethical principles of the Declaration of Helsinki. The study was also carried out in keeping with local legal requirements.

The study was conducted with Investigators and staff who were trained and experienced in the diagnosis and management of peanut allergy and anaphylaxis, and equipped and capable of performing a double-blind, placebo-controlled food challenge (DBPCFC) in children.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 January 2016
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	Australia: 24
Country: Number of subjects enrolled	Canada: 89
Country: Number of subjects enrolled	Germany: 29
Country: Number of subjects enrolled	Ireland: 20
Country: Number of subjects enrolled	United States: 194
Worldwide total number of subjects	356
EEA total number of subjects	49

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	356
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 4 to 11 years old with peanut allergy at 31 active centers in Australia, Canada, Germany, Ireland and USA. Participants were randomized in a 2:1 ratio to receive DBV712 250 micrograms (µg) or placebo.

Pre-assignment

Screening details:

Overall maximum study duration for each participant was approximately 61 weeks (6-week screening period, 53-week treatment period and 2-week follow-up period). During the screening period, participants underwent a DBPCFC up to a highest dose of 300 milligrams (mg) peanut protein to confirm their allergy and their entry peanut eliciting dose (ED).

Period 1

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

Blinding implementation details:

DBV712 250 µg and placebo patches were supplied in identical pouches and were similar in physical appearance, thereby enabling double-blind conditions.

Arms

Are arms mutually exclusive?	Yes
Arm title	DBV712 250 µg

Arm description:

Participants applied 1 new DBV712 250 µg patch for 24 hours (±4 hours) every day for 12 months. The application duration was progressively increased to a duration of 24 hours daily over a 15-day period (6 hours during the first week, 12 hours during the second week and 24 hours from the third week onwards).

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

Dosage and administration details:

The active treatment, DBV712, is a cutaneous patch (DBV712 patch) containing 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 for 24 hours (±4 hours) every day for 12 months. The application duration was progressively increased to a duration of 24 hours daily over a 15-day period (6 hours during the first week, 12 hours during the second week and 24 hours from the third week onwards).

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

Dosage and administration details:

The placebo treatment consists of a matching cutaneous patch and dry deposit formulation, in which the peanut proteins were replaced by mannitol. Application of the placebo patch at a similar time for each daily application (morning or evening) was recommended.

Number of subjects in period 1	DBV712 250 µg	Placebo
Started	238	118
Completed	213	107
Not completed	25	11
Non-compliance with investigational product (IP)	2	-
Physician decision	-	1
Adverse Event	4	-
Withdrawal by Subject	13	6
Unspecified	3	1
Lost to follow-up	3	3

Baseline characteristics

Reporting groups

Reporting group title	DBV712 250 µg
Reporting group description:	
Participants applied 1 new DBV712 250 µg patch for 24 hours (±4 hours) every day for 12 months. The application duration was progressively increased to a duration of 24 hours daily over a 15-day period (6 hours during the first week, 12 hours during the second week and 24 hours from the third week onwards).	
Reporting group title	Placebo
Reporting group description:	
Participants applied 1 new placebo patch for 24 hours (±4 hours) every day for 12 months. The application duration was progressively increased to a duration of 24 hours daily over a 15-day period (6 hours during the first week, 12 hours during the second week and 24 hours from the third week onwards).	

Reporting group values	DBV712 250 µg	Placebo	Total
Number of subjects	238	118	356
Age categorical			
Units: Subjects			
4 to 5 years	55	32	87
6 to 11 years	183	86	269
Age continuous			
Units: years			
arithmetic mean	7.4	7.3	-
standard deviation	± 2.11	± 2.30	
Gender categorical			
Units: Subjects			
Female	89	49	138
Male	149	69	218
Race			
Units: Subjects			
White	194	96	290
Black or African American	1	2	3
Asian	19	8	27
Other	24	12	36
Screening ED Subgroup			
Screening ED Subgroup 1: participants with a screening ED of 1 mg, 3 mg or 10 mg peanut protein. Screening ED Subgroup 2: participants with a screening ED of 30 mg, 100 mg or 300 mg peanut protein.			
Units: Subjects			
Screening ED Subgroup 1	41	20	61
Screening ED Subgroup 2	197	98	295

End points

End points reporting groups

Reporting group title	DBV712 250 µg
Reporting group description: Participants applied 1 new DBV712 250 µg patch for 24 hours (±4 hours) every day for 12 months. The application duration was progressively increased to a duration of 24 hours daily over a 15-day period (6 hours during the first week, 12 hours during the second week and 24 hours from the third week onwards).	
Reporting group title	Placebo
Reporting group description: Participants applied 1 new placebo patch for 24 hours (±4 hours) every day for 12 months. The application duration was progressively increased to a duration of 24 hours daily over a 15-day period (6 hours during the first week, 12 hours during the second week and 24 hours from the third week onwards).	

Primary: Difference in Percentage of Treatment Responders at Month 12; Analyzed in the Overall Population

End point title	Difference in Percentage of Treatment Responders at Month 12; Analyzed in the Overall Population
End point description: The DBPCFCs to determine ED were performed at screening and Month 12, with each challenge occurring over 2 days. The participant was gradually fed increasing amounts of standardized blinded oral formulas containing either peanut protein (during 1 of the 2 days of the challenge), or without any peanut protein (during the other day of the challenge). A participant was defined as a treatment responder if: • ED was ≥300 mg peanut protein at Month 12 DBPCFC (for screening ED subgroup 1), or • ED was ≥1,000 mg peanut protein at Month 12 DBPCFC (for screening ED subgroup 2). Participants with missing treatment response at Month 12 were imputed as non-responders. The percentage of treatment responders at Month 12 is presented. Analysis was performed in the overall population. The intent-to-treat (ITT) population was comprised of all participants who were randomized.	
End point type	Primary
End point timeframe: At Month 12	

End point values	DBV712 250 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	118		
Units: percentage of participants				
number (confidence interval 95%)	35.3 (29.5 to 41.6)	13.6 (8.5 to 20.9)		

Statistical analyses

Statistical analysis title	DBV712 versus Placebo
Statistical analysis description: Analysis of the difference in response rates between DBV712 250 µg group and Placebo group and 2-sided Newcombe 95% confidence interval (CI). P-value was obtained from a 2-sided 5% test to evaluate	

the null hypothesis of no difference in response rates between treatment groups using the Wald method. Clinical relevance was evaluated based on the lower bound of the Newcombe 95% CI of the difference in response rates $\geq 15\%$.

Comparison groups	DBV712 250 µg v Placebo
Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Wald
Parameter estimate	Difference in Response Rates (%)
Point estimate	21.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.4
upper limit	29.8

Secondary: Difference in Percentages of Treatment Responders at Month 12; Analyzed in Each Screening ED Subgroup

End point title	Difference in Percentages of Treatment Responders at Month 12; Analyzed in Each Screening ED Subgroup
End point description:	The DBPCFCs to determine ED were performed at screening and Month 12, with each challenge occurring over 2 days. The participant was gradually fed increasing amounts of blinded oral formulas containing either peanut protein (during 1 of the 2 days of the challenge), or without any peanut protein (during the other day of the challenge). A participant was defined as a treatment responder if: • ED was ≥ 300 mg peanut protein at Month 12 DBPCFC (for screening ED subgroup 1), or • ED was $\geq 1,000$ mg peanut protein at Month 12 DBPCFC (for screening ED subgroup 2). Participants with missing treatment response at Month 12 were imputed as non-responders. The percentage of treatment responders at Month 12 is presented below. Analysis was performed for each separate screening ED subgroup. The ITT population was comprised of all participants who were randomized. 'n' denotes number of participants analyzed in each screening ED subgroup.
End point type	Secondary
End point timeframe:	
At Month 12	

End point values	DBV712 250 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	118		
Units: percentage of participants				
number (confidence interval 95%)				
Screening ED subgroup 1 (n = 41, 20)	39.0 (25.7 to 54.3)	20.0 (8.1 to 41.6)		
Screening ED subgroup 2 (n = 197, 98)	34.5 (28.2 to 41.4)	12.2 (7.1 to 20.2)		

Statistical analyses

Statistical analysis title	DBV712 versus Placebo (Screening ED subgroup 1)
Statistical analysis description:	
Analysis of the difference in response rates between DBV712 250 µg group and Placebo group and 2-sided Newcombe 95% CI. P-value was obtained from a 2-sided 5% test to evaluate the null hypothesis of no difference in response rates between treatment groups using the Wald method. Clinical relevance was evaluated based on the lower bound of the Newcombe 95% CI of the difference in response rates >0.	
Comparison groups	DBV712 250 µg v Placebo
Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.105
Method	Wald
Parameter estimate	Difference in Response Rates (%)
Point estimate	19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.4
upper limit	38.4

Statistical analysis title	DBV712 versus Placebo (Screening ED subgroup 2)
Statistical analysis description:	
Analysis of the difference in response rates between DBV712 250 µg group and Placebo group and 2-sided Newcombe 95% CI. P-value was obtained from a 2-sided 5% test to evaluate the null hypothesis of no difference in response rates between treatment groups using the Wald method. Clinical relevance was evaluated based on the lower bound of the Newcombe 95% CI of the difference in response rates >0.	
Comparison groups	DBV712 250 µg v Placebo
Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Wald
Parameter estimate	Difference in Response Rates (%)
Point estimate	22.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.1
upper limit	30.8

Secondary: Cumulative Reactive Dose (CRD) of Peanut Protein at Baseline and Month 12

End point title	Cumulative Reactive Dose (CRD) of Peanut Protein at Baseline and Month 12
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End point description:

The CRD was calculated as the sum of all doses given (including any repeated and partial doses). The median CRD of peanut protein at baseline and Month 12 is presented. Analysis was performed using the

modified baseline observation carried forward method to impute missing data at Month 12. The ITT population was comprised of all participants who were randomized.

End point type	Secondary
End point timeframe:	
Baseline and Month 12	

End point values	DBV712 250 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	118		
Units: mg				
median (inter-quartile range (Q1-Q3))				
Baseline	144.0 (44.0 to 444.0)	144.0 (44.0 to 444.0)		
Month 12	444.0 (144.0 to 1444.0)	144.0 (44.0 to 444.0)		

Statistical analyses

Statistical analysis title	DBV712 versus Placebo
Statistical analysis description:	
The treatment effect was estimated using the Hodges-Lehmann estimate of the difference in median CRDs at Month 12.	
Comparison groups	Placebo v DBV712 250 µg
Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Wilcoxon rank-sum test
Parameter estimate	Difference in Median CRD
Point estimate	297
Confidence interval	
level	95 %
sides	2-sided
lower limit	130
upper limit	317

Secondary: Relative Change From Baseline in Peanut-specific Immunoglobulin E (IgE) Over Time

End point title	Relative Change From Baseline in Peanut-specific Immunoglobulin E (IgE) Over Time
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End point description:

Venous blood samples were drawn to assess peanut-specific IgE levels at baseline and Months 3, 6 and 12. The median relative changes from baseline in IgE levels for each timepoint are presented. Relative change from baseline = $100 \times (\text{value at the visit} - \text{value at baseline}) / \text{value at baseline}$. The ITT population was comprised of all participants who were randomized. Only those with non-missing data were included in the analysis. 'n' denotes number of participants analyzed for each timepoint.

End point type	Secondary
End point timeframe:	
Baseline and Months 3, 6 and 12	

End point values	DBV712 250 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	118		
Units: Relative change (percentage)				
median (inter-quartile range (Q1-Q3))				
Month 3 (n = 232, 115)	78.716 (26.557 to 174.588)	16.964 (-12.591 to 48.802)		
Month 6 (n = 229, 111)	39.716 (-3.676 to 109.690)	4.605 (-26.380 to 30.352)		
Month 12 (n = 224, 108)	2.858 (-24.739 to 61.058)	-6.919 (-31.468 to 25.291)		

Statistical analyses

No statistical analyses for this end point

Secondary: Relative Changes From Baseline in Peanut-specific Immunoglobulin G4 Subtype (IgG4) Over Time

End point title	Relative Changes From Baseline in Peanut-specific Immunoglobulin G4 Subtype (IgG4) Over Time
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End point description:

Venous blood samples were drawn to assess peanut-specific IgG4 levels at baseline and Months 3, 6 and 12. The median relative changes from baseline in IgG4 levels for each timepoint are presented. Relative change from baseline=100×(value at the visit-value at baseline)/value at baseline. The ITT population was comprised of all participants who were randomized. Only those with non-missing data were included in the analysis. 'n' denotes number of participants analyzed for each timepoint.

End point type	Secondary
End point timeframe:	
Baseline and Months 3, 6 and 12	

End point values	DBV712 250 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	118		
Units: Relative change (percentage)				
median (inter-quartile range (Q1-Q3))				
Month 3 (n = 231, 115)	127.778 (55.660 to 259.615)	14.286 (0.000 to 45.833)		

Month 6 (n = 229, 110)	258.491 (107.843 to 549.351)	11.492 (-9.677 to 42.105)		
Month 12 (n = 224, 109)	513.487 (196.458 to 1105.235)	10.496 (- 10.108 to 33.333)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) were collected from Day 1, throughout the 53-week treatment period and additional 2-week follow-up period. Overall time frame of up to 55 weeks.

Adverse event reporting additional description:

The safety population was comprised of all participants who were randomized and received at least 1 dose of IP. Adverse events occurring after the end of the treatment period were recorded only if the Investigator considered there was a causal relationship with the IP and as such, were considered also as TEAEs.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	DBV712 250 µg
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Reporting group description:

Participants applied 1 new DBV712 250 µg patch for 24 hours (±4 hours) every day for 12 months. The application duration was progressively increased to a duration of 24 hours daily over a 15-day period (6 hours during the first week, 12 hours during the second week and 24 hours from the third week onwards).

Reporting group title	Placebo
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Reporting group description:

Participants applied 1 new placebo patch for 24 hours (±4 hours) every day for 12 months. The application duration was progressively increased to a duration of 24 hours daily over a 15-day period (6 hours during the first week, 12 hours during the second week and 24 hours from the third week onwards).

Serious adverse events	DBV712 250 µg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 238 (4.20%)	6 / 118 (5.08%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	6 / 238 (2.52%)	3 / 118 (2.54%)	
occurrences causally related to treatment / all	4 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food allergy			
subjects affected / exposed	1 / 238 (0.42%)	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			

Visual impairment			
subjects affected / exposed	0 / 238 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Coeliac disease			
subjects affected / exposed	0 / 238 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Throat irritation			
subjects affected / exposed	1 / 238 (0.42%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wheezing			
subjects affected / exposed	1 / 238 (0.42%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 238 (0.42%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 238 (0.42%)	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	DBV712 250 µg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	222 / 238 (93.28%)	96 / 118 (81.36%)	
Injury, poisoning and procedural complications			

Arthropod bite subjects affected / exposed occurrences (all)	8 / 238 (3.36%) 9	6 / 118 (5.08%) 7	
Limb injury subjects affected / exposed occurrences (all)	1 / 238 (0.42%) 1	6 / 118 (5.08%) 6	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	39 / 238 (16.39%) 74	18 / 118 (15.25%) 41	
General disorders and administration site conditions Application site eczema subjects affected / exposed occurrences (all)	25 / 238 (10.50%) 29	6 / 118 (5.08%) 18	
Application site erythema subjects affected / exposed occurrences (all)	67 / 238 (28.15%) 118	20 / 118 (16.95%) 54	
Application site pruritus subjects affected / exposed occurrences (all)	83 / 238 (34.87%) 154	14 / 118 (11.86%) 30	
Application site reaction subjects affected / exposed occurrences (all)	21 / 238 (8.82%) 29	2 / 118 (1.69%) 5	
Application site swelling subjects affected / exposed occurrences (all)	38 / 238 (15.97%) 86	2 / 118 (1.69%) 18	
Application site urticaria subjects affected / exposed occurrences (all)	16 / 238 (6.72%) 24	0 / 118 (0.00%) 0	
Pyrexia subjects affected / exposed occurrences (all)	48 / 238 (20.17%) 63	22 / 118 (18.64%) 34	
Immune system disorders Allergy to animal subjects affected / exposed occurrences (all)	8 / 238 (3.36%) 11	8 / 118 (6.78%) 16	

Food allergy subjects affected / exposed occurrences (all)	21 / 238 (8.82%) 29	9 / 118 (7.63%) 14	
Anaphylactic reaction subjects affected / exposed occurrences (all)	12 / 238 (5.04%) 12	4 / 118 (3.39%) 4	
Hypersensitivity subjects affected / exposed occurrences (all)	22 / 238 (9.24%) 29	6 / 118 (5.08%) 8	
Seasonal allergy subjects affected / exposed occurrences (all)	20 / 238 (8.40%) 30	5 / 118 (4.24%) 9	
Gastrointestinal disorders			
Abdominal pain upper subjects affected / exposed occurrences (all)	17 / 238 (7.14%) 19	3 / 118 (2.54%) 4	
Abdominal pain subjects affected / exposed occurrences (all)	10 / 238 (4.20%) 16	7 / 118 (5.93%) 12	
Vomiting subjects affected / exposed occurrences (all)	31 / 238 (13.03%) 42	10 / 118 (8.47%) 12	
Diarrhoea subjects affected / exposed occurrences (all)	14 / 238 (5.88%) 18	3 / 118 (2.54%) 4	
Respiratory, thoracic and mediastinal disorders			
Asthma subjects affected / exposed occurrences (all)	30 / 238 (12.61%) 78	16 / 118 (13.56%) 28	
Cough subjects affected / exposed occurrences (all)	52 / 238 (21.85%) 97	15 / 118 (12.71%) 27	
Oropharyngeal pain subjects affected / exposed occurrences (all)	16 / 238 (6.72%) 24	8 / 118 (6.78%) 12	
Nasal congestion			

subjects affected / exposed	21 / 238 (8.82%)	10 / 118 (8.47%)	
occurrences (all)	34	16	
Rhinitis allergic			
subjects affected / exposed	27 / 238 (11.34%)	9 / 118 (7.63%)	
occurrences (all)	50	14	
Wheezing			
subjects affected / exposed	18 / 238 (7.56%)	9 / 118 (7.63%)	
occurrences (all)	26	10	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	27 / 238 (11.34%)	9 / 118 (7.63%)	
occurrences (all)	36	31	
Rash			
subjects affected / exposed	18 / 238 (7.56%)	5 / 118 (4.24%)	
occurrences (all)	24	5	
Urticaria			
subjects affected / exposed	21 / 238 (8.82%)	15 / 118 (12.71%)	
occurrences (all)	29	25	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	20 / 238 (8.40%)	10 / 118 (8.47%)	
occurrences (all)	23	11	
Gastroenteritis viral			
subjects affected / exposed	15 / 238 (6.30%)	3 / 118 (2.54%)	
occurrences (all)	17	5	
Pharyngitis streptococcal			
subjects affected / exposed	16 / 238 (6.72%)	5 / 118 (4.24%)	
occurrences (all)	23	5	
Influenza			
subjects affected / exposed	7 / 238 (2.94%)	6 / 118 (5.08%)	
occurrences (all)	8	6	
Sinusitis			
subjects affected / exposed	17 / 238 (7.14%)	3 / 118 (2.54%)	
occurrences (all)	20	3	
Upper respiratory tract infection			

subjects affected / exposed	73 / 238 (30.67%)	30 / 118 (25.42%)	
occurrences (all)	134	48	
Viral infection			
subjects affected / exposed	19 / 238 (7.98%)	3 / 118 (2.54%)	
occurrences (all)	21	3	
Viral upper respiratory tract infection			
subjects affected / exposed	42 / 238 (17.65%)	20 / 118 (16.95%)	
occurrences (all)	82	40	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 December 2015	Sections affected by important changes in the protocol as per amendment 1: - Study design - Efficacy endpoints - Safety endpoints - Exploratory endpoints - Inclusion criteria - Exclusion criteria - Criteria for withdrawal from IP and study - Prohibited prior and concomitant medication - DBPCFC stopping rules - Safety criteria - Statistical methods.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported