Clinical trial results:
A Phase IIb, Randomized, Placebo-Controlled, Dose-Finding Clinical Trial to Study the Safety and Efficacy of MK-8237 Using an Environmental Exposure Chamber in Subjects with House Dust Induced Allergic Rhinitis/Rhinoconjunctivitis

Summary

EudraCT number	2012-001855-38
Trial protocol	AT
Global end of trial date	27 August 2013

Results information

Result version number	v1
This version publication date	15 March 2016
First version publication date	28 January 2015

Trial information

Trial identification

Sponsor protocol code	8237-003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01644617
WHO universal trial number (UTN)	-
Other trial identifiers	P07627: SCH 900237, MK-8237-003: Merck Registration

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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 August 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 August 2013
Global end of trial reached?	Yes
Global end of trial date	27 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the dose-related efficacy of MK-8237 sublingual house dust mite (HDM) tablet versus placebo in the treatment of HDM-induced rhinitis based on the average total nasal symptom score (TNSS) determined during the chamber challenge session at Week 24.

Protection of trial subjects:

The study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 124
Worldwide total number of subjects	124
EEA total number of subjects	124

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 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	124
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from one study site in Austria.

Pre-assignment

Screening details:

This study enrolled male and female participants, 18 years of age and older, with a history of allergic rhinitis/rhinoconjunctivitis to house dust of 1-year duration or more (with or without asthma).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MK-8237 6 DU

Arm description:

Participants receive MK-8237 6 Development Units (DU) sublingual tablets once daily (QD), preferably at the same time each day, for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	MK-8237 6 DU sublingual tablets
Investigational medicinal product code	
Other name	SCH 900237
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use

Dosage and administration details:

One MK-8237 6 DU sublingual tablet once daily for 24 weeks

Arm title	MK-8237 12 DU

Arm description:

Participants receive MK-8237 12 DU sublingual tablets, QD, preferably at the same time each day, for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	MK-8237 12 DU sublingual tablets
Investigational medicinal product code	
Other name	SCH 900237
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use

Dosage and administration details:

One MK-8237 12 DU sublingual tablet once daily for 24 weeks

Arm title	Placebo

Arm description:

Participants receive Placebo sublingual tablets, QD, preferably at the same time each day, for 24 weeks.

Arm type	Placebo

Investigational medicinal product name	Placebo sublingual tablets
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use

Dosage and administration details:

Placebo sublingual tablets once daily for 24 weeks

Number of subjects in period 1	MK-8237 6 DU	MK-8237 12 DU	Placebo
Started	41	42	41
Completed	36	36	34
Not completed	5	6	7
Consent withdrawn by subject	4	3	1
Adverse event, non-fatal	-	3	6
Lost to follow-up	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	MK-8237 6 DU
Reporting group description:	
Participants receive MK-8237 6 Development Units (DU) sublingual tablets once daily (QD), preferably at the same time each day, for 24 weeks.	
Reporting group title	MK-8237 12 DU
Reporting group description:	
Participants receive MK-8237 12 DU sublingual tablets, QD, preferably at the same time each day, for 24 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants receive Placebo sublingual tablets, QD, preferably at the same time each day, for 24 weeks.	

Reporting group values	MK-8237 6 DU	MK-8237 12 DU	Placebo
Number of subjects	41	42	41
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	41	42	41
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	30	19	17
Male	11	23	24

Reporting group values	Total		
Number of subjects	124		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	124		
From 65-84 years	0		
85 years and over	0		

Gender categorical Units: Subjects			
Female	66		
Male	58		

End points

End points reporting groups

Reporting group title	MK-8237 6 DU
Reporting group description:	
Participants receive MK-8237 6 Development Units (DU) sublingual tablets once daily (QD), preferably at the same time each day, for 24 weeks.	
Reporting group title	MK-8237 12 DU
Reporting group description:	
Participants receive MK-8237 12 DU sublingual tablets, QD, preferably at the same time each day, for 24 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants receive Placebo sublingual tablets, QD, preferably at the same time each day, for 24 weeks.	

Primary: Average Total Nasal Symptom Score (TNSS) During Environmental Exposure Chamber (EEC) Challenge Session at Week 24

End point title	Average Total Nasal Symptom Score (TNSS) During Environmental Exposure Chamber (EEC) Challenge Session at Week 24
End point description:	
TNSS is the total score for 4 nasal symptoms (itchy nose, blocked nose, runny nose and sneezing), each scored on a 4-point scale (0=No symptoms to 3=Severe symptoms). TNSS can range from 0 to 12 points, with a higher score indicating more severe nasal symptoms. The end point was calculated based on participant diary entries over the last 4 hours of the EEC challenge session at Week 24.	
End point type	Primary
End point timeframe:	
Week 24	

End point values	MK-8237 6 DU	MK-8237 12 DU	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	36[1]	36[2]	34[3]	
Units: Score on a Scale				
least squares mean (confidence interval 95%)	5.47 (4.55 to 6.39)	3.83 (2.94 to 4.72)	7.45 (6.57 to 8.33)	

Notes:

[1] - Full Analysis Set (FAS): Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

[2] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

[3] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

Statistical analyses

Statistical analysis title	Difference in Least Squares (LS) Means at Week 24
Statistical analysis description:	
Difference in TNSS LS means at Week 24: MK-8237 6 DU vs. Placebo - Analysis via analysis of covariance (ANCOVA) with treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the	

bootstrap method.

Comparison groups	MK-8237 6 DU v Placebo
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-1.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.24
upper limit	-0.72

Statistical analysis title	Difference in LS Means at Week 24

Statistical analysis description:

Difference in TNSS LS means at Week 24: MK-8237 12 DU vs. Placebo - Analysis via ANCOVA with treatment and Baseline endpoint score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method.

Comparison groups	MK-8237 12 DU v Placebo
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-3.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.85
upper limit	-2.39

Secondary: Average Total Symptom Score (TSS) During EEC Challenge Sessions at Weeks 8, 16 and 24

End point title	Average Total Symptom Score (TSS) During EEC Challenge Sessions at Weeks 8, 16 and 24

End point description:

TSS is the sum of the TNSS and Total Ocular Symptom Score (TOSS). TOSS is the total of scores for 2 ocular symptom scores (gritty feeling/red/itchy eyes and watery eyes), each scored on a 4-point scale (0=No symptoms to 3=Severe symptoms; TOSS range: 0 to 6 points). TSS could range from 0 to 18 points, with a higher score indicating more severe nasal and ocular symptoms. The end point was calculated based on participant diary entries over the last 4 hours of the EEC challenge sessions at Weeks 8, 16 and 24.

End point type	Secondary

End point timeframe:

Week 8, Week 16, Week 24

End point values	MK-8237 6 DU	MK-8237 12 DU	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39[4]	40[5]	40[6]	
Units: Score on a Scale				
least squares mean (confidence interval 95%)				
Week 8 (n=39, 40, 39)	7.65 (6.81 to 8.48)	6.51 (5.52 to 7.51)	8.48 (7.56 to 9.39)	
Week 16 (n=36, 39, 38)	7.21 (6.05 to 8.37)	5.95 (4.92 to 6.99)	8.58 (7.46 to 9.69)	
Week 24 (n=36, 36, 34)	6.62 (5.48 to 7.77)	4.43 (3.2 to 5.66)	9.27 (7.98 to 10.57)	

Notes:

[4] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

[5] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

[6] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

Statistical analyses

Statistical analysis title	Difference in LS Means at Week 24

Statistical analysis description:

Difference in TSS LS means at Week 24: MK-8237 6 DU vs. Placebo - Analysis via ANCOVA with treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method. Number of participants included in analysis=70.

Comparison groups	MK-8237 6 DU v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-2.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.35
upper limit	-0.95

Statistical analysis title	Difference in LS Means at Week 24

Statistical analysis description:

Difference in TSS LS means at Week 24: MK-8237 12 DU vs. Placebo - Analysis via ANCOVA with treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method. Number of participants included in analysis=70.

Comparison groups	MK-8237 12 DU v Placebo

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-4.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.59
upper limit	-3.09

Statistical analysis title	Difference in LS Means at Week 8

Statistical analysis description:

Difference in TSS LS means at Week 8: MK-8237 6 DU vs. Placebo - Analysis via ANCOVA with treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method. Number of participants included in analysis=78.

Comparison groups	MK-8237 6 DU v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.181
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.06
upper limit	0.4

Statistical analysis title	Difference in LS Means at Week 8

Statistical analysis description:

Difference in TSS LS means at Week 8: MK-8237 12 DU vs. Placebo - Analysis via ANCOVA with treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method. Number of participants included in analysis=79.

Comparison groups	MK-8237 12 DU v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-1.97

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	-0.64

Statistical analysis title	Difference in LS Means at Week 16

Statistical analysis description:

Difference in TSS LS means at Week 16: MK-8237 6 DU vs. Placebo - Analysis via ANCOVA with treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method. Number of participants included in analysis=74.

Comparison groups	MK-8237 6 DU v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.091
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.96
upper limit	0.22

Statistical analysis title	Difference in LS Means at Week 16

Statistical analysis description:

Difference in TSS LS means at Week 16: MK-8237 12 DU vs. Placebo - Analysis via ANCOVA with treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method. Number of participants included in analysis=77.

Comparison groups	MK-8237 12 DU v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-2.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.12
upper limit	-1.13

Secondary: Average Total Ocular Symptom Score (TOSS) During EEC Challenge Sessions at Weeks 8, 16 and 24

End point title	Average Total Ocular Symptom Score (TOSS) During EEC Challenge Sessions at Weeks 8, 16 and 24

End point description:

TOSS is the total of scores for 2 ocular symptom scores (gritty feeling/red/itchy eyes and watery eyes), each scored on a 4-point scale (0=No symptoms to 3=Severe symptoms). TOSS could range from 0 to 6 points, with a higher score indicating more severe ocular symptoms. The end point was calculated based on participant diary entries over the last 4 hours of the EEC challenge sessions at Weeks 8, 16 and 24.

End point type	Secondary

End point timeframe:

Week 8, Week 16, Week 24

End point values	MK-8237 6 DU	MK-8237 12 DU	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39[7]	40[8]	40[9]	
Units: Score on a Scale				
least squares mean (confidence interval 95%)				
Week 8 (n=39, 40, 39)	1.45 (0.68 to 1.53)	1.18 (0.86 to 1.5)	1.79 (1.36 to 2.22)	
Week 16 (n=36, 39, 38)	1.54 (1.08 to 1.83)	1.14 (0.72 to 1.55)	1.67 (1.22 to 2.12)	
Week 24 (n=36, 36, 34)	1.1 (1.05 to 2.03)	0.61 (0.21 to 1)	1.87 (1.35 to 2.4)	

Notes:

[7] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

[8] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

[9] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

Statistical analyses

Statistical analysis title	Difference in LS Means at Week 24

Statistical analysis description:

Difference in TOSS LS means at Week 24: MK-8237 6 DU vs. Placebo - Analysis via ANCOVA with treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method. Number of participants included in analysis=70.

Comparison groups	MK-8237 6 DU v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.023
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-0.77

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.43
upper limit	-0.11

Statistical analysis title	Difference in LS Means at Week 24

Statistical analysis description:

Difference in TOSS LS means at Week 24: MK-8237 12 DU vs. Placebo - Analysis via ANCOVA with treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method. Number of participants included in analysis=70.

Comparison groups	MK-8237 12 DU v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.92
upper limit	-0.62

Statistical analysis title	Difference in LS Means at Week 8

Statistical analysis description:

Difference in TOSS LS means at Week 8: MK-8237 6 DU vs. Placebo - Analysis via ANCOVA with treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method. Number of participants included in analysis=78.

Comparison groups	MK-8237 6 DU v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.235
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.22

Statistical analysis title	Difference in LS Means at Week 8

Statistical analysis description:

Difference in TOSS LS means at Week 8: MK-8237 12 DU vs. Placebo - Analysis via ANCOVA with treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method. Number of participants included in analysis=79.

Comparison groups	MK-8237 12 DU v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.023
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.14
upper limit	-0.09

Statistical analysis title	Difference in LS Means at Week 16

Statistical analysis description:

Difference in TOSS LS means at Week 16: MK-8237 6 DU vs. Placebo - Analysis via ANCOVA with treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method. Number of participants included in analysis=74.

Comparison groups	MK-8237 6 DU v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.691
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	0.52

Statistical analysis title	Difference in LS Means at Week 16

Statistical analysis description:

Difference in TOSS LS means at Week 16: MK-8237 12 DU vs. Placebo - Analysis via ANCOVA with

treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method. Number of participants included in analysis=77.

Comparison groups	MK-8237 12 DU v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.082
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.13
upper limit	0.07

Secondary: Change from Pre-treatment in House Dust Mite (HDM)-specific Immunoglobulin E (IgE) Levels at Week 8

End point title	Change from Pre-treatment in House Dust Mite (HDM)-specific Immunoglobulin E (IgE) Levels at Week 8

End point description:

Participant IgE levels against Dermatophagoides pteronyssinus (D. pteronyssinus) and Dermatophagoides farinae (D. farinae) were assessed at Pre-treatment (Week -6) and at Week 8. The changes in HDM-specific IgE levels (in Log10 Scale) from Pre-treatment to Week 8 were calculated.

End point type	Secondary

End point timeframe:

Pre-treatment (Week -6) and Week 8

End point values	MK-8237 6 DU	MK-8237 12 DU	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39[10]	40[11]	40[12]	
Units: Log 10 kU/L				
least squares mean (confidence interval 95%)				
D. pteronyssinus	0.5 (0.41 to 0.59)	0.63 (0.51 to 0.75)	0.08 (0.03 to 0.12)	
D. farinae	0.46 (0.38 to 0.55)	0.59 (0.48 to 0.7)	0.07 (0.03 to 0.11)	

Notes:

[10] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

[11] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

[12] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

Statistical analyses

Statistical analysis title	Difference in LS Means - D. farinae

Statistical analysis description:

Difference in LS means for D. farinae IgE levels: MK-8237 6 DU vs. Placebo - Analysis via ANOVA with treatment as fixed effect and adjusted for different error variation for each treatment group.

Comparison groups	MK-8237 6 DU v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Difference in LS Means
Point estimate	0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.48

Statistical analysis title	Difference in LS Means - D. farinae

Statistical analysis description:

Difference in LS means for D. farinae IgE levels: MK-8237 12 DU vs. Placebo - Analysis via ANOVA with treatment as fixed effect and adjusted for different error variation for each treatment group.

Comparison groups	MK-8237 12 DU v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Difference in LS Means
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	0.64

Statistical analysis title	Difference in LS Means - D. pteronyssinus

Statistical analysis description:

Difference in LS means for D. pteronyssinus IgE levels: MK-8237 6 DU vs. Placebo - Analysis via ANOVA with treatment as fixed effect and adjusted for different error variation for each treatment group.

Comparison groups	MK-8237 6 DU v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Difference in LS Means
Point estimate	0.42

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	0.52

Statistical analysis title	Difference in LS Means - D. pteronyssinus

Statistical analysis description:

Difference in LS means for D. pteronyssinus IgE levels: MK-8237 12 DU vs Placebo - Analysis via ANOVA with treatment as fixed effect and adjusted for different error variation for each treatment group.

Comparison groups	MK-8237 12 DU v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Difference in LS Means
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	0.68

Secondary: Change from Pre-treatment in HDM-specific Immunoglobulin G4 (IgG4) Levels at Week 8

End point title	Change from Pre-treatment in HDM-specific Immunoglobulin G4 (IgG4) Levels at Week 8

End point description:

Participant IgG4 levels for D. pteronyssinus and D. farinae were assessed at Pre-treatment (Week -6) and Week 8. The changes in HDM-specific IgG4 levels (in Log10 Scale) from Pre-treatment (Week -6) to Week 8 were calculated.

End point type	Secondary

End point timeframe:

Pre-treatment (Week -6) and Week 8

End point values	MK-8237 6 DU	MK-8237 12 DU	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39[13]	40[14]	40[15]	
Units: Log 10 mg/L				
least squares mean (confidence interval 95%)				
D. pteronyssinus	0.19 (0.12 to 0.25)	0.23 (0.13 to 0.33)	0 (-0.01 to 0.01)	

D. farinae	0.24 (0.16 to 0.32)	0.32 (0.22 to 0.41)	-0.01 (-0.03 to 0.01)	

Notes:

[13] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

[14] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

[15] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

Statistical analyses

Statistical analysis title	Difference in LS Means - D. pteronyssinus

Statistical analysis description:

Difference in LS means in D. pteronyssinus IgG4 levels: MK-8237 6 DU vs. Placebo - Analysis via ANOVA with treatment as fixed effect and adjusted for different error variation for each treatment group.

Comparison groups	MK-8237 6 DU v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Difference in LS Means
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	0.25

Statistical analysis title	Difference in LS Means - D. pteronyssinus

Statistical analysis description:

Difference in LS means in D. pteronyssinus IgG4 levels: MK-8237 12 DU vs. Placebo - Analysis via ANOVA with treatment as fixed effect and adjusted for different error variation for each treatment group.

Comparison groups	MK-8237 12 DU v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Difference in LS Means
Point estimate	0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	0.33

Statistical analysis title	Difference in LS Means - D. farinae

Statistical analysis description:

Difference in LS means in D. farinae IgG4 levels: MK-8237 6 DU vs. Placebo - Analysis via ANOVA with treatment as fixed effect and adjusted for different error variation for each treatment group.

Comparison groups	MK-8237 6 DU v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Difference in LS Means
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	0.33

Statistical analysis title	Difference in LS Means - D. farinae

Statistical analysis description:

Difference in LS means in D. farinae IgG4 levels: MK-8237 12 DU vs. Placebo - Analysis via ANOVA with treatment as fixed effect and adjusted for different error variation for each treatment group.

Comparison groups	MK-8237 12 DU v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Difference in LS Means
Point estimate	0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	0.42

Secondary: Average TNSS During EEC Challenge Sessions at Weeks 8 and 16

End point title	Average TNSS During EEC Challenge Sessions at Weeks 8 and 16

End point description:

TNSS is the total score for 4 nasal symptoms (itchy nose, blocked nose, runny nose and sneezing), each scored on a 4-point scale (0=No symptoms to 3=Severe symptoms). TNSS can range from 0 to 12 points, with a higher score indicating more severe nasal symptoms. The end point was calculated based on participant diary entries over the last 4 hours of the EEC challenge sessions at Weeks 8 and 16.

End point type	Secondary

End point timeframe:

Week 8, Week 16

End point values	MK-8237 6 DU	MK-8237 12 DU	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39[16]	40[17]	40[18]	
Units: Score on a Scale				
least squares mean (confidence interval 95%)				
Week 8 (n=39, 40, 39)	6.16 (5.55 to 6.78)	5.34 (4.53 to 6.15)	6.71 (6.13 to 7.28)	
Week 16 (n=36, 39, 38)	5.67 (4.83 to 6.5)	4.82 (4.07 to 5.56)	6.9 (6.13 to 7.67)	

Notes:

[16] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

[17] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

[18] - FAS: Took ≥1 study drug dose and had ≥1 post-randomization efficacy measurement.

Statistical analyses

Statistical analysis title	Difference in LS Means at Week 8

Statistical analysis description:

Difference in TNSS LS means at Week 8: MK-8237 6 DU vs. Placebo - Analysis via ANCOVA with treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method. Number of participants included in analysis=78.

Comparison groups	MK-8237 6 DU v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.198
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.38
upper limit	0.29

Statistical analysis title	Difference in LS Means at Week 16

Statistical analysis description:

Difference in TNSS LS means at Week 16: MK-8237 6 DU vs. Placebo - Analysis via ANCOVA with treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method. Number of participants included in analysis=74.

Comparison groups	MK-8237 6 DU v Placebo

Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.032
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.36
upper limit	-0.11

Statistical analysis title	Difference in LS Means at Week 8

Statistical analysis description:

Difference in TNSS LS means at Week 8: MK-8237 12 DU vs. Placebo - Analysis via ANCOVA with treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method. Number of participants included in analysis=79.

Comparison groups	MK-8237 12 DU v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.34
upper limit	-0.39

Statistical analysis title	Difference in LS Means at Week 16

Statistical analysis description:

Difference in TNSS LS means at Week 16: MK-8237 12 DU vs. Placebo - Analysis via ANCOVA with treatment and Baseline end point score as fixed effects, and adjusted for different error variation for each treatment group. Treatment difference relative to Placebo was calculated by (MK-8237-Placebo)/Placebo * 100%. Confidence intervals were calculated by the bootstrap method. Number of participants included in analysis=77.

Comparison groups	MK-8237 12 DU v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-2.08

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.14
upper limit	-1.03

Secondary: Number of Participants Who Experienced At Least One Adverse Event (AE)

End point title	Number of Participants Who Experienced At Least One Adverse Event (AE)

End point description:

An AE is defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of study drug, whether or not considered related to this study drug.

End point type	Secondary

End point timeframe:

Up to 26 weeks (Up to 2 weeks after last dose of study drug)

End point values	MK-8237 6 DU	MK-8237 12 DU	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41[19]	42[20]	41[21]	
Units: Participants	36	38	32	

Notes:

[19] - All Participants as Treated (APaT): All randomized participants who took ≥1 study drug dose.

[20] - APaT: All randomized participants who took ≥1 study drug dose.

[21] - APaT: All randomized participants who took ≥1 study drug dose.

Statistical analyses

Statistical analysis title	Difference in Percentage vs. Placebo

Statistical analysis description:

Difference in percentage of participants who experienced at least one AE vs. Placebo: MK-8237 6 DU vs. Placebo - Analysis based on Miettinen & Nurminen method.

Comparison groups	MK-8237 6 DU v Placebo
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen Method
Parameter estimate	Difference in Percentages
Point estimate	9.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	26.6

Statistical analysis title	Difference in Percentage vs. Placebo

Statistical analysis description:

Difference in percentage of participants who experienced at least one AE vs. Placebo: MK-8237 12 DU vs. Placebo - Analysis based on Miettinen & Nurminen method.

Comparison groups	MK-8237 12 DU v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen Method
Parameter estimate	Difference in Percentages
Point estimate	12.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	28.9

Secondary: Number of Participants Who Discontinued Study Drug Due to an AE

End point title	Number of Participants Who Discontinued Study Drug Due to an AE

End point description:

An AE is defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of study drug, whether or not considered related to this study drug.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	MK-8237 6 DU	MK-8237 12 DU	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41[22]	42[23]	41[24]	
Units: Participants	0	3	6	

Notes:

[22] - APaT: All randomized participants who took ≥1 study drug dose.

[23] - APaT: All randomized participants who took ≥1 study drug dose.

[24] - APaT: All randomized participants who took ≥1 study drug dose.

Statistical analyses

Statistical analysis title	Difference in Percentage vs. Placebo

Statistical analysis description:

Difference in percentage of participants who discontinued study drug due to an AE vs. Placebo: MK-8237 6 DU vs. Placebo - Analysis based on Miettinen & Nurminen method.

Comparison groups	MK-8237 6 DU v Placebo

Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentages
Point estimate	-14.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.5
upper limit	-5.4

Statistical analysis title	Difference in Percentage vs. Placebo

Statistical analysis description:

Difference in percentage of participants who discontinued study drug due to an AE vs. Placebo: MK-8237 12 DU vs. Placebo - Analysis based on Miettinen & Nurminen method.

Comparison groups	MK-8237 12 DU v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentages
Point estimate	-7.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.6
upper limit	6.7

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 26 weeks (Up to 2 weeks after last dose of study drug)	
Adverse event reporting additional description:	
APaT: All randomized participants who took ≥1 study drug dose.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	MK-8237 6 DU
Reporting group description:	
Participants receive MK-8237 6 Development Units (DU) sublingual tablets once daily (QD), preferably at the same time each day, for 24 weeks	
Reporting group title	MK-8237 12 DU
Reporting group description:	
Participants receive MK-8237 12 DU sublingual tablets, QD, preferably at the same time each day, for 24 weeks	
Reporting group title	Placebo
Reporting group description:	
Participants receive Placebo sublingual tablets, QD, preferably at the same time each day, for 24 weeks	

Serious adverse events	MK-8237 6 DU	MK-8237 12 DU	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	1 / 41 (2.44%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	MK-8237 6 DU	MK-8237 12 DU	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 41 (85.37%)	36 / 42 (85.71%)	24 / 41 (58.54%)
Nervous system disorders			

Headache			
subjects affected / exposed	6 / 41 (14.63%)	7 / 42 (16.67%)	8 / 41 (19.51%)
occurrences (all)	9	9	13
Ear and labyrinth disorders			
Ear pruritus			
subjects affected / exposed	1 / 41 (2.44%)	3 / 42 (7.14%)	0 / 41 (0.00%)
occurrences (all)	1	3	0
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	2 / 41 (4.88%)	4 / 42 (9.52%)	0 / 41 (0.00%)
occurrences (all)	2	6	0
Lip swelling			
subjects affected / exposed	2 / 41 (4.88%)	8 / 42 (19.05%)	1 / 41 (2.44%)
occurrences (all)	2	9	2
Oedema mouth			
subjects affected / exposed	10 / 41 (24.39%)	10 / 42 (23.81%)	0 / 41 (0.00%)
occurrences (all)	10	10	0
Oral pruritus			
subjects affected / exposed	6 / 41 (14.63%)	6 / 42 (14.29%)	0 / 41 (0.00%)
occurrences (all)	6	7	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 41 (4.88%)	3 / 42 (7.14%)	1 / 41 (2.44%)
occurrences (all)	2	3	1
Dyspnoea			
subjects affected / exposed	8 / 41 (19.51%)	7 / 42 (16.67%)	13 / 41 (31.71%)
occurrences (all)	13	11	22
Oropharyngeal pain			
subjects affected / exposed	4 / 41 (9.76%)	4 / 42 (9.52%)	2 / 41 (4.88%)
occurrences (all)	4	5	2
Rhinitis allergic			
subjects affected / exposed	7 / 41 (17.07%)	5 / 42 (11.90%)	6 / 41 (14.63%)
occurrences (all)	8	5	7
Rhinitis seasonal			
subjects affected / exposed	3 / 41 (7.32%)	1 / 42 (2.38%)	2 / 41 (4.88%)
occurrences (all)	3	1	2

Throat irritation			
subjects affected / exposed	14 / 41 (34.15%)	22 / 42 (52.38%)	0 / 41 (0.00%)
occurrences (all)	15	26	0
Infections and infestations			
Influenza			
subjects affected / exposed	3 / 41 (7.32%)	3 / 42 (7.14%)	3 / 41 (7.32%)
occurrences (all)	5	3	3
Nasopharyngitis			
subjects affected / exposed	9 / 41 (21.95%)	12 / 42 (28.57%)	8 / 41 (19.51%)
occurrences (all)	11	16	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported