Clinical trial results:
A Phase III, multicenter, open-label, long-term trial to study the efficacy and safety of MK-4117 in Japanese subjects with eczema/dermatitis and dermal pruritus

Summary

EudraCT number	2017-000610-26
Trial protocol	Outside EU/EEA
Global end of trial date	22 March 2014

Results information

Result version number	v1 (current)
This version publication date	12 May 2017
First version publication date	12 May 2017

Trial information

Trial identification

Sponsor protocol code	4117-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01916980
WHO universal trial number (UTN)	-
Other trial identifiers	JAPIC-CTI: 132245

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 March 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This was an efficacy and safety study of up to 12 weeks of MK-4117 (desloratadine) in Japanese participants with eczema/dermatitis or dermal pruritus. The primary hypothesis of this study is that the sum of the daytime and nighttime pruritus/itch scores for both the eczema/dermatitis group and the dermal pruritus group will be significantly improved at Week 2 compared to Baseline.

Protection of trial subjects:

This 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	27 August 2013
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	Japan: 94
Worldwide total number of subjects	94
EEA total number of subjects	0

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)	14
Adults (18-64 years)	70
From 65 to 84 years	9
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Japanese participants of at least 12 years of age with eczema/dermatitis or dermal pruritus were recruited.

Pre-assignment

Screening details:

The screening period lasted up to 2 weeks. A total of 99 participants were screened and 94 were enrolled.

Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Desloratadine: Eczema/Dermatitis

Arm description:

Participants with eczema/dermatitis received desloratadine 5 mg (taken as one 5-mg tablet) by mouth once daily in the evening for up to 12 weeks. After Week 4, the dose of desloratadine could have been increased from 5 mg/day to 10 mg/day (taken as two 5-mg tablets) by mouth once daily in the evening for up to 8 weeks, if criteria for dose up-titration were met, there was insufficient anti-pruritic efficacy and there was no safety concern.

Arm type	Experimental
Investigational medicinal product name	Desloratadine 5 mg tablet
Investigational medicinal product code	
Other name	MK-4117
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One desloratadine 5 mg tablet taken by mouth in the evening (dose could have increased to two 5 mg tablets after Week 4).

Arm title	Desloratadine: Dermal Pruritis

Arm description:

Participants with dermal pruritus received desloratadine 5 mg (taken as one 5-mg tablet) by mouth once daily in the evening for up to 12 weeks. After Week 4, the dose of desloratadine could have been increased from 5 mg/day to 10 mg/day (taken as two 5-mg tablets) by mouth once daily in the evening for up to 8 weeks, if criteria for dose up-titration were met, there was insufficient anti-pruritic efficacy and there was no safety concern.

Arm type	Experimental
Investigational medicinal product name	Desloratadine 5 mg tablet
Investigational medicinal product code	
Other name	MK-4117
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One desloratadine 5 mg tablet taken by mouth in the evening (dose could have increased to two 5 mg tablets after Week 4).

Number of subjects in period 1	Desloratadine: Eczema/Dermatitis	Desloratadine: Dermal Pruritis
Started	65	29
Completed	58	25
Not completed	7	4
Consent withdrawn by subject	1	-
Adverse event, non-fatal	4	2
Lack of efficacy	2	2

Baseline characteristics

Reporting groups	
Reporting group title	Desloratadine: Eczema/Dermatitis
Reporting group description:	
Participants with eczema/dermatitis received desloratadine 5 mg (taken as one 5-mg tablet) by mouth once daily in the evening for up to 12 weeks. After Week 4, the dose of desloratadine could have been increased from 5 mg/day to 10 mg/day (taken as two 5-mg tablets) by mouth once daily in the evening for up to 8 weeks, if criteria for dose up-titration were met, there was insufficient anti-pruritic efficacy and there was no safety concern.	
Reporting group title	Desloratadine: Dermal Pruritis
Reporting group description:	
Participants with dermal pruritus received desloratadine 5 mg (taken as one 5-mg tablet) by mouth once daily in the evening for up to 12 weeks. After Week 4, the dose of desloratadine could have been increased from 5 mg/day to 10 mg/day (taken as two 5-mg tablets) by mouth once daily in the evening for up to 8 weeks, if criteria for dose up-titration were met, there was insufficient anti-pruritic efficacy and there was no safety concern.	

Reporting group values	Desloratadine: Eczema/Dermatitis	Desloratadine: Dermal Pruritis	Total
Number of subjects	65	29	94
Age Categorical Units: Subjects			
Adolescents (12-17 years)	10	4	14
Adults (18-64 years)	52	18	70
From 65-84 years	3	6	9
85 years and over	0	1	1
Age Continuous Units: years			
arithmetic mean	33	44.1	
standard deviation	± 15.2	± 21.5	-
Gender Categorical Units: Subjects			
Female	34	17	51
Male	31	12	43
Investigator-assessed Sum of Daytime and Nighttime Pruritus/Itch Scores at Baseline			
The Investigator assessed the severity of participant pruritus/itch during the daytime (0=Virtually no itching to 4=Cannot relax because of constant itching) and nighttime (0=Virtually no itching to 4=Cannot sleep because of itching) at Baseline. The sum of the daytime and nighttime pruritus/itch scores could range from 0 to 8, with a higher sum score indicating greater severity. Baseline values were assessed based on the participant diary for two days before the Baseline clinic visit and on the participant interview at the Baseline clinic visit.			
Units: Score on a Scale			
arithmetic mean	4.75	5.1	
standard deviation	± 1.1	± 1.47	-
Participant-assessed Pruritus Visual Analog Scale (VAS) Score at Baseline			
Participants assessed the degree of their pruritus using a 100-mm visual analog scale (VAS; 0mm=No itch, 100mm=Worst imaginable itch) at Baseline. Pruritus VAS scores could range from 0 to 100, with a higher score indicating more severe itching. Baseline was defined as the participant evaluation at the day of the Baseline clinic visit.			
Units: Score on a Scale			
arithmetic mean	60.42	60.79	

standard deviation	± 18.94	± 24.45	-

End points

End points reporting groups

Reporting group title	Desloratadine: Eczema/Dermatitis

Reporting group description:

Participants with eczema/dermatitis received desloratadine 5 mg (taken as one 5-mg tablet) by mouth once daily in the evening for up to 12 weeks. After Week 4, the dose of desloratadine could have been increased from 5 mg/day to 10 mg/day (taken as two 5-mg tablets) by mouth once daily in the evening for up to 8 weeks, if criteria for dose up-titration were met, there was insufficient anti-pruritic efficacy and there was no safety concern.

Reporting group title	Desloratadine: Dermal Pruritis

Reporting group description:

Participants with dermal pruritus received desloratadine 5 mg (taken as one 5-mg tablet) by mouth once daily in the evening for up to 12 weeks. After Week 4, the dose of desloratadine could have been increased from 5 mg/day to 10 mg/day (taken as two 5-mg tablets) by mouth once daily in the evening for up to 8 weeks, if criteria for dose up-titration were met, there was insufficient anti-pruritic efficacy and there was no safety concern.

Primary: Change From Baseline in Pruritus/Itch Score (Sum of Daytime and Nighttime Scores) Assessed by the Investigator at Week 2

End point title	Change From Baseline in Pruritus/Itch Score (Sum of Daytime and Nighttime Scores) Assessed by the Investigator at Week 2[1]

End point description:

The Investigator assessed the severity of participant pruritus/itch during the daytime (0=Virtually no itching to 4=Cannot relax because of constant itching) and nighttime (0=Virtually no itching to 4=Cannot sleep because of itching). The sum of the daytime and nighttime pruritus/itch scores could range from 0 to 8, with a higher sum score indicating greater severity. The change from Baseline in the sum of the daytime and nighttime pruritus/itch scores at Week 2 clinic visit was calculated. The Full Analysis Set (FAS) population consisted of all participants who received at least one dose of study drug and had a Baseline or at least one post-Baseline observation for Investigator-assessed pruritus/itch score.

End point type	Primary

End point timeframe:

Baseline Visit and Week 2

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, only descriptive statistics are presented.

End point values	Desloratadine: Eczema/Dermatitis	Desloratadine: Dermal Pruritis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	29		
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-1.63 (-2.01 to -1.25)	-2.17 (-2.74 to -1.61)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Experienced at Least One Adverse Event (AE)

End point title	Percentage of Participants Who Experienced at Least One Adverse Event (AE)[2]

End point description:

An AE is any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a study drug or protocol-specified procedure, whether or not considered related to the study drug or protocol-specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a pre-existing condition that is temporally associated with the use of the study drug is also an AE. The All-Participants-as-Treated (APaT) population consisted of all participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Up to 14 weeks (up to 2 weeks after the last dose of study drug)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, only descriptive statistics are presented.

End point values	Desloratadine: Eczema/Dermatitis	Desloratadine: Dermal Pruritis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	29		
Units: Percentage of Participants				
number (not applicable)	53.8	48.3		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Discontinued Study Drug Due to an AE

End point title	Percentage of Participants Who Discontinued Study Drug Due to an AE[3]

End point description:

An adverse event is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a pre-existing condition that is temporally associated with the use of the study drug is also an AE. The APaT population consisted of all participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Up to 12 weeks

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, only descriptive statistics are presented.

End point values	Desloratadine: Eczema/Dermatitis	Desloratadine: Dermal Pruritis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	29		
Units: Percentage of Participants				
number (not applicable)	6.2	6.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pruritus/Itch Score (Sum of Daytime and Nighttime Scores) Assessed by the Investigator at Day 3, Week 1, Week 4, Week 6, Week 8 and Week 12

End point title	Change From Baseline in Pruritus/Itch Score (Sum of Daytime and Nighttime Scores) Assessed by the Investigator at Day 3, Week 1, Week 4, Week 6, Week 8 and Week 12

End point description:

The Investigator assessed the severity of participant pruritus/itch during the daytime (0=Virtually no itching to 4=Cannot relax because of constant itching) and nighttime (0=Virtually no itching to 4=Cannot sleep because of itching). The sum of the daytime and nighttime pruritus/itch scores could range from 0 to 8, with a higher sum score indicating greater severity. The changes from Baseline in the sum of the daytime and nighttime pruritus/itch scores at the Day 3, Week 1, Week 4, Week 6, Week 8 and Week 12 clinic visits were calculated. The FAS population consisted of all participants who received at least one dose of study drug and had a Baseline or at least one post-Baseline observation for Investigator-assessed pruritus/itch score.

End point type	Secondary

End point timeframe:

Baseline Visit and Day 3 Visit, Week 1 Visit, Week 4 Visit, Week 6 Visit, Week 8 Visit, Week 12 Visit

End point values	Desloratadine: Eczema/Dermatitis	Desloratadine: Dermal Pruritis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	29		
Units: Score on a Scale				
least squares mean (confidence interval 95%)				
Change from Baseline at Day 3 (n=65, 29)	-0.83 (-1.18 to -0.49)	-1.59 (-2.1 to -1.07)		
Change from Baseline at Week 1 (n=65, 29)	-1.29 (-1.66 to -0.92)	-2.07 (-2.62 to -1.52)		
Change from Baseline at Week 4 (n=63, 28)	-1.88 (-2.29 to -1.47)	-2.39 (-3.01 to -1.78)		
Change from Baseline at Week 6 (n=62, 26)	-2.33 (-2.72 to -1.94)	-2.48 (-3.07 to -1.89)		
Change from Baseline at Week 8 (n=61, 25)	-2.18 (-2.59 to -1.76)	-3.15 (-3.79 to -2.52)		
Change from Baseline at Week 12 (n=58, 25)	-2.51 (-2.89 to -2.14)	-3.47 (-4.04 to -2.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Moderate or Remarkable Improvement in the Global Improvement Rate of Pruritus/Itch Assessed by the Investigator at Day 3, Week 1, Week 2, Week 4, Week 6, Week 8 and Week 12

End point title	Percentage of Participants With Moderate or Remarkable Improvement in the Global Improvement Rate of Pruritus/Itch Assessed by the Investigator at Day 3, Week 1, Week 2, Week 4, Week 6, Week 8 and Week 12

End point description:

The global improvement judgment criteria were used to assess overall improvement in pruritus/itch. The Investigator assessed the degree of severity of pruritus/itch based on 5 grades (1=Remarkably improved to 5=Aggravated) at Baseline and subsequent clinic visits. The percentages of participants who were remarkably improved (Grade 1=Pruritus/itch disappeared) or moderately improved (Grade 2=Pruritus/itch was greatly improved) at the Day 3, Week 1, Week 2, Week 4, Week 6, Week 8 and Week 12 clinic visits were calculated. The FAS population consisted of all participants who received at least one dose of study drug and had a Baseline or at least one post-Baseline observation for Investigator-assessed Global Improvement.

End point type	Secondary

End point timeframe:

Baseline Visit and Day 3 Visit, Week 1 Visit, Week 2 Visit, Week 4 Visit, Week 6 Visit, Week 8 Visit, Week 12 Visit

End point values	Desloratadine: Eczema/Dermatitis	Desloratadine: Dermal Pruritis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	29		
Units: Percentage of Participants				
number (not applicable)				
Day 3	16.9	34.5		
Week 1	29.2	51.7		
Week 2	33.8	51.7		
Week 4	50.8	62.1		
Week 6	60	62.1		
Week 8	63.1	62.1		
Week 12	69.2	62.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Pruritus/Itch Visual Analog Scale (VAS) Score Recorded by Participants at Day 3, Week 1, Week 2, Week 4, Week 6, Week 8 and Week 12

End point title	Change From Baseline in the Pruritus/Itch Visual Analog Scale (VAS) Score Recorded by Participants at Day 3, Week 1, Week 2, Week 4, Week 6, Week 8 and Week 12

End point description:

Participants assessed the degree of their pruritus using a 100-mm visual analog scale (VAS; 0mm=No itch, 100mm=Worst imaginable itch) at Baseline and subsequent clinic visits. Pruritus/itch VAS scores could range from 0 to 100, with a higher score indicating more severe pruritus/itching. The changes from Baseline in the VAS scores for pruritus/itch at the Day 3, Week 1, Week 2, Week 4, Week 6, Week 8 and Week 12 clinic visits were calculated. The FAS population consisted of all participants who received at least one dose of study drug and had a Baseline or at least one post-Baseline observation for participant-assessed pruritus/itch VAS score.

End point type	Secondary

End point timeframe:

Baseline Visit and Day 3 Visit, Week 1 Visit, Week 2 Visit, Week 4 Visit, Week 6 Visit, Week 8 Visit, Week 12 Visit

End point values	Desloratadine: Eczema/Dermatitis	Desloratadine: Dermal Pruritis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	29		
Units: Score on a Scale				
least squares mean (confidence interval 95%)				
Change from Baseline at Day 3 (n=65, 29)	-10.03 (-15.22 to -4.84)	-21.9 (-29.66 to -14.13)		
Change from Baseline at Week 1 (n=65, 29)	-12.17 (-17.92 to -6.42)	-24.72 (-33.33 to -16.12)		
Change from Baseline at Week 2 (n=63, 29)	-18.95 (-25.18 to -12.72)	-28.45 (-37.72 to -19.18)		
Change from Baseline at Week 4 (n=63, 28)	-22.36 (-29.01 to -15.71)	-27.74 (-37.66 to -17.82)		
Change from Baseline at Week 6 (n=62, 26)	-27.26 (-33.2 to -21.32)	-30.71 (-39.7 to -21.72)		
Change from Baseline at Week 8 (n=61, 25)	-29.87 (-36.55 to -23.2)	-32.44 (-42.6 to -22.29)		
Change from Baseline at Week 12 (n=58, 25)	-33.02 (-39.65 to -26.39)	-38.74 (-48.76 to -28.73)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 14 weeks (up to 2 weeks after the last dose of study drug)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Eczema/Dermatitis
Reporting group description: -	
Reporting group title	Dermal Pruritus
Reporting group description: -	

Serious adverse events	Eczema/Dermatitis	Dermal Pruritus	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 65 (1.54%)	0 / 29 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm skin			
subjects affected / exposed	1 / 65 (1.54%)	0 / 29 (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	Eczema/Dermatitis	Dermal Pruritus	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 65 (24.62%)	6 / 29 (20.69%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	4 / 65 (6.15%)	0 / 29 (0.00%)	
occurrences (all)	4	0	
Skin and subcutaneous tissue disorders			
Seborrhoeic dermatitis			

subjects affected / exposed occurrences (all)	0 / 65 (0.00%) 0	2 / 29 (6.90%) 2	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	13 / 65 (20.00%) 16	4 / 29 (13.79%) 4	

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