Clinical trial results:
A randomized, open-label, comparative study to evaluate an intermittent dosing regimen of fluticasone propionate 0.05% cream (twice per week) in reducing the risk of relapse when added to regular daily moisturization using Physiogel® Lotion in paediatric subjects with stabilized atopic dermatitis

Summary

EudraCT number	2017-001574-42
Trial protocol	Outside EU/EEA
Global end of trial date	15 February 2015

Results information

Result version number	v1 (current)
This version publication date	21 October 2017
First version publication date	21 October 2017

Trial information

Trial identification

Sponsor protocol code	117291

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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	08 October 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the risk of AD relapse can be significantly reduced by extended intermittent dosing with Fluticasone propionate 0.05% cream in addition to regular emollient therapy in the maintenance treatment (20 weeks) of atopic dermatitis as compared with application of physiogel lotion alone.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 December 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	China: 123
Worldwide total number of subjects	123
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)	6
Children (2-11 years)	115
Adolescents (12-17 years)	2
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Number of enrolled participants n=123 in Acute Phase and n=107 in Maintenance Phase (ITT Population).

Pre-assignment

Screening details:

Eligible participants (par.) received twice daily (BID) fluticasone propionate 0.05% (FP) cream up to 4 weeks (wk) (in Acute Phase), then par. received (1:1) either emollient BID plus FP cream once daily (OD) twice a wk, or emollient BID up to 20 wk (Maintenance Phase). Par. who did not relapse received emollient BID up to 12 wk (Follow-up Phase).

Period 1

Period 1 title	Acute Phase
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	FP 0.05% cream

Arm description:

Participants who satisfied eligibility criteria received FP 0.05% cream BID up to 4 weeks. FP 0.05% cream was applied to affected sites and any newly occurring atopic dermatitis (AD) sites. Investigator assessed Eczema Area, AD Severity, Visual Skin Assessment, and conducted physical examination, vital sign measurement in the Acute Phase. The efficacy and safety in the Acute Phase was assessed every 2 weeks up to 4 weeks or until treatment success.

Arm type	Experimental
Investigational medicinal product name	Fluticasone proprionate (FP) 0.05%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

All participants in ACUTE phase were administered FP 0.05% cream twice daily treatment. In MAINTENANCE phase, randomized participants were given FP 0.05% cream once daily twice a week. FP 0.05% cream was applied to all healed sites and any newly occurring sites.

Number of subjects in period 1	FP 0.05% cream
Started	123
Completed–not entered Maintenance Phase	4 [1]
Completed	111
Not completed	12
Physician decision	1
ACCEPTED OTHER TOPIC THERAPIES	1
NOT ACHIEVED "TREATMENT SUCCESS"	1
Lost to follow-up	4

Missing	1
Withdrawal by subject	4

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This milestone is included to state that 4 participants completed the acute phase but did not enter the maintenance phase.

Period 2

Period 2 title	Maintenance Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Emollient plus FP 0.05% cream

Arm description:

Participants with treatment success during the Acute Phase were enrolled in the Maintenance Phase. Treatment success is defined as participants with Physician Static Global Assessment (PSGA) <=1; and the improvement >=2 compared to Baseline (the six-point scale of PSGA score range from 0 to 5 where 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe, 5=very severe). During the Maintenance Phase, the participants received emollient BID plus FP 0.05% cream OD twice a week up to 20 weeks. FP 0.05% cream was applied to all healed sites and any newly occurring sites. Emollient was applied before the application of FP 0.05% cream to the affected and unaffected areas.

Arm type	Experimental
Investigational medicinal product name	Emollient
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Emollient twice daily was applied before application of FP 0.05% cream to the affected and unaffected areas in MAINTENANCE phase and FOLLOW-UP phase.

Investigational medicinal product name	Fluticasone proprionate (FP) 0.05%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

All participants in ACUTE phase were administered FP 0.05% cream twice daily treatment. In MAINTENANCE phase, randomized participants were given FP 0.05% cream once daily twice a week. FP 0.05% cream was applied to all healed sites and any newly occurring sites.

Arm title	Emollient

Arm description:

Participants with treatment success during the Acute Phase were enrolled in the Maintenance Phase. Treatment success is defined as PSGA <=1; and the improvement >=2 compared to Baseline (the six-point scale of PSGA score range from 0 to 5 where 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe, 5=very severe). The participants received emollient BID up to 20 weeks.

Arm type	Active comparator

Investigational medicinal product name	Emollient
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Emollient twice daily was applied before application of FP 0.05% cream to the affected and unaffected areas in MAINTENANCE phase and FOLLOW-UP phase.

Number of subjects in period 2[2]	Emollient plus FP 0.05% cream	Emollient
Started	54	53
Completed	48	51
Not completed	6	2
Lost to follow-up	4	1
Missing	1	-
Withdrawal by subject	1	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Four participants had completed the acute phase but did not enter the maintenance phase.

Period 3

Period 3 title	Follow-up Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Follow-up: Emollient

Arm description:

Participants who completed the study treatment in the Maintenance Phase in either treatment group without a relapse, were entered into the Follow-up Phase. Emollient was applied BID up to 12 weeks.

Arm type	Active comparator
Investigational medicinal product name	Emollient
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Emollient twice daily was applied before application of FP 0.05% cream to the affected and unaffected areas in MAINTENANCE phase and FOLLOW-UP phase.

Number of subjects in period 3[3]	Follow-up: Emollient
Started	66
Completed	64
Not completed	2
Physician decision	1
Withdrawal by subject	1

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Forty-one participants had atopic dermatitis relapse hence could not enter the follow-up phase.

Baseline characteristics

Reporting groups	
Reporting group title	Acute Phase
Reporting group description:	
Acute Phase	

Reporting group values	Acute Phase	Total	
Number of subjects	123	123	
Age categorical Units: Subjects			
Age continuous			
Age continuous description			
Units: years			
arithmetic mean	4.8		
standard deviation	± 2.58	-	
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	63	63	
Male	60	60	
Race/Ethnicity, Customized Units: Subjects			
Chinese	118	118	
Other	5	5	

End points

End points reporting groups

Reporting group title	FP 0.05% cream
Reporting group description:	
Participants who satisfied eligibility criteria received FP 0.05% cream BID up to 4 weeks. FP 0.05% cream was applied to affected sites and any newly occurring atopic dermatitis (AD) sites. Investigator assessed Eczema Area, AD Severity, Visual Skin Assessment, and conducted physical examination, vital sign measurement in the Acute Phase. The efficacy and safety in the Acute Phase was assessed every 2 weeks up to 4 weeks or until treatment success.	
Reporting group title	Emollient plus FP 0.05% cream
Reporting group description:	
Participants with treatment success during the Acute Phase were enrolled in the Maintenance Phase. Treatment success is defined as participants with Physician Static Global Assessment (PSGA) <=1; and the improvement >=2 compared to Baseline (the six-point scale of PSGA score range from 0 to 5 where 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe, 5=very severe). During the Maintenance Phase, the participants received emollient BID plus FP 0.05% cream OD twice a week up to 20 weeks. FP 0.05% cream was applied to all healed sites and any newly occurring sites. Emollient was applied before the application of FP 0.05% cream to the affected and unaffected areas.	
Reporting group title	Emollient
Reporting group description:	
Participants with treatment success during the Acute Phase were enrolled in the Maintenance Phase. Treatment success is defined as PSGA <=1; and the improvement >=2 compared to Baseline (the six-point scale of PSGA score range from 0 to 5 where 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe, 5=very severe). The participants received emollient BID up to 20 weeks.	
Reporting group title	Follow-up: Emollient
Reporting group description:	
Participants who completed the study treatment in the Maintenance Phase in either treatment group without a relapse, were entered into the Follow-up Phase. Emollient was applied BID up to 12 weeks.	

Primary: Time to the first relapse of AD during the Maintenance Phase

End point title	Time to the first relapse of AD during the Maintenance Phase
End point description:	
Time to the first relapse of AD is defined as the number of days from start of the FP treatment in Maintenance Phase until AD relapse. AD relapse is defined as participants with PSGA exacerbation score >=2 (the six-point scale of PSGA score range from 0 to 5 where 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe, 5=very severe) compared to PSGA score of treatment success during Acute Phase. Participants with treatment success are defined as participants with PSGA <=1; and the improvement >=2 compared to Baseline. 99999 indicates that data were not available. ITT Population: all participants who were randomized into the Maintenance Phase. Only participants available at the specified time point were analyzed.	
End point type	Primary
End point timeframe:	
From the start of treatment up to Week 20 during the Maintenance Phase	

End point values	Emollient plus FP 0.05% cream	Emollient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[1]	53[2]		
Units: Days				
median (confidence interval 95%)	99999 (-99999	142.0 (50.0 to		

	to 99999)	150.0)

Notes:

[1] - ITT Population

[2] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Emollient plus FP 0.05% cream v Emollient
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	13.4993
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.1113
upper limit	44.325

Secondary: Median time to the first relapse of AD during the Maintenance Phase and Follow-up Phase

End point title	Median time to the first relapse of AD during the Maintenance Phase and Follow-up Phase

End point description:

Median time to the first relapse of AD during the Maintenance Phase and Follow-up Phase is defined as the number of days from start of the FP treatment until AD relapse during the Maintenance Phase and Follow-up Phase. AD relapse is defined as participants with PSGA exacerbation score >=2 (the six-point scale of PSGA score range from 0 to 5 where 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe, 5=very severe) compared to PSGA score of treatment success during the Acute Phase. 99999 indicates that data were not available.

End point type	Secondary

End point timeframe:

From the start of treatment up to Week 32 during the Maintenance Phase and Follow-up Phase

End point values	Emollient plus FP 0.05% cream	Emollient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[3]	53[4]		
Units: Days				
median (confidence interval 95%)	99999 (-99999 to 99999)	142.0 (50.0 to 99999)		

Notes:

[3] - ITT Population. Only participants available at the specified time point were analyzed.

[4] - ITT Population. Only participants available at the specified time point were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Emollient plus FP 0.05% cream v Emollient
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	4.9524
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.4258
upper limit	10.1105

Secondary: Numbers of recurrent participants at the end of the Maintenance Phase (Week 20)

End point title	Numbers of recurrent participants at the end of the Maintenance Phase (Week 20)

End point description:

The number of participants with AD recurrent/relapse at the end of Maintenance Phase is presented. AD relapse is defined as participants with PSGA exacerbation score >=2 (the six-point scale of PSGA: 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe, 5=very severe) compared to PSGA score of treatment success. Participants with treatment success is defined as participants with PSGA <=1; and the improvement >=2 compared to Baseline.

End point type	Secondary

End point timeframe:

From Week 0 (or treatment success, if earlier) to Week 20

End point values	Emollient plus FP 0.05% cream	Emollient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[5]	53[6]		
Units: Participants	3	30		

Notes:

[5] - ITT Population

[6] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Emollient plus FP 0.05% cream v Emollient
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Fisher exact
Confidence interval	
level	95 %

Secondary: Numbers of recurrent participants at the end of the Follow-up Phase (Week 32)

End point title	Numbers of recurrent participants at the end of the Follow-up Phase (Week 32)

End point description:

The number of participants with AD recurrent/relapse at the end of the Follow-up Phase is presented. AD relapse is defined as participants with PSGA exacerbation score >=2 (the six-point scale of PSGA: 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe, 5=very severe) compared to PSGA score of treatment success. Participants with treatment success is defined as participants with PSGA <=1; and the improvement >=2 compared to Baseline.

End point type	Secondary

End point timeframe:

From Week 20 to Week 32

End point values	Emollient plus FP 0.05% cream	Emollient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[7]	53[8]		
Units: Participants	10	32		

Notes:

[7] - ITT Population

[8] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Emollient plus FP 0.05% cream v Emollient
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Chi-squared
Confidence interval	
level	95 %

Secondary: Number of participants with “treatment success” during the Acute Phase

End point title	Number of participants with “treatment success” during the Acute Phase

End point description:

The number of participants with "treatment success” during the Acute Phase is presented. Participants with treatment success are defined as participants with PSGA <=1; and the improvement >=2 (the six-point scale of PSGA: 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe, 5=very severe) compared to Baseline in the Acute Phase of the study.

End point type	Secondary

End point timeframe:

From the start of treatment up to Visit 4 (Week 0) or treatment success (depends on which time point comes first)

End point values	FP 0.05% cream			
Subject group type	Reporting group			
Number of subjects analysed	123[9]			
Units: Participants	107			

Notes:

[9] - Enrolled Population: all participants who were enrolled into the Acute Phase of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Quality of Life (QoL) at the end of the Maintenance Phase

End point title	Change from Baseline in Quality of Life (QoL) at the end of the Maintenance Phase

End point description:

Infant's Dermatitis Quality of Life Index (IDQOL) and Children's Dermatology Life Quality Index (CDLQI) were used to evaluate quality of life for participants of age between 1 to 16 years. IDQOL and CDLQI questionnaires were designed for infants (below the age of 4 years) and children (age 4 to age 16) with atopic dermatitis, respectively. The IDQOL and CDLQI were calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score in each questionnaire, the more quality of life is impaired. The change from Baseline in the QoL score is based on each questionnaire at the end of the Maintenance Phase and is calculated as the score at the end of the Maintenance Phase minus the Baseline score. Baseline is defined as QoL scores obtained at Visit 4 (end of Acute Phase). A QOL is equal to IDQOL if the age of a participant is < 4 years and it is equal to CDLQI if the age of a participant is between 4 and 16 years.

End point type	Secondary

End point timeframe:

Baseline and Week 20

End point values	Emollient plus FP 0.05% cream	Emollient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[10]	53[11]		
Units: Scores on a scale				
arithmetic mean (standard deviation)	-0.4 (± 4.40)	2.2 (± 4.68)		

Notes:

[10] - ITT Population

[11] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Emollient plus FP 0.05% cream v Emollient
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Confidence interval	
level	95 %

Secondary: Change from Baseline in QoL at the end of the Follow-up Phase

End point title	Change from Baseline in QoL at the end of the Follow-up Phase

End point description:

Infant's IDQOL and Children's CDLQI were used to evaluate quality of life for participants of age between 1 to 16 years. IDQOL and CDLQI questionnaires were designed for infants (below the age of 4 years) and children (age 4 to age 16) with AD, respectively. The IDQOL and CDLQI were calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score in each questionnaire, the more quality of life is impaired. The change from Baseline in QoL score is based on each questionnaire at the end of the Follow-up Phase and is calculated as the score at the end of the Follow-up Phase minus the Baseline score. Baseline is defined as QoL scores obtained at Visit 4 (end of Acute Phase). A QOL is equal to IDQOL if the age of a participant is < 4 years and it is equal to CDLQI if the age of a participant is between 4 and 16 years.

End point type	Secondary

End point timeframe:

Baseline and Week 32

End point values	Emollient plus FP 0.05% cream	Emollient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[12]	53[13]		
Units: Scores on a scale				
arithmetic mean (standard deviation)	0.0 (± 4.97)	2.2 (± 5.10)		

Notes:

[12] - ITT Population

[13] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Emollient plus FP 0.05% cream v Emollient
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Confidence interval	
level	95 %

Secondary: Number of participants with post-study assessment of skin emollients using questionnaire

End point title	Number of participants with post-study assessment of skin emollients using questionnaire

End point description:

Participants from each group completed the post-study questionnaire to rate the skin emollients (gel, lotion, cream, ointment, solution and foam) used in the past based on their experience. Participants rated skin emollients on a 5-point scale (5= "liked the best", 4= "second best", 3= "third best", 2= "fourth best, 1= "liked the least", N/A=Does not apply to me).

End point type	Secondary

End point timeframe:

At early withdrawal or end of the therapy visit (up to Week 32)

End point values	Emollient plus FP 0.05% cream	Emollient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[14]	53[15]		
Units: Participants				
Gel, 1	2	1		
Gel, 2	2	1		
Gel, 3	2	2		
Gel, 4	2	2		
Gel, 5	1	0		
Gel, N/A	39	44		
Lotion, 1	1	1		
Lotion, 2	0	1		
Lotion, 3	7	2		
Lotion, 4	8	12		
Lotion, 5	27	26		
Lotion, N/A	5	8		
Cream, 1	1	0		
Cream, 2	1	2		
Cream, 3	7	2		
Cream, 4	12	18		
Cream, 5	6	5		

Cream, N/A	21	23		
Ointment, 1	1	3		
Ointment, 2	7	3		
Ointment, 3	5	10		
Ointment, 4	3	3		
Ointment, 5	10	11		
Ointment, N/A	22	20		
Solution, 1	0	1		
Solution, 2	1	0		
Solution, 3	4	5		
Solution, 4	4	2		
Solution, 5	1	0		
Solution, N/A	38	42		
Foam, 1	4	2		
Foam, 2	1	1		
Foam, 3	1	0		
Foam, 4	0	0		
Foam, 5	0	0		
Foam, N/A	42	47		

Notes:

[14] - ITT Population

[15] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with post-study assessment of lotion qualities (1) using questionnaire

End point title	Number of participants with post-study assessment of lotion qualities (1) using questionnaire

End point description:

Participants from each group completed the post-study questionnaire to rate the qualities of the lotion as compared with other skin emollients used in the past based on their experience. Each participant was asked the following Questions (Q). Q 1: This product is easier to use than other skin emollients; Q 2: When I apply this product I am able to start my daily activities quicker than with other skin emollients; Q 3: This product leaves my skin feeling softer than other skin emollients; Q 4: I am able to apply this product to larger body surface areas than other skin emollients; Q 5: This product disappears into my skin quicker than when I apply other skin emollients. Participants rated the qualities of the lotion based on a 5 point scale (5= "Strongly Agree", 4= "Agree", 3= "Neutral", 2= "Disagree", 1= "Strongly Disagree" N/A=Does not apply to me). Participant's rating for each question were summarized.

End point type	Secondary

End point timeframe:

At early withdrawal or end of the therapy visit (up to Week 32)

End point values	Emollient plus FP 0.05% cream	Emollient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[16]	53[17]		
Units: Participants				
Q 1, 1	0	0		

Q 1, 2	0	4		
Q 1, 3	5	13		
Q 1, 4 or 5	39	29		
Q 1, N/A	4	4		
Q 2, 1	0	1		
Q 2, 2	1	2		
Q 2, 3	5	13		
Q 2, 4 or 5	38	29		
Q 2, N/A	4	5		
Q 3, 1	0	0		
Q 3, 2	1	3		
Q 3, 3	4	9		
Q 3, 4 or 5	39	34		
Q 3, N/A	4	4		
Q 4, 1	0	1		
Q 4, 2	0	1		
Q 4, 3	6	7		
Q 4, 4 or 5	38	37		
Q 4, N/A	4	4		
Q 5, 1	0	2		
Q 5, 2	0	2		
Q 5, 3	6	10		
Q 5, 4 or 5	38	32		
Q 5, N/A	4	4		

Notes:

[16] - Enrolled Population

[17] - Enrolled Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with post-study assessment of lotion qualities (2) using questionnaire

End point title	Number of participants with post-study assessment of lotion qualities (2) using questionnaire

End point description:

Participants from each group completed the post-study questionnaire to rate the qualities of the lotion as compared with other skin emollients used in the past based on their experience. Each participant was asked the following Questions (Q). Q 1: It leaves my skin feeling soft and smooth; Q 2: There is nothing left on my skin; Q 3: Does not feel greasy; Q 4: Disappears into my skin quickly after I put it on; Q 5: Easy to apply; Q 6: Fragrance-free; Q 7: Spreadability; Q 8: Lack of stickiness. Participants rated the qualities of the lotion based on a 5 point scale (5= “Strongly Agree”, 4= “Agree”, 3= “Neutral”, 2= “Disagree", 1= “Strongly Disagree” N/A=Does not apply to me). Participant's rating for each question were summarized.

End point type	Secondary

End point timeframe:

At early withdrawal or end of the therapy visit (up to Week 32)

End point values	Emollient plus FP 0.05% cream	Emollient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[18]	53[19]		
Units: Participants				
Q 1, 1	0	0		
Q 1, 2	1	1		
Q 1, 3	3	11		
Q 1, 4 or 5	44	37		
Q 1, N/A	0	1		
Q 2, 1	0	0		
Q 2, 2	3	4		
Q 2, 3	1	8		
Q 2, 4 or 5	44	38		
Q 2, N/A	0	0		
Q 3, 1	0	2		
Q 3, 2	3	3		
Q 3, 3	2	10		
Q 3, 4 or 5	43	35		
Q 3, N/A	0	0		
Q 4, 1	0	2		
Q 4, 2	1	3		
Q 4, 3	2	7		
Q 4, 4 or 5	45	38		
Q 4, N/A	0	0		
Q 5, 1	0	2		
Q 5, 2	1	1		
Q 5, 3	2	5		
Q 5, 4 or 5	45	42		
Q 5, N/A	0	0		
Q 6, 1	0	0		
Q 6, 2	0	0		
Q 6, 3	1	5		
Q 6, 4 or 5	47	45		
Q 6, N/A	0	0		
Q 7, 1	0	0		
Q 7, 2	1	0		
Q 7, 3	2	9		
Q 7, 4 or 5	45	41		
Q 7, N/A	0	0		
Q 8, 1	0	2		
Q 8, 2	3	3		
Q 8, 3	2	10		
Q 8, 4 or 5	43	35		
Q 8, N/A	0	0		

Notes:

[18] - ITT Population

[19] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in cutaneous atrophy sign score, epidermal thickening /lichenification sign score and abnormal pigmentation score using Visual Analogue Scale (VAS) at the end of the Acute Phase

End point title	Change from Baseline in cutaneous atrophy sign score, epidermal thickening /lichenification sign score and abnormal pigmentation score using Visual Analogue Scale (VAS) at the end of the Acute Phase

End point description:

Investigator evaluated and scored the signs of cutaneous atrophy (CA), epidermal thickening/lichenification (ET/L) and abnormal pigmentation (AP) using Visual Analogue Scale (ranging from 0 to 10, higher values represent a worse outcome) based on their subjective judgment. The change from Baseline in each signs (Cutaneous atrophy, epidermal thickening / lichenification and abnormal pigmentation) score at the end of the Acute Phase (Visit 4 [Week 0 or treatment success, depend on which time point comes first) ±2day]) and is calculated as the score at Visit 4 minus the Baseline score. Baseline is defined as the VAS score for each sign obtained before the first dose of study drug in the Acute Phase of the study (Visit 2). Summation of the VAS scores for each sign (CA, ET/L and AP) was done to calculate the Total VAS score (ranging from 0 to 30, higher values represent a worse outcome) at Visit 4 of the Acute Phase of the study.

End point type	Secondary

End point timeframe:

From the start of treatment up to Visit 4 (Week 0) or treatment success (depends on which time point comes first)

End point values	FP 0.05% cream			
Subject group type	Reporting group			
Number of subjects analysed	123[20]			
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Visit 4, CA	-0.3 (± 1.12)			
Visit 4, ET/L	-1.9 (± 1.57)			
Visit 4, AP	-0.7 (± 1.47)			
Visit 4, Total VAS Score	-2.9 (± 3.14)			

Notes:

[20] - Enrolled Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in cutaneous atrophy sign score, epidermal thickening /lichenification sign score and abnormal pigmentation score using Visual Analogue Scale (VAS) at the end of the Maintenance Phase and Follow-up Phase

End point title	Change from Baseline in cutaneous atrophy sign score, epidermal thickening /lichenification sign score and abnormal pigmentation score using Visual Analogue Scale (VAS) at the end of the Maintenance Phase and Follow-up Phase

End point description:

Investigator evaluated and scored the signs of cutaneous atrophy (CA), epidermal thickening/lichenification (ET/L) and abnormal pigmentation (AP) using the Visual Analogue Scale (ranging from 0 to 10, higher values represent a worse outcome) based on their subjective judgment. The change from Baseline in each sign (Cutaneous atrophy, epidermal thickening / lichenification and

abnormal pigmentation) score at the end of the Maintenance Phase and Follow-up Phase and is calculated as the score at the end of the Maintenance and Follow-up Phase minus the Baseline score. Baseline is defined as VAS score for each sign obtained at Visit 4 (end of Acute Phase). Summation of VAS scores for each sign (CA, ET/L and AP) was done to calculate the Total VAS score (ranging from 0 to 30, higher values represent a worse outcome) at the Maintenance and Follow-up phase of study. The missing value was imputed using last-observation-carry-forward (LOCF) method.

End point type	Secondary

End point timeframe:

Baseline, Week 20 and Week 32

End point values	Emollient plus FP 0.05% cream	Emollient		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[21]	53[22]		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 20, CA	-0.1 (± 0.44)	-0.2 (± 1.01)		
Week 20, ET/L	-0.4 (± 1.49)	0.5 (± 1.51)		
Week 20, AP	-0.4 (± 1.42)	0.0 (± 1.32)		
Week 32, CA	-0.1 (± 0.58)	-0.2 (± 1.03)		
Week 32, ET/L	0.1 (± 1.19)	0.6 (± 1.53)		
Week 32, AP	-0.3 (± 1.23)	0.0 (± 1.35)		
Week 20, Total VAS Score	-0.9 (± 2.61)	0.3 (± 2.75)		
Week 32, Total VAS Score	-0.3 (± 2.09)	0.4 (± 2.82)		

Notes:

[21] - ITT Population

[22] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Emollient plus FP 0.05% cream v Emollient
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.701 [23]
Method	Wilcoxon (Mann-Whitney)
Confidence interval	
level	95 %

Notes:

[23] - Week 20, CA

Statistical analysis title	Statistical analysis 2
Comparison groups	Emollient plus FP 0.05% cream v Emollient

Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0042 [24]
Method	Wilcoxon (Mann-Whitney)
Confidence interval	
level	95 %

Notes:
[24] - Week 20, ET/L

Statistical analysis title	Statistical analysis 3
Comparison groups	Emollient plus FP 0.05% cream v Emollient
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.081 [25]
Method	Wilcoxon (Mann-Whitney)
Confidence interval	
level	95 %

Notes:
[25] - Week 20, AP

Statistical analysis title	Statistical analysis 4
Comparison groups	Emollient plus FP 0.05% cream v Emollient
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2799 [26]
Method	Wilcoxon (Mann-Whitney)
Confidence interval	
level	95 %

Notes:
[26] - Week 32, CA

Statistical analysis title	Statistical analysis 5
Comparison groups	Emollient plus FP 0.05% cream v Emollient
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1375 [27]
Method	Wilcoxon (Mann-Whitney)
Confidence interval	
level	95 %

Notes:
[27] - Week 32, ET/L

Statistical analysis title	Statistical analysis 6
Comparison groups	Emollient plus FP 0.05% cream v Emollient

Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.11 [28]
Method	Wilcoxon (Mann-Whitney)
Confidence interval	
level	95 %

Notes:

[28] - Week 32, AP

Statistical analysis title	Statistical analysis 7
Comparison groups	Emollient plus FP 0.05% cream v Emollient
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0394 [29]
Method	Wilcoxon (Mann-Whitney)
Confidence interval	
level	95 %

Notes:

[29] - Week 20, Total VAS Score

Statistical analysis title	Statistical analysis 8
Comparison groups	Emollient plus FP 0.05% cream v Emollient
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2237 [30]
Method	Wilcoxon (Mann-Whitney)
Confidence interval	
level	95 %

Notes:

[30] - Week 32, Total VAS Score

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from the start of study drug until follow-up (last dose of study treatment (emollient), up to Week 32).

Adverse event reporting additional description:

SAEs and non-serious AEs were collected in participants of the Safety Population, comprised of all participants who received study therapy during the Acute Phase, Maintenance Phase and Follow-up Phase and have a safety assessment in the Acute Phase, Maintenance Phase and Follow-up Phase of the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	FP 0.05% cream

Reporting group description:

Participants who satisfied eligibility criteria received FP 0.05% cream BID up to 4 weeks. FP 0.05% cream was applied to affected sites and any newly occurring atopic dermatitis (AD) sites. Investigator assessed Eczema Area, AD Severity, Visual Skin Assessment, and conducted physical examination, vital sign measurement in the Acute Phase. The efficacy and safety of FP 0.05% cream was assessed every 2 weeks up to 4 weeks or until treatment success.

Reporting group title	Emollient plus FP 0.05% cream

Reporting group description:

Participants with treatment success during the Acute Phase were enrolled in the Maintenance Phase. Treatment success is defined as participants with Physician Static Global Assessment (PSGA) less than or equal to 1; and the improvement greater than or equal to 2 compared to Baseline (the six-point scale of PSGA score range from 0 to 5 where 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe, 5=very severe). During the Maintenance Phase, the participants received emollient BID plus FP 0.05% cream OD twice a week up to 20 weeks. FP 0.05% cream was applied to all healed sites and any newly occurring sites. Emollient was applied before the application of FP 0.05% cream to the affected and unaffected areas.

Reporting group title	Emollient

Reporting group description:

Participants with treatment success during the Acute Phase were enrolled in the Maintenance Phase. Treatment success is defined as PSGA less than or equal to 1; and the improvement greater than or equal to 2 compared to Baseline (the six-point scale of PSGA score range from 0 to 5 where 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe, 5=very severe). The participants received emollient BID up to 20 weeks.

Reporting group title	Follow-up: Emollient

Reporting group description:

Participants who completed the study treatment in the Maintenance Phase in either treatment group without a relapse, were entered into the Follow-up Phase. Emollient was applied BID up to 12 weeks.

Serious adverse events	FP 0.05% cream	Emollient plus FP 0.05% cream	Emollient
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 116 (0.00%)	2 / 53 (3.77%)	0 / 53 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 116 (0.00%)	1 / 53 (1.89%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 116 (0.00%)	1 / 53 (1.89%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious mononucleosis			
subjects affected / exposed	0 / 116 (0.00%)	1 / 53 (1.89%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mycoplasma infection			
subjects affected / exposed	0 / 116 (0.00%)	1 / 53 (1.89%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Follow-up: Emollient		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 66 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infectious mononucleosis			

subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mycoplasma infection			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	FP 0.05% cream	Emollient plus FP 0.05% cream	Emollient
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 116 (3.45%)	9 / 53 (16.98%)	9 / 53 (16.98%)
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	0 / 116 (0.00%)	1 / 53 (1.89%)	1 / 53 (1.89%)
occurrences (all)	0	1	1
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 116 (0.00%)	0 / 53 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 116 (0.00%)	4 / 53 (7.55%)	3 / 53 (5.66%)
occurrences (all)	0	5	3
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 116 (0.86%)	0 / 53 (0.00%)	2 / 53 (3.77%)
occurrences (all)	1	0	2
Abdominal distension			
subjects affected / exposed	0 / 116 (0.00%)	0 / 53 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 116 (0.00%)	0 / 53 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1

Retching			
subjects affected / exposed	0 / 116 (0.00%)	0 / 53 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 116 (0.00%)	1 / 53 (1.89%)	3 / 53 (5.66%)
occurrences (all)	0	1	3
Rhinorrhoea			
subjects affected / exposed	0 / 116 (0.00%)	1 / 53 (1.89%)	1 / 53 (1.89%)
occurrences (all)	0	1	1
Rhinitis allergic			
subjects affected / exposed	0 / 116 (0.00%)	0 / 53 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Laryngeal pain			
subjects affected / exposed	0 / 116 (0.00%)	0 / 53 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 116 (0.00%)	0 / 53 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 116 (0.00%)	0 / 53 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 116 (1.72%)	3 / 53 (5.66%)	3 / 53 (5.66%)
occurrences (all)	2	3	7
Tonsillitis			
subjects affected / exposed	1 / 116 (0.86%)	1 / 53 (1.89%)	0 / 53 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 116 (0.00%)	0 / 53 (0.00%)	2 / 53 (3.77%)
occurrences (all)	0	0	2
Exanthema subitum			
subjects affected / exposed	0 / 116 (0.00%)	1 / 53 (1.89%)	0 / 53 (0.00%)
occurrences (all)	0	1	0

Herpes virus infection			
subjects affected / exposed	0 / 116 (0.00%)	1 / 53 (1.89%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	0 / 116 (0.00%)	1 / 53 (1.89%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 53 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Laryngitis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 53 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Follow-up: Emollient		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 66 (16.67%)		
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 66 (1.52%)		
occurrences (all)	2		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 66 (6.06%)		
occurrences (all)	4		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 66 (1.52%)		
occurrences (all)	1		
Abdominal distension			
subjects affected / exposed	1 / 66 (1.52%)		
occurrences (all)	1		
Abdominal pain			

subjects affected / exposed occurrences (all) Retching subjects affected / exposed occurrences (all)	0 / 66 (0.00%) 0 0 / 66 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all) Rhinitis allergic subjects affected / exposed occurrences (all) Laryngeal pain subjects affected / exposed occurrences (all)	 1 / 66 (1.52%) 1 0 / 66 (0.00%) 0 1 / 66 (1.52%) 1 1 / 66 (1.52%) 1		
Skin and subcutaneous tissue disorders Dermatitis allergic subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	 0 / 66 (0.00%) 0 1 / 66 (1.52%) 1		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Tonsillitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Exanthema subitum	 3 / 66 (4.55%) 3 0 / 66 (0.00%) 0 2 / 66 (3.03%) 2		

subjects affected / exposed	0 / 66 (0.00%)		
occurrences (all)	0		
Herpes virus infection			
subjects affected / exposed	1 / 66 (1.52%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 66 (1.52%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences (all)	0		
Laryngitis			
subjects affected / exposed	1 / 66 (1.52%)		
occurrences (all)	2		

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