Clinical trial results:
Open Label Exploratory Study to Evaluate the Effect of Dupilumab on Skin Barrier Function in Patients With Moderate to Severe Atopic Dermatitis

Summary

EudraCT number	2020-000314-15
Trial protocol	Outside EU/EEA
Global end of trial date	17 June 2021

Results information

Result version number	v1 (current)
This version publication date	11 January 2022
First version publication date	11 January 2022

Trial information

Trial identification

Sponsor protocol code	LPS15991

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04447417
WHO universal trial number (UTN)	U1111-1244-1409

Notes:

Sponsors

Sponsor organisation name	Sanofi-aventis Recherche & Développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin Cedex, France, 91380
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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	15 July 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate changes in skin barrier function with transepidermal water loss (TEWL) assessed after skin tape stripping (STS) in pre-defined lesional skin in subjects with moderate to severe atopic dermatitis (AD) treated with dupilumab.

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of adults and paediatric subjects. The parent(s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parent(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimised. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimise distress and discomfort. Adult subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 July 2020
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	United States: 16
Country: Number of subjects enrolled	Canada: 36
Worldwide total number of subjects	52
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)	12
Adults (18-64 years)	40
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was conducted at 2 centers in the United States and Canada. A total of 52 eligible subjects were enrolled between 16 July 2020 and 19 January 2021 under the AD subjects cohort or the healthy volunteers cohort.

Pre-assignment

Screening details:

Healthy volunteer’s cohort received no treatment and was considered as a reference comparator group.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Healthy Volunteer

Arm description:

Healthy volunteers with age, gender, location of targeted skin lesion area and study site matched to a selected atopic dermatitis (AD) subjects, received no treatment, but were monitored in similar way as AD subjects.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Atopic Dermatitis Patients

Arm description:

Subjects with moderate to severe AD and aged 18 years and older received dupilumab 600 milligrams (mg) (loading dose) subcutaneous (SC) injection on Day 1, followed by dupilumab 300 mg SC injection every 2 weeks (Q2W) through Week 14 (i.e., at Day 15, 29, 43, 57 and 85).
Subjects aged greater than or equal to (>=) 12 to less than (<) 18 years received treatment based on their body weight: <60 kilograms (kg) and >=60 kg - received dupilumab 400 mg and 600 mg (loading dose) SC injection on Day 1, respectively, followed by dupilumab 200 mg and 300 mg SC injection Q2W through Week 14 (i.e., at Day 15, 29, 43, 57 and 85).

Arm type	Experimental
Investigational medicinal product name	Dupilumab
Investigational medicinal product code	SAR231893
Other name	Dupixent®/REGN668
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dupilumab loading dose 600 mg and 400 mg as SC injections, respectively on Day 1. Subsequent doses of dupilumab 200 mg and 300 mg SC injection Q2W through Week 14 (i.e., at Day 15, 29, 43, 57 and 85).

Number of subjects in period 1	Healthy Volunteer	Atopic Dermatitis Patients
Started	26	26
Completed	23	26
Not completed	3	0
Consent withdrawn by subject	1	-
Failure to meet inclusion criteria	1	-
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Healthy Volunteer
Reporting group description:	
Healthy volunteers with age, gender, location of targeted skin lesion area and study site matched to a selected atopic dermatitis (AD) subjects, received no treatment, but were monitored in similar way as AD subjects.	
Reporting group title	Atopic Dermatitis Patients
Reporting group description:	
Subjects with moderate to severe AD and aged 18 years and older received dupilumab 600 milligrams (mg) (loading dose) subcutaneous (SC) injection on Day 1, followed by dupilumab 300 mg SC injection every 2 weeks (Q2W) through Week 14 (i.e., at Day 15, 29, 43, 57 and 85). Subjects aged greater than or equal to (>=) 12 to less than (<) 18 years received treatment based on their body weight: <60 kilograms (kg) and >=60 kg - received dupilumab 400 mg and 600 mg (loading dose) SC injection on Day 1, respectively, followed by dupilumab 200 mg and 300 mg SC injection Q2W through Week 14 (i.e., at Day 15, 29, 43, 57 and 85).	

Reporting group values	Healthy Volunteer	Atopic Dermatitis Patients	Total
Number of subjects	26	26	52
Age categorical			
Analysis was performed on safety population: all enrolled subjects who actually received at least one dose of investigational medicinal product (IMP) or had at least one transepidermal water loss (TEWL)/skin tape stripping (STS) assessment and all healthy volunteers who had at least one TEWL/STS assessment performed.			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	33.4	32.2	
standard deviation	± 16.4	± 17.2	-
Gender categorical			
Units: Subjects			
Female	11	11	22
Male	15	15	30
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	0	2	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	4	2	6
White	21	21	42
More than one race	0	1	1
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Healthy Volunteer

Reporting group description:

Healthy volunteers with age, gender, location of targeted skin lesion area and study site matched to a selected atopic dermatitis (AD) subjects, received no treatment, but were monitored in similar way as AD subjects.

Reporting group title	Atopic Dermatitis Patients

Reporting group description:

Subjects with moderate to severe AD and aged 18 years and older received dupilumab 600 milligrams (mg) (loading dose) subcutaneous (SC) injection on Day 1, followed by dupilumab 300 mg SC injection every 2 weeks (Q2W) through Week 14 (i.e., at Day 15, 29, 43, 57 and 85).
Subjects aged greater than or equal to (>=) 12 to less than (<) 18 years received treatment based on their body weight: <60 kilograms (kg) and >=60 kg - received dupilumab 400 mg and 600 mg (loading dose) SC injection on Day 1, respectively, followed by dupilumab 200 mg and 300 mg SC injection Q2W through Week 14 (i.e., at Day 15, 29, 43, 57 and 85).

Primary: Percent Change From Baseline in Transepidermal Water Loss After 5 Skin Tape Stripping on Lesional Skin (LS) in AD Patients at Week 16

End point title	Percent Change From Baseline in Transepidermal Water Loss After 5 Skin Tape Stripping on Lesional Skin (LS) in AD Patients at Week 16[1][2]

End point description:

TEWL assessment: noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise skin barrier function (SBF). TEWL combined with STS measures SBF. With STS, the uppermost layers of skin are peeled away using adhesive discs. LS areas for TEWL assessment and STS was identified at Baseline (predefined skin area). Within predefined LS areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined LS areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on 1st spot. Percent Change from Baseline at Week 16 in TEWL after 5 STS on LS (1st spot) in AD subjects were reported in this endpoint. mITT:AD subjects, had at least 1 dose of IMP and healthy volunteers, had at least 1 TEWL/STS. If prohibited therapies used, only visits prior to rescue therapy were considered. Number of subjects analysed=subjects evaluable.

End point type	Primary

End point timeframe:

Baseline, Week 16

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: As the end-point was descriptive in nature no statistical analysis was provided.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Healthy Volunteer arm as pre-specified in protocol.

End point values	Atopic Dermatitis Patients			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: percent change				
arithmetic mean (standard deviation)	-54.6 (± 18.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in TEWL After 20 STS on Lesional and Non-lesional Skin (Non-LS) in AD Patients at Week 16

End point title	Percent Change From Baseline in TEWL After 20 STS on Lesional and Non-lesional Skin (Non-LS) in AD Patients at Week 16[3]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The LS and non-LS areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined LS and non-LS areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment (3 spots on LS, 3 spots on non-LS). TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined LS and non-LS areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Percent change from Baseline at Week 16 in TEWL after 20 STS on LS and non-LS (1st spot) in AD subjects were reported in this endpoint. Analysed on modified intent-to-treat (mITT) population. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data for this endpoint was not planned to be collected and analysed for Healthy Volunteer arm as pre-specified in protocol.

End point values	Atopic Dermatitis Patients			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: percent change				
arithmetic mean (standard deviation)				
Lesional skin (n = 7)	-47.7 (± 20.1)			
Non-Lesional skin (n = 21)	16.6 (± 91.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change in TEWL After 20 STS on Lesional and Non-lesional Skin in AD Patients at Week 16

End point title	Absolute Change in TEWL After 20 STS on Lesional and Non-lesional Skin in AD Patients at Week 16[4]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The LS and non-LS areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined LS and non-LS areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment (3 spots on LS, 3 spots on non-LS). TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined LS and non-LS areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Absolute change from Baseline at Week 16 in TEWL after 20 STS on LS and non-LS (first spot) in AD subjects were reported in this endpoint. Analysis was performed on mITT population. Here, 'n'=subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Healthy Volunteer arm as pre-specified in protocol.

End point values	Atopic Dermatitis Patients			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: grams per square metre per hour				
arithmetic mean (standard deviation)				
Lesional skin (n = 7)	-42.6 (± 22.1)			
Non-Lesional skin (n = 21)	-2.1 (± 26.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in TEWL After 20 STS on Normal Skin in Healthy Volunteers at Week 16

End point title	Percent Change From Baseline in TEWL After 20 STS on Normal Skin in Healthy Volunteers at Week 16[5]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The normal skin areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined normal skin areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined normal skin areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Percent change from Baseline at Week 16 in TEWL after 20 STS on normal skin (first spot) in healthy volunteers were reported in this endpoint. Analysis was performed on mITT population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Atopic Dermatitis Patients arm as pre-specified in the protocol.

End point values	Healthy Volunteer			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: percent change				
arithmetic mean (standard deviation)	-5.8 (± 46.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in TEWL After 20 STS on Normal Skin in Healthy Volunteers at Week 16

End point title	Absolute Change From Baseline in TEWL After 20 STS on Normal Skin in Healthy Volunteers at Week 16[6]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The normal skin areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined normal skin areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined normal skin areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Absolute change from Baseline at Week 16 in TEWL after 20 STS on normal skin (first spot) in healthy volunteers were reported in this endpoint. Analysis was performed on mITT population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Atopic Dermatitis Patients arm as pre-specified in the protocol.

End point values	Healthy Volunteer			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: grams per square metre per hour				
arithmetic mean (standard deviation)	-8.0 (± 19.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in TEWL After 15 STS on Lesional and Non-lesional Skin in AD Patients at Week 16

End point title	Percent Change From Baseline in TEWL After 15 STS on Lesional and Non-lesional Skin in AD Patients at Week 16[7]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is

used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The LS and non-LS areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined LS and non-LS areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment (3 spots on LS, 3 spots on non-LS). TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined LS and non-LS areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Percent change from Baseline at Week 16 in TEWL after 15 STS on LS and non-LS (first spot) in AD subjects were reported in this endpoint. Analysis was performed on mITT population. Here, 'n'=subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data for this endpoint was not planned to be collected and analysed for Healthy Volunteer arm as pre-specified in protocol.

End point values	Atopic Dermatitis Patients			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: percent change				
arithmetic mean (standard deviation)				
Lesional skin (n = 7)	-51.2 (± 17.4)			
Non-Lesional skin (n = 21)	25.1 (± 116.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in TEWL After 15 STS on Lesional and Non-lesional Skin in AD Patients at Week 16

End point title	Absolute Change From Baseline in TEWL After 15 STS on Lesional and Non-lesional Skin in AD Patients at Week 16[8]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The LS and non-LS areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined LS and non-LS areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment (3 spots on LS, 3 spots on non-LS). TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined LS and non-LS areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Absolute change from Baseline at Week 16 in TEWL after 15 STS on LS and non-LS (first spot) in AD subjects were reported in this endpoint. Analysis was performed on mITT population. Here, 'n'=subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data for this endpoint was not planned to be collected and analysed for Healthy Volunteer arm as pre-specified in protocol.

End point values	Atopic Dermatitis Patients			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: grams per square metre per hour				
arithmetic mean (standard deviation)				
Lesional skin (n = 7)	-43.1 (± 20.6)			
Non-Lesional skin (n = 21)	-2.0 (± 23.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in TEWL After 15 STS on Normal Skin in Healthy Volunteers at Week 16

End point title	Percent Change From Baseline in TEWL After 15 STS on Normal Skin in Healthy Volunteers at Week 16[9]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The normal skin areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined normal skin areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined normal skin areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Percent change from Baseline at Week 16 in TEWL after 15 STS on normal skin (first spot) in healthy volunteers were reported in this endpoint. Analysis was performed on mITT population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Atopic Dermatitis Patients arm as pre-specified in the protocol.

End point values	Healthy Volunteer			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: percent change				
arithmetic mean (standard deviation)	-7.2 (± 35.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in TEWL After 15 STS on Normal Skin in Healthy Volunteers at Week 16

End point title	Absolute Change From Baseline in TEWL After 15 STS on

	Normal Skin in Healthy Volunteers at Week 16[10]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The normal skin areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined normal skin areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined normal skin areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Absolute change from Baseline at Week 16 in TEWL after 15 STS on normal skin (first spot) in healthy volunteers were reported in this endpoint. Analysis was performed on mITT population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Atopic Dermatitis Patients arm as pre-specified in the protocol.

End point values	Healthy Volunteer			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: grams per square metre per hour				
arithmetic mean (standard deviation)	-4.5 (± 11.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in TEWL After 10 STS on Lesional and Non-lesional Skin in AD Patients at Week 16

End point title	Percent Change From Baseline in TEWL After 10 STS on Lesional and Non-lesional Skin in AD Patients at Week 16[11]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The LS and non-LS areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined LS and non-LS areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment (3 spots on LS, 3 spots on non-LS). TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined LS and non-LS areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Percent change from Baseline at Week 16 in TEWL after 10 STS on LS and non-LS (first spot) in AD subjects were reported in this endpoint. Analysis was performed on mITT population. Here, 'n'=subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Healthy Volunteer arm as pre-specified in protocol.

End point values	Atopic Dermatitis Patients			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: percent change				
arithmetic mean (standard deviation)				
Lesional skin (n = 20)	-54.9 (± 17.5)			
Non-Lesional skin (n = 21)	26.2 (± 111.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in TEWL After 10 STS on Lesional and Non-lesional Skin in AD Patients at Week 16

End point title	Absolute Change From Baseline in TEWL After 10 STS on Lesional and Non-lesional Skin in AD Patients at Week 16[12]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The LS and non-LS areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined LS and non-LS areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment (3 spots on LS, 3 spots on non-LS). TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined LS and non-LS areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Absolute change from Baseline at Week 16 in TEWL after 10 STS on LS and non-LS (first spot) in AD subjects were reported in this endpoint. Anlysis was performed on mITT population. Here, 'n'=subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Healthy Volunteer arm as pre-specified in protocol.

End point values	Atopic Dermatitis Patients			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: grams per square metre per hour				
arithmetic mean (standard deviation)				
Lesional skin (n = 20)	-41.2 (± 20.4)			
Non-Lesional skin (n = 21)	-0.5 (± 17.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in TEWL After 10 STS on Normal Skin in Healthy Volunteers at Week 16

End point title	Absolute Change From Baseline in TEWL After 10 STS on Normal Skin in Healthy Volunteers at Week 16[13]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The normal skin areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined normal skin areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined normal skin areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Absolute change from Baseline at Week 16 in TEWL after 10 STS on normal skin (first spot) in healthy volunteers were reported in this endpoint. Analysis was performed on mITT population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Atopic Dermatitis Patients arm as pre-specified in the protocol.

End point values	Healthy Volunteer			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: grams per square metre per hour				
arithmetic mean (standard deviation)	-0.8 (± 4.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in TEWL After 10 STS on Normal Skin in Healthy Volunteers at Week 16

End point title	Percent Change From Baseline in TEWL After 10 STS on Normal Skin in Healthy Volunteers at Week 16[14]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The normal skin areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined normal skin areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined normal skin areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Percent change from Baseline at Week 16 in TEWL after 10 STS on normal skin (first spot) in healthy volunteers were reported in this endpoint. Analysis was performed on mITT population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Atopic Dermatitis Patients arm as pre-specified in the protocol.

End point values	Healthy Volunteer			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percent change				
arithmetic mean (standard deviation)	-2.0 (± 23.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in TEWL After 5 STS on Non-lesional Skin in AD Patients at Week 16

End point title	Percent Change From Baseline in TEWL After 5 STS on Non-lesional Skin in AD Patients at Week 16[15]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The non-LS areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined non-LS areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined non-LS areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Percent change from Baseline at Week 16 in TEWL after 5 STS on non-LS (first spot) in AD subjects were reported in this endpoint. Analysis was performed on mITT population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Healthy Volunteer arm as pre-specified in protocol.

End point values	Atopic Dermatitis Patients			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: percent change				
arithmetic mean (standard deviation)	17.6 (± 82.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in TEWL After 5 STS on Lesional Skin in AD Patients at Week 16

End point title	Absolute Change From Baseline in TEWL After 5 STS on Lesional Skin in AD Patients at Week 16[16]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The LS areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined LS areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined LS areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Absolute change from Baseline at Week 16 in TEWL after 5 STS on LS (first spot) in AD subjects were reported in this endpoint. Analysis was performed on mITT population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Healthy Volunteer arm as pre-specified in protocol.

End point values	Atopic Dermatitis Patients			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: grams per square metre per hour				
arithmetic mean (standard deviation)	-35.1 (± 17.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in TEWL After 5 STS on Non-lesional Skin in AD Patients at Week 16

End point title	Absolute Change From Baseline in TEWL After 5 STS on Non-lesional Skin in AD Patients at Week 16[17]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The non-LS areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined non-LS areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined non-LS areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Absolute change from Baseline at Week 16 in TEWL after 5 STS on non-LS (first spot) in AD subjects were reported in this endpoint. Analysis was performed on mITT population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Healthy Volunteer arm as pre-specified in protocol.

End point values	Atopic Dermatitis Patients			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: grams per square metre per hour				
arithmetic mean (standard deviation)	-0.8 (± 13.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in TEWL After 5 STS on Normal Skin in Healthy Volunteers at Week 16

End point title	Absolute Change From Baseline in TEWL After 5 STS on Normal Skin in Healthy Volunteers at Week 16[18]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The normal skin areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined normal skin areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined normal skin areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Absolute change from Baseline at Week 16 in TEWL after 5 STS on normal skin (first spot) in healthy volunteers were reported in this endpoint. Analysis was performed on mITT population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Atopic Dermatitis Patients arm as pre-specified in the protocol.

End point values	Healthy Volunteer			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: grams per square metre per hour				
arithmetic mean (standard deviation)	0.0 (± 2.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in TEWL After 5 STS on Normal Skin in Healthy Volunteers at Week 16

End point title	Percent Change From Baseline in TEWL After 5 STS on Normal Skin in Healthy Volunteers at Week 16[19]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, the uppermost layers of the skin are peeled away using adhesive discs. The normal skin areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within the predefined normal skin areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined normal skin areas at specified time points. STS assessment at Baseline (Week 0, Day 1) and Week 16 was conducted on first spot. Percent change from Baseline at Week 16 in TEWL after 5 STS on normal skin (first spot) in healthy volunteers were reported in this endpoint. Analysis was performed on mITT population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Atopic Dermatitis Patients arm as pre-specified in the protocol.

End point values	Healthy Volunteer			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: percent change				
arithmetic mean (standard deviation)	1.2 (± 21.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in TEWL Before STS on Lesional and Non-lesional Skin in AD Patients at Day 4, 8, 11, 15, 22, 29, 43, 57, 85 and Week 16

End point title	Percent Change From Baseline in TEWL Before STS on Lesional and Non-lesional Skin in AD Patients at Day 4, 8, 11, 15, 22, 29, 43, 57, 85 and Week 16[20]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. LS and non-LS areas for TEWL assessment were identified at Baseline ('predefined skin area'). Within predefined LS and non-LS areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment (3 spots on LS, 3 spots on non-LS). TEWL was measured prior to STS on pre-defined LS and non-LS areas at specified time points. At each visit, before STS, all three spots were assessed, and their value was averaged to derive a single value. Percent change from Baseline at specified time points in TEWL before STS on LS and non-LS in AD subjects were reported in this endpoint. Analysis was performed on mITT population. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Day 4, 8, 11, 15, 22, 29, 43, 57, 85 and Week 16

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Healthy Volunteer arm as pre-specified in protocol.

End point values	Atopic Dermatitis Patients			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: percent change				
arithmetic mean (standard deviation)				
Lesional skin: Day 4 (n = 24)	-0.7 (± 30.1)			
Lesional skin: Day 8 (n = 25)	-5.3 (± 42.1)			
Lesional skin: Day 11 (n =24)	-12.9 (± 32.6)			
Lesional skin: Day 15 (n = 25)	-16.3 (± 34.5)			
Lesional skin: Day 22 (n = 25)	-37.8 (± 20.6)			
Lesional skin: Day 29 (n = 24)	-35.1 (± 19.9)			
Lesional skin: Day 43 (n = 23)	-40.6 (± 21.4)			
Lesional skin: Day 57 (n = 23)	-42.1 (± 20.9)			
Lesional skin: Day 85 (n = 21)	-42.7 (± 23.8)			
Lesional skin: Week 16 (n = 21)	-48.7 (± 22.6)			
Non-Lesional skin: Day 4 (n = 24)	25.2 (± 40.6)			
Non-Lesional skin: Day 8 (n = 25)	27.9 (± 59.5)			
Non-Lesional skin: Day 11 (n = 24)	20.1 (± 46.8)			
Non-Lesional skin: Day 15 (n = 25)	24.0 (± 56.1)			
Non-Lesional skin: Day 22 (n = 25)	14.5 (± 47.8)			
Non-Lesional skin: Day 29 (n = 24)	6.4 (± 47.0)			
Non-Lesional skin: Day 43 (n= 23)	5.6 (± 57.2)			
Non-Lesional skin: Day 57 (n = 23)	17.8 (± 85.4)			
Non-Lesional skin: Day 85 (n = 21)	27.5 (± 99.1)			
Non-Lesional skin: Week 16 (n = 21)	18.8 (± 85.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline up to Week 16 in TEWL Before STS on Lesional and Non-lesional Skin in AD Patients at Day 4, 8, 11, 15, 22, 29, 43, 57, 85 and Week 16

End point title	Absolute Change From Baseline up to Week 16 in TEWL Before STS on Lesional and Non-lesional Skin in AD Patients at Day 4, 8, 11, 15, 22, 29, 43, 57, 85 and Week 16[21]

End point description:

TEWL assessment: noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. LS and non-LS areas for TEWL assessment were identified at Baseline ('predefined skin area'). Within predefined LS and non-LS areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment (3 spots on LS, 3 spots on non-LS). TEWL was measured prior to STS on pre-defined LS and non-LS areas at specified time points. At each visit, before STS, all three spots

were assessed, and their value was averaged to derive a single value. Absolute change from Baseline at specified time points in TEWL before STS on LS and non-LS in AD subjects were reported in this endpoint. Analysis was performed on mITT population. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Day 4, 8, 11, 15, 22, 29, 43, 57, 85 and Week 16

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Healthy Volunteer arm as pre-specified in protocol.

End point values	Atopic Dermatitis Patients			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: grams per square metre per hour				
arithmetic mean (standard deviation)				
Lesional skin: Day 4 (n = 24)	-3.0 (± 14.0)			
Lesional skin: Day 8 (n = 25)	-5.6 (± 18.8)			
Lesional skin: Day 11 (n = 24)	-8.2 (± 16.0)			
Lesional skin: Day 15 (n = 25)	-10.4 (± 16.6)			
Lesional skin: Day 22 (n = 25)	-19.3 (± 14.0)			
Lesional skin: Day 29 (n = 24)	-17.7 (± 14.4)			
Lesional skin: Day 43 (n = 23)	-20.9 (± 14.9)			
Lesional skin: Day 57 (n = 23)	-20.9 (± 14.0)			
Lesional skin: Day 85 (n = 21)	-22.4 (± 16.7)			
Lesional skin: Week 16 (n = 21)	-24.3 (± 16.3)			
Non-Lesional skin: Day 4 (n = 24)	2.7 (± 7.6)			
Non-Lesional skin: Day 8 (n = 25)	3.8 (± 11.0)			
Non-Lesional skin: Day 11 (n = 24)	2.1 (± 10.1)			
Non-Lesional skin: Day 15 (n = 25)	2.6 (± 11.5)			
Non-Lesional skin: Day 22 (n = 25)	0.4 (± 8.9)			
Non-Lesional skin: Day 29 (n = 24)	-1.2 (± 11.1)			
Non-Lesional skin: Day 43 (n = 23)	-1.7 (± 9.4)			
Non-Lesional skin: Day 57 (n = 23)	-0.9 (± 13.0)			
Non-Lesional skin: Day 85 (n = 21)	1.0 (± 15.3)			
Non-Lesional skin: Week 16 (n = 21)	-0.7 (± 12.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in TEWL Before STS on Normal Skin in Healthy Volunteers at Day 4, 8, 11, 15, 22, 29, 43, 57, 85 and Week 16

End point title	Percent Change From Baseline in TEWL Before STS on Normal Skin in Healthy Volunteers at Day 4, 8, 11, 15, 22, 29, 43, 57, 85 and Week 16[22]

End point description:

TEWL assessment: noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. Normal skin areas for TEWL assessment were identified at Baseline ('predefined skin area'). Within predefined normal skin areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL was measured prior to STS on pre-defined normal skin areas at specified time points. At each visit, before STS, all three spots were assessed, and their value was averaged to derive a single value. Percent change from Baseline at specified time points in TEWL before STS on normal skin in healthy volunteers were reported in this endpoint. Analysis was performed on mITT population. Here, number of subjects analysed = subjects evaluable for this endpoint and 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Day 4, 8, 11, 15, 22, 29, 43, 57, 85 and Week 16

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Atopic Dermatitis Patients arm as pre-specified in the protocol.

End point values	Healthy Volunteer			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: percent change				
arithmetic mean (standard deviation)				
Day 4 (n = 24)	42.6 (± 44.4)			
Day 8 (n = 23)	20.5 (± 38.4)			
Day 11 (n = 23)	15.9 (± 31.0)			
Day 15 (n = 23)	16.6 (± 25.1)			
Day 22 (n = 23)	18.5 (± 32.2)			
Day 29 (n = 23)	8.0 (± 20.2)			
Day 43 (n = 23)	4.0 (± 26.2)			
Day 57 (n = 23)	20.3 (± 31.9)			
Day 85 (n = 23)	6.0 (± 21.8)			
Week 16 (n = 23)	4.3 (± 25.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in TEWL Before STS on Normal Skin in Healthy Volunteers at Day 4, 8, 11, 15, 22, 29, 43, 57, 85 and Week 16

End point title	Absolute Change From Baseline in TEWL Before STS on Normal Skin in Healthy Volunteers at Day 4, 8, 11, 15, 22, 29, 43, 57, 85 and Week 16[23]

End point description:

TEWL assessment: noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. Normal skin areas for TEWL assessment were identified at Baseline ('predefined skin area'). Within predefined normal skin areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL was measured prior to STS on pre-defined normal skin areas at specified time points. At each visit, before STS, all three spots were assessed, and their value was averaged to derive a single value. Absolute change from Baseline at specified time points in TEWL before STS on normal skin in healthy volunteers were reported in this endpoint. Analysis was performed on mITT population. Here, number of subjects analysed = subjects evaluable for this endpoint and 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Day 4, 8, 11, 15, 22, 29, 43, 57, 85 and Week 16

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Atopic Dermatitis Patients arm as pre-specified in the protocol.

End point values	Healthy Volunteer			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: grams per square metre per hour				
arithmetic mean (standard deviation)				
Day 4 (n = 24)	3.9 (± 4.6)			
Day 8 (n = 23)	1.4 (± 3.1)			
Day 11 (n = 23)	1.2 (± 3.3)			
Day 15 (n = 23)	1.5 (± 2.7)			
Day 22 (n = 23)	1.4 (± 2.5)			
Day 29 (n = 23)	0.4 (± 2.2)			
Day 43 (n = 23)	-0.1 (± 2.7)			
Day 57 (n = 23)	1.6 (± 4.0)			
Day 85 (n = 23)	0.1 (± 2.7)			
Week 16 (n = 23)	0.4 (± 2.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in TEWL After 5, 10, 15 and 20 STS on Lesional and Non-lesional Skin in AD Patients at Day 15, 29, 57, 85 and Week 16

End point title	Percent Change From Baseline in TEWL After 5, 10, 15 and 20 STS on Lesional and Non-lesional Skin in AD Patients at Day 15, 29, 57, 85 and Week 16[24]

End point description:

TEWL assessment: noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, uppermost layers of skin are peeled away using adhesive discs. LS and non-LS areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within predefined LS and non-LS areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment(3 spots on LS, 3 spots on non-LS). TEWL: measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined LS and non-LS areas at specified time points. STS assessment was done at Baseline (Week 0, Day 1), Day 57 and Week 16 on 1st spot; at Day 15 on 2nd spot and at Day 29 and Day 85 on 3rd spot. Percent change from Baseline at specified time points in TEWL after STS on LS and non-LS in AD subjects were reported in this endpoint. mITT population. Here, 'n' = subjects with available data.

End point type	Secondary

End point timeframe:

Baseline, Day 15, 29, 57, 85 and Week 16

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Healthy Volunteer

arm as pre-specified in protocol.

End point values	Atopic Dermatitis Patients			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: percent change				
arithmetic mean (standard deviation)				
Lesional skin: After 5 STS: Day 15 (n = 25)	-25.1 (± 34.0)			
Lesional skin: After 5 STS: Day 29 (n = 24)	-38.9 (± 23.4)			
Lesional skin: After 5 STS: Day 57 (n = 23)	-45.6 (± 23.5)			
Lesional skin: After 5 STS: Day 85 (n = 20)	-50.6 (± 26.7)			
Lesional skin: After 5 STS: Week 16 (n = 21)	-54.6 (± 18.0)			
Lesional skin: After 10 STS: Day 15 (n = 24)	-18.5 (± 30.7)			
Lesional skin: After 10 STS: Day 29 (n = 24)	-32.5 (± 29.1)			
Lesional skin: After 10 STS: Day 57 (n = 23)	-46.7 (± 22.4)			
Lesional skin: After 10 STS: Day 85 (n = 21)	-47.0 (± 25.6)			
Lesional skin: After 10 STS: Week 16 (n =20)	-54.9 (± 17.5)			
Lesional skin: After 15 STS: Day 15 (n = 9)	-14.5 (± 24.8)			
Lesional skin: After 15 STS: Day 29 (n = 10)	-33.0 (± 17.7)			
Lesional skin: After 15 STS: Day 57 (n = 8)	-39.1 (± 22.3)			
Lesional skin: After 15 STS: Day 85 (n = 7)	-43.4 (± 24.4)			
Lesional skin: After 15 STS: Week 16 (n = 7)	-51.2 (± 17.4)			
Lesional skin: After 20 STS: Day 15 (n = 9)	-11.6 (± 27.9)			
Lesional skin: After 20 STS: Day 29 (n = 10)	-29.1 (± 18.8)			
Lesional skin: After 20 STS: Day 57 (n = 9)	-37.4 (± 22.9)			
Lesional skin: After 20 STS: Day 85 (n = 7)	-38.8 (± 28.2)			
Lesional skin: After 20 STS: Week 16 (n = 7)	-47.7 (± 20.1)			
Non-Lesional skin: After 5 STS: Day 15 (n = 24)	49.8 (± 100.0)			
Non-Lesional skin: After 5 STS: Day 29 (n = 23)	8.0 (± 46.1)			
Non-Lesional skin: After 5 STS: Day 57 (n = 22)	22.8 (± 89.0)			
Non-Lesional skin: After 5 STS: Day 85 (n = 20)	33.7 (± 106.8)			
Non-Lesional skin: After 5 STS: Week 16 (n = 20)	17.6 (± 82.2)			

Non-Lesional skin: After 10 STS: Day 15 (n = 25)	55.1 (± 109.3)			
Non-Lesional skin: After 10 STS: Day 29 (n = 24)	4.5 (± 52.9)			
Non-Lesional skin: After 10 STS: Day 57 (n = 23)	18.6 (± 91.0)			
Non-Lesional skin: After 10 STS: Day 85 (n = 21)	31.0 (± 116.3)			
Non-Lesional skin: After 10 STS: Week 16 (n = 21)	26.2 (± 111.8)			
Non-Lesional skin: After 15 STS: Day 15 (n = 25)	70.9 (± 128.3)			
Non-Lesional skin: After 15 STS: Day 29 (n = 24)	2.4 (± 58.9)			
Non-Lesional skin: After 15 STS: Day 57 (n = 23)	23.5 (± 104.4)			
Non-Lesional skin: After 15 STS: Day 85 (n = 21)	34.7 (± 112.0)			
Non-Lesional skin: After 15 STS: Week 16 (n = 21)	25.1 (± 116.5)			
Non-Lesional skin: After 20 STS: Day 15 (n = 25)	53.1 (± 96.0)			
Non-Lesional skin: After 20 STS: Day 29 (n = 24)	-3.8 (± 53.2)			
Non-Lesional skin: After 20 STS: Day 57 (n = 23)	14.3 (± 80.7)			
Non-Lesional skin: After 20 STS: Day 85 (n = 21)	30.4 (± 104.9)			
Non-Lesional skin: After 20 STS: Week 16 (n = 21)	16.6 (± 91.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in TEWL After 5, 10, 15 and 20 STS on Lesional and Non-lesional Skin in AD Patients at Day 15, 29, 57, 85 and Week 16

End point title	Absolute Change From Baseline in TEWL After 5, 10, 15 and 20 STS on Lesional and Non-lesional Skin in AD Patients at Day 15, 29, 57, 85 and Week 16[25]

End point description:

TEWL assessment: noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, uppermost layers of skin are peeled away using adhesive discs. LS and non-LS areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within predefined LS and non-LS areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment(3 spots on LS, 3 spots on non-LS). TEWL: measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined LS and non-LS areas at specified time points. STS assessment was done at Baseline (Week 0, Day 1), Day 57 and Week 16 on 1st spot; at Day 15 on 2nd spot and at Day 29 and Day 85 on 3rd spot. Absolute change from Baseline at specified time points in TEWL after STS on LS and non-LS in AD subjects were reported in this endpoint. mITT population. Here, 'n'=subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Day 15, 29, 57, 85 and Week 16

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data for this endpoint was not planned to be collected and analysed for Healthy Volunteer arm as pre-specified in protocol.

End point values	Atopic Dermatitis Patients			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: grams per square metre per hour				
arithmetic mean (standard deviation)				
Lesional skin: After 5 STS: Day 15 (n = 25)	-19.4 (± 21.8)			
Lesional skin: After 5 STS: Day 29 (n = 24)	-27.1 (± 20.2)			
Lesional skin: After 5 STS: Day 57 (n = 23)	-29.4 (± 19.1)			
Lesional skin: After 5 STS: Day 85 (n = 20)	-34.8 (± 21.6)			
Lesional skin: After 5 STS: Week 16 (n = 21)	-35.1 (± 17.1)			
Lesional skin: After 10 STS: Day 15 (n = 24)	-17.7 (± 24.5)			
Lesional skin: After 10 STS: Day 29 (n = 24)	-28.3 (± 25.9)			
Lesional skin: After 10 STS: Day 57 (n = 23)	-35.6 (± 23.2)			
Lesional skin: After 10 STS: Day 85 (n = 21)	-36.2 (± 21.3)			
Lesional skin: After 10 STS: Week 16 (n = 20)	-41.2 (± 20.4)			
Lesional skin: After 15 STS: Day 15 (n = 9)	-13.3 (± 23.9)			
Lesional skin: After 15 STS: Day 29 (n = 10)	-27.0 (± 16.3)			
Lesional skin: After 15 STS: Day 57 (n = 8)	-31.4 (± 22.1)			
Lesional skin: After 15 STS: Day 85 (n = 7)	-33.7 (± 18.1)			
Lesional skin: After 15 STS: Week 16 (n = 7)	-43.1 (± 20.6)			
Lesional skin: After 20 STS: Day 15 (n = 9)	-13.6 (± 26.3)			
Lesional skin: After 20 STS: Day 29 (n = 10)	-25.5 (± 16.1)			
Lesional skin: After 20 STS: Day 57 (n = 9)	-33.3 (± 23.4)			
Lesional skin: After 20 STS: Day 85 (n = 7)	-32.2 (± 22.5)			
Lesional skin: After 20 STS: Week 16 (n = 7)	-42.6 (± 22.1)			
Non-Lesional skin: After 5 STS: Day 15 (n = 24)	8.2 (± 22.1)			
Non-Lesional skin: After 5 STS: Day 29 (n = 23)	-1.0 (± 10.2)			
Non-Lesional skin: After 5 STS: Day 57 (n = 22)	0.2 (± 14.8)			
Non-Lesional skin: After 5 STS: Day 85 (n = 20)	3.4 (± 18.2)			
Non-Lesional skin: After 5 STS: Week 16 (n = 20)	-0.8 (± 13.6)			

Non-Lesional skin: After 10 STS: Day 15 (n = 25)	10.6 (± 29.0)			
Non-Lesional skin: After 10 STS: Day 29 (n = 24)	-2.6 (± 14.2)			
Non-Lesional skin: After 10 STS: Day 57 (n = 23)	-1.8 (± 18.2)			
Non-Lesional skin: After 10 STS: Day 85 (n = 21)	2.4 (± 24.3)			
Non-Lesional skin: After 10 STS: Week 16 (n = 21)	-0.5 (± 17.9)			
Non-Lesional skin: After 15 STS: Day 15 (n = 25)	17.7 (± 37.6)			
Non-Lesional skin: After 15 STS: Day 29 (n = 24)	-4.8 (± 20.5)			
Non-Lesional skin: After 15 STS: Day 57 (n = 23)	-1.2 (± 25.5)			
Non-Lesional skin: After 15 STS: Day 85 (n = 21)	3.8 (± 31.0)			
Non-Lesional skin: After 15 STS: Week 16 (n = 21)	-2.0 (± 23.5)			
Non-Lesional skin: After 20 STS: Day 15 (n = 25)	18.6 (± 37.7)			
Non-Lesional skin: After 20 STS: Day 29 (n = 24)	-7.5 (± 25.2)			
Non-Lesional skin: After 20 STS: Day 57 (n = 23)	-0.8 (± 27.7)			
Non-Lesional skin: After 20 STS: Day 85 (n = 21)	5.5 (± 38.2)			
Non-Lesional skin: After 20 STS: Week 16 (n = 21)	-2.1 (± 26.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in TEWL After 5, 10, 15 and 20 STS on Normal Skin in Healthy Volunteers at Day 15, 29, 57, 85 and Week 16

End point title	Percent Change From Baseline in TEWL After 5, 10, 15 and 20 STS on Normal Skin in Healthy Volunteers at Day 15, 29, 57, 85 and Week 16[26]

End point description:

TEWL assessment: noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, uppermost layers of skin are peeled away using adhesive discs. Normal skin areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within predefined normal skin areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined normal skin areas at specified time points. STS assessment was done at Baseline (Week 0, Day 1), Day 57 and Week 16 on 1st spot; at Day 15 on 2nd spot and at Day 29 and Day 85 on 3rd spot. Percent change from Baseline at specified time points in TEWL after STS on normal skin in healthy volunteers were reported in this endpoint. mITT population. Here, number of subjects analysed=subjects evaluable and 'n'=subjects with data a for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Day 15, 29, 57, 85 and Week 16

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data for this endpoint was not planned to be collected and analysed for Atopic Dermatitis Patients arm as pre-specified in the protocol.

End point values	Healthy Volunteer			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: percent change				
arithmetic mean (standard deviation)				
After 5 STS: Day 15 (n = 23)	15.9 (± 27.8)			
After 5 STS: Day 29 (n= 23)	5.2 (± 24.5)			
After 5 STS: Day 57 (n = 23)	16.0 (± 27.6)			
After 5 STS: Day 85 (n = 23)	5.8 (± 26.3)			
After 5 STS: Week 16 (n = 23)	1.2 (± 21.9)			
After 10 STS: Day 15 (n = 22)	17.6 (± 31.3)			
After 10 STS: Day 29 (n = 21)	6.8 (± 27.8)			
After 10 STS: Day 57 (n = 22)	13.7 (± 25.9)			
After 10 STS: Day 85 (n = 22)	3.1 (± 26.8)			
After 10 STS: Week 16 (n = 22)	-2.0 (± 23.5)			
After 15 STS: Day 15 (n =21)	32.3 (± 80.8)			
After 15 STS: Day 29 (n = 22)	1.6 (± 37.1)			
After 15 STS: Day 57 (n =23)	15.3 (± 49.1)			
After 15 STS: Day 85 (n = 23)	1.7 (± 60.2)			
After 15 STS: Week 16 (n = 23)	-7.2 (± 35.8)			
After 20 STS: Day 15 (n = 23)	44.2 (± 107.8)			
After 20 STS: Day 29 (n = 22)	31.1 (± 94.8)			
After 20 STS: Day 57 (n = 23)	22.0 (± 63.2)			
After 20 STS: Day 85 (n = 23)	8.5 (± 89.4)			
After 20 STS: Week 16 (n = 23)	-5.8 (± 46.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in TEWL After 5, 10, 15 and 20 STS on Normal Skin in Healthy Volunteers at Day 15, 29, 57, 85 and Week 16

End point title	Absolute Change From Baseline in TEWL After 5, 10, 15 and 20 STS on Normal Skin in Healthy Volunteers at Day 15, 29, 57, 85 and Week 16[27]

End point description:

TEWL assessment: noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. With STS, uppermost layers of skin are peeled away using adhesive discs. Normal skin areas for TEWL assessment and STS were identified at Baseline ('predefined skin area'). Within predefined normal skin areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined normal skin areas at specified time points. STS assessment was done at Baseline (Week 0, Day 1), Day 57 and Week 16 on 1st spot; at Day 15 on 2nd spot and at Day 29 and Day 85 on 3rd spot. Absolute change from Baseline at specified time points in TEWL after STS on normal skin in healthy volunteers were reported in this endpoint. mITT population. Here, number of subjects analysed=subjects evaluable and 'n'=subjects with data a for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Day 15, 29, 57, 85 and Week 16

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Atopic Dermatitis Patients arm as pre-specified in the protocol.

End point values	Healthy Volunteer			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: grams per square metre per hour				
arithmetic mean (standard deviation)				
After 5 STS: Day 15 (n = 23)	1.7 (± 3.8)			
After 5 STS: Day 29 (n = 23)	0.2 (± 2.9)			
After 5 STS: Day 57 (n = 23)	1.6 (± 4.2)			
After 5 STS: Day 85 (n = 23)	0.1 (± 3.3)			
After 5 STS: Week 16 (n = 23)	0.0 (± 2.7)			
After 10 STS: Day 15 (n = 22)	2.1 (± 5.5)			
After 10 STS: Day 29 (n = 21)	0.4 (± 4.0)			
After 10 STS: Day 57 (n = 22)	1.5 (± 5.4)			
After 10 STS: Day 85 (n = 22)	-0.4 (± 4.2)			
After 10 STS: Week 16 (n = 22)	-0.8 (± 4.0)			
After 15 STS: Day 15 (n = 21)	3.3 (± 15.0)			
After 15 STS: Day 29 (n = 22)	-1.9 (± 8.8)			
After 15 STS: Day 57 (n = 23)	0.5 (± 12.8)			
After 15 STS: Day 85 (n = 23)	-3.0 (± 12.7)			
After 15 STS: Week 16 (n = 23)	-4.5 (± 11.1)			
After 20 STS: Day 15 (n = 23)	5.6 (± 22.4)			
After 20 STS: Day 29 (n = 22)	1.9 (± 20.5)			
After 20 STS: Day 57 (n = 23)	0.0 (± 19.7)			
After 20 STS: Day 85 (n = 23)	-5.2 (± 23.3)			
After 20 STS: Week 16 (n = 23)	-8.0 (± 19.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Area Under the Curve (AUC) of TEWL on Lesional and Non-lesional Skin in AD Patients at Day 15, 29, 57, 85 and Week 16

End point title	Percent Change From Baseline in Area Under the Curve (AUC) of TEWL on Lesional and Non-lesional Skin in AD Patients at Day 15, 29, 57, 85 and Week 16[28]

End point description:

TEWL assessment: noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. TEWL AUC done over defined number of STS was used to reflect the overall integrity of the stratum corneum. LS and non-LS areas for TEWL assessment and STS was identified at Baseline ('predefined skin area'). Within the predefined LS and non-LS areas, 3 closely adjacent nonoverlapping spots identified for subsequent SBF assessment (3 spots on LS, 3 spots on non-LS). TEWL was measured prior to STS and after 5, 10, 15 and 20 STS on pre-defined LS and non-LS areas at specified time points. TEWL AUC was a composite measure before

and after 5, 10, 15 and 20 STS at each specified time point. AUC of TEWL: calculated for each visit using trapezoidal rule. Percent change from Baseline at specified time points in TEWL AUC in AD subjects were reported in this endpoint. mITT population. Here, 'n'=subjects with available data for each category.

End point type	Secondary

End point timeframe:

Baseline, Day 15, 29, 57, 85 and Week 16

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Healthy Volunteer arm as pre-specified in protocol.

End point values	Atopic Dermatitis Patients			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: percent change				
arithmetic mean (standard deviation)				
Lesional skin: Day 15 (n = 25)	-17.0 (± 37.5)			
Lesional skin: Day 29 (n = 24)	-20.5 (± 39.3)			
Lesional skin: Day 57 (n = 23)	-24.3 (± 49.2)			
Lesional skin: Day 85 (n = 21)	-24.5 (± 56.9)			
Lesional skin: Week 16 (n = 21)	-29.2 (± 43.5)			
Non-Lesional skin: Day 15 (n = 25)	52.4 (± 99.9)			
Non-Lesional skin: Day 29 (n = 24)	1.0 (± 48.8)			
Non-Lesional skin: Day 57 (n = 23)	17.7 (± 89.4)			
Non-Lesional skin: Day 85 (n = 21)	29.5 (± 105.6)			
Non-Lesional skin: Week 16 (n = 21)	19.4 (± 97.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Area Under the Curve of TEWL on Lesional and Non-lesional Skin in AD Patients at Day 15, 29, 57, 85 and Week 16

End point title	Absolute Change From Baseline in Area Under the Curve of TEWL on Lesional and Non-lesional Skin in AD Patients at Day 15, 29, 57, 85 and Week 16[29]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. TEWL AUC done over defined number of STS was used to reflect the overall integrity of the stratum corneum. LS and non-LS areas for TEWL assessment and STS was identified at Baseline ('predefined skin area'). Within the predefined LS and non-LS areas, 3 closely adjacent nonoverlapping spots identified for subsequent SBF assessment (3 spots on LS, 3 spots on non-LS). TEWL was measured prior to STS and after 5,10,15 and 20 STS on pre-defined LS and non-LS areas at specified time points. TEWL AUC was a composite measure before and after 5, 10, 15 and 20 STS at each specified time point. AUC of TEWL: calculated for each visit using trapezoidal rule. Absolute change from Baseline at specified time points in TEWL AUC in AD subjects were reported in this endpoint. Analysed on mITT population. Here, 'n'=subjects with available data.

End point type	Secondary

End point timeframe:

Baseline, Day 15, 29, 57, 85 and Week 16

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data for this endpoint was not planned to be collected and analysed for Healthy Volunteer arm as pre-specified in protocol.

End point values	Atopic Dermatitis Patients			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: grams per square metre per hour				
arithmetic mean (standard deviation)				
Lesional skin: Day 15 (n = 25)	-229.6 (± 400.8)			
Lesional skin: Day 29 (n = 24)	-278.0 (± 384.1)			
Lesional skin: Day 57 (n = 23)	-292.3 (± 409.2)			
Lesional skin: Day 85 (n = 21)	-284.8 (± 448.7)			
Lesional skin: Week 16 (n = 21)	-321.2 (± 464.2)			
Non-Lesional skin: Day 15 (n = 25)	230.9 (± 536.0)			
Non-Lesional skin: Day 29 (n = 24)	-66.2 (± 299.3)			
Non-Lesional skin: Day 57 (n = 23)	-22.4 (± 380.9)			
Non-Lesional skin: Day 85 (n = 21)	59.1 (± 483.9)			
Non-Lesional skin: Week 16 (n = 21)	-27.7 (± 348.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Area Under the Curve of TEWL on Normal Skin in Healthy Volunteers at Day 15, 29, 57, 85 and Week 16

End point title	Percent Change From Baseline in Area Under the Curve of TEWL on Normal Skin in Healthy Volunteers at Day 15, 29, 57, 85 and Week 16[30]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. TEWL AUC done over defined number of STS was used to reflect the overall integrity of the stratum corneum. Normal skin areas for TEWL assessment and STS was identified at Baseline ('predefined skin area'). Within the predefined normal skin areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL measured prior to STS and after 5,10,15 and 20 STS on pre-defined normal skin areas at specified time points. TEWL AUC was a composite measure before and after 5, 10, 15 and 20 STS at each specified time point. AUC of TEWL: calculated for each visit using trapezoidal rule. Percent Change from Baseline at specified time points in TEWL AUC in healthy volunteers were reported in this endpoint. Analysed on mITT population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Day 15, 29, 57, 85 and Week 16

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Atopic Dermatitis Patients arm as pre-specified in the protocol.

End point values	Healthy Volunteer			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: percent change				
arithmetic mean (standard deviation)				
Day 15	23.3 (± 51.2)			
Day 29	2.6 (± 39.6)			
Day 57	14.0 (± 36.2)			
Day 85	1.0 (± 45.6)			
Week 16	-5.5 (± 30.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in TEWL Area Under the Curve (AUC) on Normal Skin in Healthy Volunteers at Day 15, 29, 57, 85 and Week 16

End point title	Absolute Change From Baseline in TEWL Area Under the Curve (AUC) on Normal Skin in Healthy Volunteers at Day 15, 29, 57, 85 and Week 16[31]

End point description:

TEWL assessment: a noninvasive in vivo measurement of water loss across stratum corneum that is used to characterise SBF. TEWL combined with STS measures SBF. TEWL AUC done over defined number of STS was used to reflect the overall integrity of the stratum corneum. Normal skin areas for TEWL assessment and STS was identified at Baseline ('predefined skin area'). Within the predefined normal skin areas, 3 closely adjacent non-overlapping spots identified for subsequent SBF assessment. TEWL measured prior to STS and after 5,10,15 and 20 STS on pre-defined normal skin areas at specified time points. TEWL AUC was a composite measure before and after 5, 10, 15 and 20 STS at each specified time point. AUC of TEWL: calculated for each visit using trapezoidal rule. Absolute change from Baseline at specified time points in TEWL AUC in healthy volunteers were reported in this endpoint. Analysed on mITT population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Day 15, 29, 57, 85 and Week 16

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Atopic Dermatitis Patients arm as pre-specified in the protocol.

End point values	Healthy Volunteer			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: grams per square metre per hour				
arithmetic mean (standard deviation)				
Day 15	49.6 (± 157.9)			
Day 29	-17.7 (± 133.2)			
Day 57	20.9 (± 145.2)			
Day 85	-31.2 (± 148.4)			
Week 16	-46.5 (± 125.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For AD subjects: from first dose (i.e., Day 1) of IMP administration up to end of treatment visit (i.e., Day 113). For healthy volunteers: from signature of consent form to end of study (i.e., from screening to Day 141)

Adverse event reporting additional description:

Reported adverse events (AEs) and deaths were treatment-emergent AEs (TEAEs) that occurred, worsened or became serious during TEAE period of AD subjects (defined as time from 1st IMP administration to end of treatment) and for healthy volunteers: from signature of consent form to end of study. Analysis was performed on safety population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Atopic Dermatitis Patients

Reporting group description:

Subjects with moderate to severe AD and aged 18 years and older received dupilumab 600 milligrams (mg) (loading dose) subcutaneous (SC) injection on Day 1, followed by dupilumab 300 mg SC injection every 2 weeks (Q2W) through Week 14 (i.e., at Day 15, 29, 43, 57 and 85).
Subjects aged greater than or equal to (>=) 12 to less than (<) 18 years received treatment based on their body weight: <60 kilograms (kg) and >=60 kg - received dupilumab 400 mg and 600 mg (loading dose) SC injection on Day 1, respectively, followed by dupilumab 200 mg and 300 mg SC injection Q2W through Week 14 (i.e., at Day 15, 29, 43, 57 and 85).

Reporting group title	Healthy volunteer

Reporting group description:

Healthy volunteers with age, gender, location of targeted skin lesion area and study site matched to a selected atopic dermatitis (AD) subjects, received no treatment, but were monitored in similar way as AD subjects.

Serious adverse events	Atopic Dermatitis Patients	Healthy volunteer	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Atopic Dermatitis Patients	Healthy volunteer	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 26 (76.92%)	13 / 26 (50.00%)	
Investigations			

Blood Pressure Abnormal			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Dental Restoration Failure			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Foreign Body In Eye			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Limb Injury			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Vascular disorders			
Hypertension			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Injection Site Reaction			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	5 / 26 (19.23%)	0 / 26 (0.00%)	
occurrences (all)	6	0	
Medical Device Site Erythema			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Medical Device Site Haemorrhage			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	2 / 26 (7.69%)	2 / 26 (7.69%)	
occurrences (all)	2	2	
Medical Device Site Pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Medical Device Site Urticaria			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	2	
Immune system disorders			
Food Allergy			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Eye disorders			
Conjunctivitis Allergic			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Dry Eye			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Noninfective Conjunctivitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Abdominal Pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Food Poisoning			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Nausea			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Breast Tenderness			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dermatitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Dermatitis Atopic			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Ecchymosis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 26 (0.00%)	3 / 26 (11.54%)	
occurrences (all)	0	3	
Petechiae			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Skin Burning Sensation			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			

Insomnia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Anxiety			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 26 (11.54%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Back Pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Myalgia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Pain In Extremity			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Osteoporosis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Herpes Zoster			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Covid-19			

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Abscess Limb			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Hordeolum			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Upper Respiratory Tract Infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Tooth Abscess			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 July 2020	The following changes were done: • To further characterise the treatment effect of dupilumab in adolescent and adult subjects with moderate to severe AD in reference to matched healthy controls, a proteomics assessment and a transcriptomics assessment from skin tape strips were added. • These assessments allowed for better assessment of the mechanism of dupilumab in AD. To have comparable data in lesional skin and nonlesional skin of AD subjects as well as in normal skin of healthy volunteers, the number of skin tape strips collected was set to 20 for each skin area. • In response to the global COVID-19 pandemic, benefit-risk assessment in the context of COVID-19 was introduced. Implementation of temporary or alternative mechanisms such as phone contact, virtual visits, online meetings, use of local clinic or laboratory locations, and home visits by skilled staff (as permitted per local regulations) were allowed to ensure the study continuity and protect subjects' safety. No waivers to deviate from protocol enrollment criteria due to COVID19 were granted. Remote monitoring was implemented when onsite monitoring was not allowed. All temporary mechanisms utilised and deviations from planned study procedures were documented as being related to the COVID-19 pandemic.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported