EU Clinical Trials Register

Clinical trial results:
A Multi-center, Exploratory Study to Assess Dupilumab Effect on Pruritus Neuro-mechanisms in Patients With Atopic Dermatitis

Summary

EudraCT number	2020-003542-36
Trial protocol	DE
Global end of trial date	30 August 2022

Results information

Result version number	v1 (current)
This version publication date	24 August 2023
First version publication date	24 August 2023

Trial information

Trial identification

Sponsor protocol code	LPS16763

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04823130
WHO universal trial number (UTN)	U1111-1251-5658

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	10 October 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assess change in neuronal architecture following long term treatment with dupilumab in skin biopsies from atopic dermatitis (AD) subjects with chronic pruritus.

Protection of trial subjects:

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	22 April 2021
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: 23
Country: Number of subjects enrolled	Germany: 31
Worldwide total number of subjects	54
EEA total number of subjects	31

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	46

From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 3 active sites in the United States and Germany. A total of 54 subjects were enrolled between 22 April 2021 to 30 March 2022 under the dupilumab or the healthy subjects arm groups.

Pre-assignment

Screening details:

Healthy subjects were considered as a reference comparator group and received no treatment. Healthy subjects underwent a 7-day observational period following collection of the skin biopsy on Day 1. Only safety data was collected for the healthy subjects and no other endpoints were assessed.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Healthy Subjects: Control

Arm description:

Healthy subjects with site, age, gender, race, location of targeted lesional and non-lesional skin area matched to selected AD subjects, received no treatment, and were considered as a control group.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Subjects With AD: Dupilumab

Arm description:

Subjects with moderate to severe AD received dupilumab 600 milligrams (mg) subcutaneous (SC) injection on Day 1, followed by dupilumab 300 mg SC injection every 2 weeks (Q2W) from Week 3 to Week 15.

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 600 mg SC injection on Day 1 followed by dupilumab 300 mg SC injection Q2W.

Number of subjects in period 1	Healthy Subjects: Control	Subjects With AD: Dupilumab
Started	19	35
Safety Population	13	31
Completed	10	28
Not completed	9	7
Failure to meet inclusion criteria	6	4
Other-unspecified	1	-

Withdrawal by Subject	2	3

Baseline characteristics

Reporting groups

Reporting group title	Healthy Subjects: Control
Reporting group description:	

Healthy subjects with site, age, gender, race, location of targeted lesional and non-lesional skin area matched to selected AD subjects, received no treatment, and were considered as a control group.

Reporting group title	Subjects With AD: Dupilumab
Reporting group description:	

Subjects with moderate to severe AD received dupilumab 600 milligrams (mg) subcutaneous (SC) injection on Day 1, followed by dupilumab 300 mg SC injection every 2 weeks (Q2W) from Week 3 to Week 15.

Reporting group values	Healthy Subjects: Control	Subjects With AD: Dupilumab	Total
Number of subjects	19	35	54
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	41.3	41.2	
standard deviation	± 14.1	± 18.1	-
Gender categorical			
Units: Subjects			
Female	13	19	32
Male	6	16	22
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	19	33	52
More than one race	0	1	1
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Healthy Subjects: Control
Reporting group description:	

Healthy subjects with site, age, gender, race, location of targeted lesional and non-lesional skin area matched to selected AD subjects, received no treatment, and were considered as a control group.

Reporting group title	Subjects With AD: Dupilumab
Reporting group description:	

Subjects with moderate to severe AD received dupilumab 600 milligrams (mg) subcutaneous (SC) injection on Day 1, followed by dupilumab 300 mg SC injection every 2 weeks (Q2W) from Week 3 to Week 15.

Primary: Change From Baseline in Intraepidermal Nerve Fiber Density on Lesional Skin at Week 17

End point title	Change From Baseline in Intraepidermal Nerve Fiber Density on Lesional Skin at Week 17[1][2]
End point description:	

Skin biopsies were used to analyse the epidermal nerve fiber density. Nerve fibers were visualised by staining consecutive sections for the pan-axonal marker protein gene product 9.5 (PGP9.5); and the basement membrane was visualised by staining for collagen type 4. Quantification of intraepidermal nerve fiber density was calculated by assessing nerve fibers crossing the basement membrane per square millimetre (F/mm^2). Analysis was performed on modified intent-to-treat (mITT) population which included all AD subjects who received at least 1 dose of investigational medicinal product (IMP) who had at least 1 skin biopsy performed, irrespective of compliance with study protocol and procedures, and who did not use prohibited therapies for AD from screening to end of study. Here, 'number of subjects analysed' = subjects with available data for this endpoint and 'n' = subjects with available data for each specified category.

End point type	Primary
End point timeframe:	

Baseline, Week 17

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 endpoint was descriptive in nature, no statistical analyses was reported.

[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 subjects' arm.

End point values	Subjects With AD: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: F/mm^2				
arithmetic mean (standard deviation)				
Baseline (n=27)	8.4567 (± 7.2502)			
Change at Week 17 (n=20)	4.2618 (± 6.7538)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Change From Baseline in Nerve Fiber Branching on Lesional Skin at Week 17

End point title	Percentage of Subjects With Change From Baseline in Nerve Fiber Branching on Lesional Skin at Week 17[3][4]

End point description:

Skin biopsies were used to analyse the epidermal nerve fiber branching. Nerve fibers were visualised by staining consecutive sections for the pan-axonal marker PGP9.5; and the basement membrane was visualised by staining for collagen type 4. Branching of epidermal nerve fibers was assessed semi-quantitatively by classifying subjects into 4 groups depending on the predominant intraepidermal nerve fiber branching pattern as follows: only linear (100% linear), mainly linear (>60% linear), mainly branched (>60% branched), only branched (100% branched). Percentage of subjects with change in nerve fiber branching status from baseline on lesional skin at Week 17 are reported in this endpoint. Analysis was performed on mITT population. Here, 'number of subjects analysed' = subjects with available data for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Week 17

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analyses was reported.

[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 subjects' arm.

End point values	Subjects With AD: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: percentage of subjects				
number (not applicable)				
Only linear	0			
Mainly linear	60.0			
Mainly branched	40.0			
Branched fibers	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Intraepidermal Nerve Fiber Density on Lesional Skin at Weeks 3 and 21

End point title	Change From Baseline in Intraepidermal Nerve Fiber Density on Lesional Skin at Weeks 3 and 21[5]

End point description:

Skin biopsies were used to analyse the epidermal nerve fiber density. Nerve fibers were visualised by staining consecutive sections for the pan-axonal marker PGP9.5; and the basement membrane was visualised by staining for collagen type 4. Quantification of intraepidermal nerve fiber density was calculated by assessing nerve fibers crossing the basement membrane per square millimetre (F/mm^2).

End point type	Secondary

End point timeframe:

Baseline, Weeks 3 and 21

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 'healthy subjects' arm.

End point values	Subjects With AD: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: F/mm^2				
arithmetic mean (standard deviation)	()			

Notes:

[6] - Data was not collected and analysed for this endpoint as no optional biopsies done at Week 3 and 21.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Nerve Fiber Branching on Lesional Skin at Weeks 3 and 21

End point title	Change From Baseline in Nerve Fiber Branching on Lesional Skin at Weeks 3 and 21[7]

End point description:

Skin biopsies were used to analyse the epidermal nerve fiber branching. Nerve fibers were visualised by staining consecutive sections for the pan-axonal marker PGP9.5, and the basement membrane was visualised by staining for collagen type 4. Branching of epidermal nerve fibers was assessed semi-quantitatively by classifying subjects into 4 groups depending on the predominant intraepidermal nerve fiber branching pattern as follows: only linear (100% linear), mainly linear (>60% linear), mainly branched (>60% branched), only branched (100% branched).

End point type	Secondary

End point timeframe:

Baseline, Weeks 3 and 21

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 subjects' arm.

End point values	Subjects With AD: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	0[8]			
Units: percent branching				
number (not applicable)				

Notes:

[8] - Data was not collected and analysed for this endpoint as no optional biopsies done at Week 3 and 21.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Peak Pruritus Assessed by Numeric Rating

Scale (NRS) at Weeks 17 and 21

End point title	Change From Baseline in Peak Pruritus Assessed by Numeric Rating Scale (NRS) at Weeks 17 and 21[9]

End point description:

Peak Pruritus NRS was an assessment tool used to report the intensity of subject's pruritus (itch) during a daily recall period. Subjects were asked to rate their worst itch on a 0 ("No itch") to 10 ("Worst itch imaginable") NRS by answering the following question: "On a scale of 0 to 10, with 0 being 'no itch' and 10 being the 'worst itch imaginable', how would you rate your itch at the worst moment during the previous 24 hours?". Higher scores indicated greater severity. Analysis was performed on mITT population. Here, 'number of subjects analysed' = subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 17 and 21

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 'healthy subjects' arm.

End point values	Subjects With AD: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 17	-6.6 (± 3.6)			
Week 21	-7.4 (± 1.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Eczema and Severity Index (EASI) Total Score at Weeks 17 and 21

End point title	Change From Baseline in Eczema and Severity Index (EASI) Total Score at Weeks 17 and 21[10]

End point description:

EASI was a validated measure used to assess the severity and extent of AD. Four AD disease characteristics (erythema, thickness [induration, papulation, and edema], scratching [excoriation], and lichenification) were each assessed for severity by the Investigator on a scale of "0" (absent) through "3" (severe). EASI area score was based upon percent (%) body surface area (BSA) with AD in each body region: 0, 1 (1% to 9%), 2 (10% to 29%), 3 (30% to 49%), 4 (50% to 69%), 5 (70% to 89%), and 6 (90% to 100%). Total EASI score was derived as the sum of the 4 region scores and ranged from 0 (minimum) to 72 (maximum). Higher scores indicated greater severity of AD. Analysis was performed on mITT population. Here, 'number of subjects analysed' = subjects with available data for this endpoint and 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Weeks 17 and 21

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 'healthy subjects' arm.

End point values	Subjects With AD: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 17 (n=12)	-18.9 (± 6.4)			
Week 21 (n=10)	-19.5 (± 6.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Scoring Atopic Dermatitis (SCORAD) Total Score at Weeks 17 and 21

End point title	Change From Baseline in Scoring Atopic Dermatitis (SCORAD) Total Score at Weeks 17 and 21[11]

End point description:

SCORAD: standardise extent & severity of AD consists of 3 components i.e., A =extent or affected BSA assessed as % of each defined body area and reported as sum of all areas, with maximum score of 100%. B=severity of 6 specific symptoms of AD (redness, swelling, oozing/crusting, excoriation, skin thickening/lichenification, dryness) assessed using following scale: none(0), mild(1), moderate(2), or severe(3) (for maximum of 18 total points) & C=subjective symptoms scored by subjects on VAS, where "0"=no itch (or no sleeplessness) & "10"=worst imaginable itch (or sleeplessness) with maximum score of 20. SCORAD total score was calculated using these 3 aspects: extent (A: 0-100), severity (B: 0-18), & subjective symptoms (C: 0-20) using formula: A/5 + 7*B/2+ C. SCORAD total score ranged from 0 to 103, where 0 = no disease to 103 = severe disease. Higher values of SCORAD represent worse outcome. mITT. 'Number of subjects analysed' = subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 17 and 21

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 subjects' arm.

End point values	Subjects With AD: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	19[12]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 17 (n=19)	-77.2 (± 32.3)			
Week 21 (n=15)	-81.3 (± 35.0)			

Notes:

[12] - Here, 'n' = subjects with available data for each specified category.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient-Reported Outcomes Measurement Information (PROMIS-itch) Total Score at Weeks 17 and 21

End point title	Change From Baseline in Patient-Reported Outcomes Measurement Information (PROMIS-itch) Total Score at Weeks 17 and 21[13]

End point description:

PROMIS-itch represents a novel suite of participant-reported outcome (PRO) measures for the itch. The PROMIS-Itch severity score consists of 7 questions: 4 questions scored on a scale of 1 to 5: 1) How intense was your itch at its worst; 2) How intense was your itch in general; 3) What is your level of itch right now; 4) How often did you feel the itch; and rest 3 questions (same questions as 1 to 3 mentioned before but scaled on a scale of 0 to 10) were scored on a scale of 0 to 10. Higher scores for each question indicated worse outcome. The total PROMIS-itch score was calculated as the sum of the 7 questions and ranged from 4 (better outcome) to 50 (worse outcome), where a higher score indicated worse condition. Analysis was performed on mITT population. Here, 'number of subjects analysed' = subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 17 and 21

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 'healthy subjects' arm.

End point values	Subjects With AD: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 17	-30.8 (± 9.0)			
Week 21	-28.8 (± 11.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient Oriented Eczema Measure (POEM) Total Score at Weeks 17 and 21

End point title	Change From Baseline in Patient Oriented Eczema Measure (POEM) Total Score at Weeks 17 and 21[14]

End point description:

The POEM was a 7-item, validated questionnaire used in clinical practice and clinical trials to assess disease symptoms in children and adults with AD. The format is subject response to 7 items (dryness, itching, flaking, cracking, sleep loss, bleeding, and weeping) based on symptom frequency during the past week (i.e., 0 = 'no days', 1 = '1 to 2 days', 2 = '3 to 4 days', 3 = '5 to 6' days, and 4 = 'every day'). The sum of the 7 items gives the total POEM score of 0 (absent disease) to 28 (severe disease). Higher scores indicated more severe disease and poor quality of life. Analysis was performed on mITT population. Here, 'number of subjects analysed' = subjects with available data for this endpoint and 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Weeks 17 and 21

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 'healthy subjects' arm.

End point values	Subjects With AD: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 17 (n=14)	-17.2 (± 5.3)			
Week 21 (n=13)	-16.1 (± 5.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dermatology Life Quality Index (DLQI) Total Score at Weeks 17 and 21

End point title	Change From Baseline in Dermatology Life Quality Index (DLQI) Total Score at Weeks 17 and 21[15]

End point description:

DLQI was a 10-item PRO questionnaire that measured the impact of AD disease symptoms and treatment on quality of life. Each question was evaluated on a 4-point scale ranged from 0 to 3 where, 0 = not at all, 1= a little, 2= a lot, 3= very much, where higher scores indicated more impact on quality of life. Scores from all 10 questions were added up to give DLQI total score that ranged from 0 (not at all) to 30 (very much). Higher scores indicated more impact on quality of life of subjects. Analysis was performed on mITT population. Here, 'number of subjects analysed' = subjects with available data for this endpoint and 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Weeks 17 and 21

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 subjects' arm.

End point values	Subjects With AD: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 17 (n=17)	-16.1 (± 7.4)			
Week 21 (n=16)	-14.8 (± 8.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Atopic Dermatitis Control Tool (ADCT) Total Score at Weeks 17 and 21

End point title	Change From Baseline in Atopic Dermatitis Control Tool (ADCT) Total Score at Weeks 17 and 21[16]

End point description:

ADCT was a PRO questionnaire designed to assess subject-self-perceived control of their eczema. ADCT contained 6 items allowing a comprehensive coverage of the dimensions defining AD control, i.e., overall severity of AD symptoms, frequency of intense episodes of itching, extent of AD related bother, impact on sleep, impact on daily activities, impact on mood or emotions. Each item of the ADCT is rated from 0 (no problem) to 4 (worst) Likert scale and is equally weighted. The sum of the 6 items gives the total score that ranged from 0 (best disease control) to 24 (worst disease control). Higher scores indicate lower AD control. Analysis was performed on mITT population. Here, 'number of subjects analysed' = subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 17 and 21

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 subjects' arm.

End point values	Subjects With AD: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 17	-17.9 (± 4.1)			
Week 21	-15.9 (± 6.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Sleep Quality Numerical Rating Scale at Weeks 17 and 21

End point title	Change From Baseline in Sleep Quality Numerical Rating Scale at Weeks 17 and 21[17]

End point description:

Sleep quality NRS was used to assess the quality of the subject's previous night's sleep using a 0 ("Worst possible sleep") to 10 ("Best possible sleep") NRS. Subjects were asked to complete the following question upon awakening: "Select the number (0 to 10) that best describes the quality of your sleep last night". Higher score indicated better outcome. Analysis was performed on mITT population. Here, 'number of subjects analysed' = subjects with available data for this endpoint and 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Weeks 17 and 21

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 subjects' arm.

End point values	Subjects With AD: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 17 (n=3)	0.7 (± 5.0)			
Week 21 (n=5)	3.0 (± 5.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Skin Pain Numerical Rating Scale at Weeks 17 and 21

End point title	Change From Baseline in Skin Pain Numerical Rating Scale at Weeks 17 and 21[18]

End point description:

Skin pain NRS was used to assess subject's skin pain at its worst in the past 24 hours using a 0 ("Not at all") to 10 ("Very much") NRS. Subjects were asked the following question: "Think about all the areas of your skin with eczema. How much did your skin burn at its worst in the past 24 hours?" Lower score indicated better outcome. Analysis was performed on mITT population. Here, 'number of subjects analysed' = subjects with available data for this endpoint and 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Weeks 17 and 21

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 'healthy subjects' arm.

End point values	Subjects With AD: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 17 (n=3)	-5.3 (± 2.9)			
Week 21 (n=4)	-5.3 (± 2.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Skin Sensitivity Numerical Rating Scale at Weeks 17 and 21

End point title	Change From Baseline in Skin Sensitivity Numerical Rating Scale at Weeks 17 and 21[19]

End point description:

Skin sensitivity NRS was a 1 item PRO measure asking the subjects to rate their skin sensitivity to touch using a 0 ("Normal") to 10 ("Extremely sensitive") NRS. Subjects were asked the following question: "Think about all the areas of your skin with eczema. How sensitive was your skin at its worst in the past 24 hours?" Lower score indicated better outcome. Analysis was performed on mITT population. Here, 'number of subjects analysed' = subjects with available data for this endpoint and 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Weeks 17 and 21

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 'healthy subjects' arm.

End point values	Subjects With AD: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 17 (n=3)	-7.7 (± 1.5)			
Week 21 (n=4)	-7.3 (± 2.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Skin Burning Numerical Rating Scale at Weeks 17 and 21

End point title	Change From Baseline in Skin Burning Numerical Rating Scale at Weeks 17 and 21[20]

End point description:

Skin burning NRS was a 1-item PRO measure asking subjects to rate the burning sensation of their skin in the past 24 hours using a 0 ("Not at all") to 10 ("Very much") NRS. Subjects were asked the following question: "Think about all the areas of your skin with eczema. How much did your skin burn at its worst in the past 24 hours?" Lower score indicated better outcome. Analysis was performed on mITT population. Here, 'number of subjects analysed' = subjects with available data for this endpoint and 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Weeks 17 and 21

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 subjects'

arm.

End point values	Subjects With AD: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 17 (n=3)	-4.3 (± 1.5)			
Week 21 (n=4)	-5.5 (± 2.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Change of Greater Than or Equal to (>=4) Point in Pruritus Numerical Rating Scale From Baseline at Weeks 17 and 21

End point title	Percentage of Subjects With Change of Greater Than or Equal to (>=4) Point in Pruritus Numerical Rating Scale From Baseline at Weeks 17 and 21[21]

End point description:

Pruritus NRS was an assessment tool used to report the intensity of subject's pruritus (itch) during a daily recall period. Subjects were asked to rate their worst itch on a 0 ("No itch") to 10 ("Worst itch imaginable") NRS by answering the following question: "On a scale of 0 to 10, with 0 being 'no itch' and 10 being the 'worst itch imaginable', how would you rate your itch at the worst moment during the previous 24 hours?". Higher scores indicated greater severity. Percentage of subjects with change of >=4 point in pruritus NRS scale from baseline at Weeks 17 and 21 are reported in this endpoint. Analysis was performed on mITT population. Here, 'number of subjects analysed' = subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 17 and 21

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 subjects' arm.

End point values	Subjects With AD: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: percentage of subjects				
number (not applicable)				
Week 17	0			
Week 21	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For Dupilumab group subjects: from first dose (i.e., Day 1) of IMP administration up to end of study visit (i.e., up to Week 21). For healthy participants: from Baseline up to end of study for healthy subjects group (i.e., at Day 8)

Adverse event reporting additional description:

Analysis was performed on safety population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Healthy Subjects

Reporting group description:

Healthy subjects with site, age, gender, race, location of targeted lesional and non-lesional skin area matched to selected AD subjects, received no treatment, and were considered as a control group.

Reporting group title	Subjects With AD: Dupilumab

Reporting group description:

Subjects with moderate to severe AD received dupilumab 600 mg SC injection on Day 1, followed by dupilumab 300 mg SC injection Q2W from Week 3 to Week 15.

Serious adverse events	Healthy Subjects	Subjects With AD: Dupilumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Respiratory, thoracic and mediastinal disorders			
Pulmonary Embolism			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Healthy Subjects	Subjects With AD: Dupilumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	24 / 31 (77.42%)	

Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	0 / 13 (0.00%)	7 / 31 (22.58%)	
occurrences (all)	0	9	
Hypoaesthesia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Injection Site Mass			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Injection Site Swelling			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Eye disorders			
Conjunctivitis Allergic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Eye Pruritus			
subjects affected / exposed	0 / 13 (0.00%)	2 / 31 (6.45%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Abdominal Pain Upper			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Food Poisoning			

subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 13 (0.00%)	2 / 31 (6.45%)	
occurrences (all)	0	3	
Toothache			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Dermatitis Atopic			
subjects affected / exposed	0 / 13 (0.00%)	3 / 31 (9.68%)	
occurrences (all)	0	3	
Eczema			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Neurodermatitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Pain Of Skin			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Psoriasis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			

Back Pain		
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	1
Bursitis		
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	1
Infections and infestations		
Asymptomatic Covid-19		
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	1
Bronchitis		
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	1
Conjunctivitis		
subjects affected / exposed	0 / 13 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	2
Cystitis		
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	1
Impetigo		
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	1
Nasopharyngitis		
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	1
Oral Herpes		
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	1
Rhinitis		
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	1
Sinusitis		
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	1
Suspected Covid-19		

subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Tinea Infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Urinary Tract Infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	

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