Clinical trial results:
A Randomized, Double-blind, Placebo-controlled, Multi-center, Parallel-group Study to Evaluate the Efficacy, Safety and Pharmacokinetics of Dupilumab Compared to Placebo in Japanese Patients With Atopic Dermatitis Aged 6 Months to <18 Years Whose Disease is not Adequately Controlled With Existing Therapies

Summary

EudraCT number	2020-002601-26
Trial protocol	Outside EU/EEA
Global end of trial date	28 October 2023

Results information

Result version number	v1 (current)
This version publication date	12 May 2024
First version publication date	12 May 2024

Trial information

Trial identification

Sponsor protocol code	EFC16823

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04678882
WHO universal trial number (UTN)	U1111-1301-1257

Notes:

Sponsors

Sponsor organisation name	Sanofi K.K.
Sponsor organisation address	3-20-2, Nishi Shinjuku, Shinjuku-ku, Tokyo, Japan, 163-1488
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 December 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 October 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of dupilumab administered concomitantly with topical corticosteroids (TCS).

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of pediatric participants. 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 minimized. 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 minimize distress and discomfort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 January 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	Japan: 62
Worldwide total number of subjects	62
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)	1
Children (2-11 years)	44
Adolescents (12-17 years)	17
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 19 centers in Japan. A total of 75 participants were screened from 15 February 2021 to 02 August 2021, of which 13 were screen failures. Screen failures were mainly due to not meeting inclusion criteria.

Pre-assignment

Screening details:

62 participants were randomized in 1:1 ratio to receive dupilumab or placebo in randomization treatment period.Randomization was stratified by age categories:≥6 months-<6 years,≥6 years-<12 years,≥12 years.For age group of ≥6 years-<12 years,randomization was further stratified by baseline Investigator's Global Assessment(IGA) score(3 versus 4).

Period 1

Period 1 title	Randomization Treatment Period(16 Weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo (Randomization Treatment Period)

Arm description:

Participants received placebo matched to dupilumab subcutaneously (SC) every 2 weeks (q2w) with placebo loading dose for ≥30 kilograms (kg) body weight at baseline; placebo matched to dupilumab SC every 4 weeks (q4w) for ≥5 to <30 kg body weight at baseline, for up to 16 weeks during the randomization treatment period.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo was administered SC as an identical formulation to the active 200 or 300 mg formulation without dupilumab to deliver placebo in 1.14 or 2 milliliters (mL) respectively, up to 16 weeks during the randomization treatment period. SC injection sites were alternated among the different quadrants of the abdomen (avoiding navel and waist areas), upper thighs, and upper arms so that the same site was not injected for 2 consecutive administrations.

Arm title	Dupilumab (Randomization Treatment Period)

Arm description:

Participants received dupilumab 300 milligrams (mg) SC q2w with 600 mg loading dose for ≥60 kg body weight at baseline; dupilumab 200 mg SC q2w with 400 mg loading dose for ≥30 to <60 kg body weight at baseline; dupilumab 300 mg SC q4w for ≥15 to <30 kg body weight at baseline; and dupilumab 200 mg SC q4w for ≥5 to <15 kg body weight at baseline, for up to 16 weeks during the randomization treatment period.

Arm type	Experimental
Investigational medicinal product name	Dupilumab
Investigational medicinal product code	SAR231893
Other name	Dupixent
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Dupilumab was supplied as 175 or 150 milligram per milliliter (mg/mL) solution in prefilled syringes to deliver 200 mg in 1.14 mL or 300 mg in 2 mL respectively, and was administered SC up to 16 weeks during the randomization treatment period. SC injection sites were alternated among the different quadrants of the abdomen (avoiding navel and waist areas), upper thighs, and upper arms so that the same site was not injected for 2 consecutive administrations.

Number of subjects in period 1	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)
Started	32	30
Completed	32	28
Not completed	0	2
Adverse Event: Not Related to COVID-19	-	1
Withdrawal by Subject	-	1

Period 2

Period 2 title	Open-label Extension Period(Week 17-EOS)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Dupilumab (Open-label Extension Period)

Arm description:

Participants who received placebo during the randomization treatment period and who entered the open-label extension (OLE) period, received dupilumab 300 mg SC q2w with 600 mg loading dose for ≥60 kg body weight; dupilumab 200 mg SC q2w with 400 mg loading dose for ≥30 to <60 kg body weight; dupilumab 300 mg SC q4w for ≥15 to <30 kg body weight; and dupilumab 200 mg SC q4w for ≥5 to <15 kg body weight, for 3 years or until approval of the indication in Japan.

Arm type	Experimental
Investigational medicinal product name	Dupilumab
Investigational medicinal product code	SAR231893
Other name	Dupixent
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Dupilumab was supplied as 175 or 150 mg/mL solution in prefilled syringes to deliver 200 mg in 1.14 mL or 300 mg in 2 mL respectively, and was administered SC during the OLE period for 3 years or until approval of the indication in Japan. SC injection sites were alternated among the different quadrants of the abdomen (avoiding navel and waist areas), upper thighs, and upper arms so that the same site was not injected for 2 consecutive administrations.

Arm title	Dupilumab/Dupilumab (Open-label Extension Period)

Arm description:

Participants who received dupilumab during the randomization treatment period and who entered the

OLE period, received dupilumab 300 mg SC q2w with 300 mg loading dose for ≥60 kg body weight; dupilumab 200 mg SC q2w with 200 mg loading dose for ≥30 to <60 kg body weight; dupilumab 300 mg SC q4w for ≥15 to <30 kg body weight; and dupilumab 200 mg SC q4w for ≥5 to <15 kg body weight, for 3 years or until approval of the indication in Japan.

Arm type	Experimental
Investigational medicinal product name	Dupilumab
Investigational medicinal product code	SAR231893
Other name	Dupixent
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Dupilumab was supplied as 175 or 150 mg/mL solution in prefilled syringes to deliver 200 mg in 1.14 mL or 300 mg in 2 mL respectively, and was administered SC during the OLE period for 3 years or until approval of the indication in Japan. SC injection sites were alternated among the different quadrants of the abdomen (avoiding navel and waist areas), upper thighs, and upper arms so that the same site was not injected for 2 consecutive administrations.

Number of subjects in period 2	Placebo/Dupilumab (Open-label Extension Period)	Dupilumab/Dupilumab (Open-label Extension Period)
Started	32	28
Completed	30	26
Not completed	2	2
Not Related to COVID-19	1	1
Withdrawal by Subject	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo (Randomization Treatment Period)
Reporting group description:	
Participants received placebo matched to dupilumab subcutaneously (SC) every 2 weeks (q2w) with placebo loading dose for ≥30 kilograms (kg) body weight at baseline; placebo matched to dupilumab SC every 4 weeks (q4w) for ≥5 to <30 kg body weight at baseline, for up to 16 weeks during the randomization treatment period.	
Reporting group title	Dupilumab (Randomization Treatment Period)
Reporting group description:	
Participants received dupilumab 300 milligrams (mg) SC q2w with 600 mg loading dose for ≥60 kg body weight at baseline; dupilumab 200 mg SC q2w with 400 mg loading dose for ≥30 to <60 kg body weight at baseline; dupilumab 300 mg SC q4w for ≥15 to <30 kg body weight at baseline; and dupilumab 200 mg SC q4w for ≥5 to <15 kg body weight at baseline, for up to 16 weeks during the randomization treatment period.	

Reporting group values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)	Total
Number of subjects	32	30	62
Age Categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	9.6	10.0	
standard deviation	± 4.2	± 4.1	-
Gender Categorical			
Units: Subjects			
Female	11	12	23
Male	21	18	39

End points

End points reporting groups

Reporting group title	Placebo (Randomization Treatment Period)

Reporting group description:

Participants received placebo matched to dupilumab subcutaneously (SC) every 2 weeks (q2w) with placebo loading dose for ≥30 kilograms (kg) body weight at baseline; placebo matched to dupilumab SC every 4 weeks (q4w) for ≥5 to <30 kg body weight at baseline, for up to 16 weeks during the randomization treatment period.

Reporting group title	Dupilumab (Randomization Treatment Period)

Reporting group description:

Participants received dupilumab 300 milligrams (mg) SC q2w with 600 mg loading dose for ≥60 kg body weight at baseline; dupilumab 200 mg SC q2w with 400 mg loading dose for ≥30 to <60 kg body weight at baseline; dupilumab 300 mg SC q4w for ≥15 to <30 kg body weight at baseline; and dupilumab 200 mg SC q4w for ≥5 to <15 kg body weight at baseline, for up to 16 weeks during the randomization treatment period.

Reporting group title	Placebo/Dupilumab (Open-label Extension Period)

Reporting group description:

Participants who received placebo during the randomization treatment period and who entered the open-label extension (OLE) period, received dupilumab 300 mg SC q2w with 600 mg loading dose for ≥60 kg body weight; dupilumab 200 mg SC q2w with 400 mg loading dose for ≥30 to <60 kg body weight; dupilumab 300 mg SC q4w for ≥15 to <30 kg body weight; and dupilumab 200 mg SC q4w for ≥5 to <15 kg body weight, for 3 years or until approval of the indication in Japan.

Reporting group title	Dupilumab/Dupilumab (Open-label Extension Period)

Reporting group description:

Participants who received dupilumab during the randomization treatment period and who entered the OLE period, received dupilumab 300 mg SC q2w with 300 mg loading dose for ≥60 kg body weight; dupilumab 200 mg SC q2w with 200 mg loading dose for ≥30 to <60 kg body weight; dupilumab 300 mg SC q4w for ≥15 to <30 kg body weight; and dupilumab 200 mg SC q4w for ≥5 to <15 kg body weight, for 3 years or until approval of the indication in Japan.

Subject analysis set title	Placebo/Dupilumab (Dupilumab Exposure Period)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received placebo matched to dupilumab SC q2w with placebo loading dose for ≥30 kg body weight at baseline; placebo matched to dupilumab SC q4w for ≥5 to <30 kg body weight at baseline, for up to 16 weeks during the randomization treatment period. Participants then entered the OLE period and received dupilumab 300 mg SC q2w with 600 mg loading dose for ≥60 kg body weight; dupilumab 200 mg SC q2w with 400 mg loading dose for ≥30 to <60 kg body weight; dupilumab 300 mg SC q4w for ≥15 to <30 kg body weight; and dupilumab 200 mg SC q4w for ≥5 to <15 kg body weight, for 3 years or until approval of the indication in Japan.

Subject analysis set title	Dupilumab /Dupilumab (Dupilumab Exposure Period)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received dupilumab 300 mg SC q2w with 600 mg loading dose for ≥60 kg body weight at baseline; dupilumab 200 mg SC q2w with 400 mg loading dose for ≥30 to <60 kg body weight at baseline; dupilumab 300 mg SC q4w for ≥15 to <30 kg body weight at baseline; and dupilumab 200 mg SC q4w for ≥5 to <15 kg body weight at baseline, for up to 16 weeks during the randomization treatment period. Participants then entered the OLE period and received dupilumab 300 mg SC q2w with 300 mg loading dose for ≥60 kg body weight; dupilumab 200 mg SC q2w with 200 mg loading dose for ≥30 to <60 kg body weight; dupilumab 300 mg SC q4w for ≥15 to <30 kg body weight; and dupilumab 200 mg SC q4w for ≥5 to <15 kg body weight, for 3 years or until approval of the indication in Japan.

Primary: Percentage of Participants With Eczema Area and Severity Index (EASI)-75 (≥75% Improvement From Baseline EASI) at Week 16

End point title	Percentage of Participants With Eczema Area and Severity Index (EASI)-75 (≥75% Improvement From Baseline EASI) at Week 16

End point description:

EASI score was a validated measure used to assess severity and extent of atopic dermatitis (AD). The 4

AD disease characteristics (erythema, thickness [induration, papulation, edema], scratching [excoriation], lichenification) were assessed for severity on scale of 0 (absent) to 3 (severe). Area of AD involvement was assessed as percentage by body area of head, trunk, upper limbs, lower limbs, and converted to score of 0 to 6. In each body region, area was expressed as 0, 1 (1% to 9%), 2 (10% to 29%), 3 (30% to 49%), 4 (50% to 69%), 5 (70% to 89%), or 6 (90% to 100%). For each body region, EASI score = (sum of the 4 AD disease characteristics scores) multiplied by (area of AD involvement score). Total EASI score ranged from 0 to 72, higher scores indicated increased extent and severity of AD. The Intent-to-treat (ITT) population included all randomized participants analyzed according to treatment group allocated by randomization regardless if the treatment kit was used or not.

End point type	Primary

End point timeframe:

Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	30		
Units: percentage of participants				
number (not applicable)	18.8	43.3		

Statistical analyses

Statistical analysis title	Dupilumab versus Placebo
Comparison groups	Placebo (Randomization Treatment Period) v Dupilumab (Randomization Treatment Period)
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0304 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response rate difference
Point estimate	25.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.26
upper limit	46.9

Notes:

[1] - A hierarchical testing procedure was used to control the overall type-I error. Testing was then performed sequentially in order the outcome measure is reported and continued when previous outcome measure was statistically significant at two-sided 0.05.

[2] - Cochran-Mantel-Haenszel(CMH) test was performed on association between responder status and intervention group, adjusted by randomization strata(≥6 months-<6 years,≥6 years-<12 years and IGA=3, ≥6 years-<12 years and IGA=4, and ≥12years at baseline).

Secondary: Percent Change in EASI Score From Baseline to Week 16

End point title	Percent Change in EASI Score From Baseline to Week 16

End point description:

EASI score was validated measure used to assess severity and extent of AD.The 4 AD disease characteristics (erythema,thickness[induration,papulation,edema],scratching[excoriation],lichenification)

were assessed for severity on scale of 0(absent) to 3(severe). Area of AD involvement was assessed as percentage by body area of head,trunk,upper limbs,lower limbs, and converted to score of 0-6. In each body region, area was expressed as 0,1(1%-9%),2(10%-29%),3(30%-49%),4(50%-69%),5(70%-89%), or 6(90%-100%). For each body region, EASI score=(sum of the 4 AD disease characteristics scores) multiplied by (area of AD involvement score). Total EASI score ranged 0-72, higher scores=increased extent and severity of AD. Baseline value=last available value before study drug administration. ITT population=all randomized participants analyzed according to treatment group allocated by randomization regardless if treatment kit was used or not. Only those participants with data available were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	29		
Units: percent change				
least squares mean (standard error)	-23.27 (± 7.81)	-62.65 (± 7.87)		

Statistical analyses

Statistical analysis title	Dupilumab Versus Placebo
Comparison groups	Placebo (Randomization Treatment Period) v Dupilumab (Randomization Treatment Period)
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.0003 [4]
Method	ANCOVA
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	-39.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-60.57
upper limit	-18.19

Notes:

[3] - A hierarchical testing procedure was used to control the overall type-I error. Testing was then performed sequentially in order the outcome measure is reported and continued when previous outcome measure was statistically significant at two-sided 0.05.

[4] - Covariance model with treatment group (placebo vs pooled dupilumab), randomization strata defined as (≥6 months to <6 years, ≥6 years to <12 years and IGA=3, ≥6 years to <12 years and IGA=4, and ≥12 years), and baseline EASI score as covariates.

Secondary: Percent Change From Baseline to Week 16 in Weekly Average of Daily Worst Itch Numerical Rating Scale (NRS) for Participants Aged ≥6 Years to <12 Years old

End point title	Percent Change From Baseline to Week 16 in Weekly Average

	of Daily Worst Itch Numerical Rating Scale (NRS) for Participants Aged ≥6 Years to <12 Years old

End point description:

The worst itch scale was a simple assessment tool used to report the intensity of their pruritus (itch). This was a 11-point scale (0 to 10) in which 0 indicated no itching while 10 indicated worst itching possible, and higher scores indicated greater severity. Participants were asked the following 2 questions: "What was the worst itch you had today?" and "What was the worst itch you had last night?". The daily worst itch score was calculated as the worse of the scores for the 2 questions. Baseline worst itch average score for maximum itch intensity was determined based on the average of daily worst itch scores for maximum itch intensity during the 7 days immediately preceding randomization. The baseline value was defined as the last available value before study drug administration. Only participants from ITT population aged ≥6 years to <12 years old with data available were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	14		
Units: percent change				
least squares mean (standard error)	-6.16 (± 9.65)	-39.45 (± 10.14)		

Statistical analyses

Statistical analysis title	Dupilumab Versus Placebo
Comparison groups	Placebo (Randomization Treatment Period) v Dupilumab (Randomization Treatment Period)
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.0117 [6]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-33.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-59.15
upper limit	-7.42

Notes:

[5] - A hierarchical testing procedure was used to control the overall type-I error. Testing was then performed sequentially in order the outcome measure is reported and continued when previous outcome measure was statistically significant at two-sided 0.05.
[6] - Covariance model with treatment group (placebo vs pooled dupilumab), randomization strata defined as (IGA=3 vs 4), and baseline NRS score as covariates.

Secondary: Percentage of Participants With Investigator's Global Assessment (IGA) 0 or 1 at Week 16

End point title	Percentage of Participants With Investigator's Global Assessment (IGA) 0 or 1 at Week 16

End point description:

The IGA was a static 5-point assessment instrument used in clinical studies to rate the severity of AD globally. The ratings (0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, 4 = severe) were an overall assessment of the skin lesions based on erythema and papulation/infiltration. Higher score indicated more severe disease. The ITT population included all randomized participants analyzed according to the treatment group allocated by randomization regardless if the treatment kit was used or not.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	30		
Units: percentage of participants				
number (not applicable)	9.4	10.0		

Statistical analyses

Statistical analysis title	Dupilumab Versus Placebo
Comparison groups	Placebo (Randomization Treatment Period) v Dupilumab (Randomization Treatment Period)
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.8476 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response rate difference
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.73
upper limit	16.66

Notes:

[7] - A hierarchical testing procedure was used to control the overall type-I error. Testing was then performed sequentially in order the outcome measure is reported and continued when previous outcome measure was statistically significant at two-sided 0.05.

[8] - CMH test was performed on association between responder status and intervention group, adjusted by randomization strata (≥6 months to <6 years, ≥6 years to <12 years old and IGA=3, ≥6 years to <12 years old and IGA=4, and ≥12 years at baseline).

Secondary: Percent Change From Baseline to Week 16 in Weekly Average of Daily Worst Pruritus Using the Peak Pruritus NRS for Participants Aged ≥12 Years to <18 Years old

End point title	Percent Change From Baseline to Week 16 in Weekly Average of Daily Worst Pruritus Using the Peak Pruritus NRS for Participants Aged ≥12 Years to <18 Years old

End point description:

The peak pruritus NRS was a simple assessment tool used report the intensity of their pruritus (itch) during a 24-hour recall period. Participants were asked the following question: For maximum itch intensity: "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?". Participants answered the question on the scale of 0 (no itch) to 10 (worst itch imaginable), where higher scores indicated greater severity. Baseline pruritus NRS average score for maximum itch intensity was determined based on the average of daily NRS scores for maximum itch intensity during the 7 days immediately preceding randomization. The baseline value was defined as the last available value before study drug administration. Only participants from ITT population aged ≥12 years to <18 years old were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	9		
Units: percent change				
least squares mean (standard error)	-22.20 (± 6.73)	-20.91 (± 6.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Week 16 in Weekly Average of Daily Worst Scratch/Itch NRS for Participants Aged ≥6 Months to <6 Years old

End point title	Percent Change From Baseline to Week 16 in Weekly Average of Daily Worst Scratch/Itch NRS for Participants Aged ≥6 Months to <6 Years old

End point description:

The worst scratch/itch scale was an assessment tool that parents/caregivers of children aged ≥6 months to <6 years old used to report intensity of their child pruritus(scratch/itch) on 11-point scale (0-10) in which 0=no scratching/itching while 10=worst scratching/itching possible; higher scores indicated greater severity. Parents/caregivers were asked following instructions: "Answer the question below based on what you observe and what your child tells you (if applicable)", and following question: "How would you rate your child's scratching/itching at its worst in past 24 hours?". Baseline worst itch scratch/itch average score for maximum itch intensity was determined based on average of daily worst scratch/itch scores for maximum itch intensity during 7 days immediately preceding randomization. The baseline value was defined as the last available value before study drug administration. Only participants from ITT population aged ≥6 months to <6 years old were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	4		
Units: percent change				
least squares mean (standard error)	-10.88 (± 6.38)	-16.53 (± 7.93)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Week 16 in Weekly Average of Daily Worst Pruritus Using Peak Pruritus NRS (Participants Aged ≥12Years[Yr]-<18Yr), Worst Itch NRS (Participants Aged ≥6Yr-<12Yr), and Worst Scratch/Itch NRS (Participants Aged ≥6 Months-<6Yr)

End point title	Percent Change From Baseline to Week 16 in Weekly Average of Daily Worst Pruritus Using Peak Pruritus NRS (Participants Aged ≥12Years[Yr]-<18Yr), Worst Itch NRS (Participants Aged ≥6Yr-<12Yr), and Worst Scratch/Itch NRS (Participants Aged ≥6 Months-<6Yr)

End point description:

Participants were asked certain questions for each scale that was used to report the intensity of pruritus (scratch/itch): the peak pruritus NRS for participants aged ≥12 years to <18 years old, the worst itch scale for participants aged ≥6 years to <12 years old, and the worst scratch/itch scale for participants aged ≥6 months to <6 years old. Participants or their parents/caregivers answered the questions on the scale of 0 (no itch) to 10 (worst itch imaginable), where higher scores indicated greater severity. The results of worst pruritus NRS across 3 age categories were pooled as a single indicator. The baseline value was defined as the last available value before study drug administration. The ITT population included all randomized participants analyzed according to the treatment group allocated by randomization regardless if the treatment kit was used or not. Only those participants with data available were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	27		
Units: percent change				
least squares mean (standard error)	-10.38 (± 5.83)	-31.85 (± 6.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With EASI-50 (≥50% Improvement From Baseline) and EASI-90 (≥90% Improvement From Baseline) at Week 16

End point title	Percentage of Participants With EASI-50 (≥50% Improvement From Baseline) and EASI-90 (≥90% Improvement From Baseline) at Week 16

End point description:

EASI score was a validated measure used to assess severity and extent of AD. The 4 AD disease characteristics (erythema, thickness [induration, papulation, edema], scratching [excoriation], lichenification) were assessed for severity on scale of 0 (absent) to 3 (severe). Area of AD involvement was assessed as percentage by body area of head, trunk, upper limbs, lower limbs, and converted to score of 0 to 6. In each body region, area was expressed as 0, 1 (1% to 9%), 2 (10% to 29%), 3 (30% to 49%), 4 (50% to 69%), 5 (70% to 89%), or 6 (90% to 100%). For each body region, EASI score = (sum of the 4 AD disease characteristics scores) multiplied by (area of AD involvement score). Total EASI score ranged from 0 to 72, higher scores indicated increased extent and severity of AD. The ITT population included all randomized participants analyzed according to the treatment group allocated by randomization regardless if the treatment kit was used or not.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	30		
Units: percentage of participants				
number (not applicable)				
EASI-50	31.3	73.3		
EASI-90	12.5	6.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 16 in Percent Body Surface Area (BSA) Affected by Atopic Dermatitis

End point title	Change from Baseline to Week 16 in Percent Body Surface Area (BSA) Affected by Atopic Dermatitis

End point description:

Body surface area affected by AD was assessed for each section of the body using the rule of nines. The possible highest score for each region is: head and neck [9%], anterior trunk [18%], back [18%], upper limbs [18%], lower limbs [36%], and genitals [1%] and was reported as a percentage of all major body sections combined. The baseline value was defined as the last available value before study drug administration. The ITT population included all randomized participants analyzed according to the treatment group allocated by randomization regardless if the treatment kit was used or not. Only those participants with data available were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	29		
Units: percent BSA				
least squares mean (standard error)	-8.56 (± 3.85)	-27.28 (± 3.84)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 16 in Children's Dermatology Life Quality Index (CDLQI) (≥4 years)

End point title	Change from Baseline to Week 16 in Children's Dermatology Life Quality Index (CDLQI) (≥4 years)

End point description:

CDLQI was a validated questionnaire designed to measure impact of skin disease on Quality of Life (QOL) in children aged ≥4 years of age. To complete the questionnaire, participants provided responses to 10 questions that focused on domains such as symptoms feelings associated with disease, impact of disease on leisure, school or holidays, personal relationships, sleep, and side effects of treatment for the skin disease. 9 questions were scored as follows: Very much = 3, Quite a lot = 2, Only a little = 1, Not at all or unanswered = 0. Question 7 had an added possible response, which was scored as 3. CDLQI for a participant is sum of score of each question with maximum of 30 and minimum of 0. Higher score indicated greater impact on the QOL. The baseline value was defined as the last available value before study drug administration. Only participants from ITT population aged ≥4 years old with data available were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	25		
Units: score on a scale				
least squares mean (standard error)	0.44 (± 0.77)	-2.81 (± 0.76)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 16 in Infants' Dermatitis Quality of Life Index (IDQOL) (<4 years)

End point title	Change from Baseline to Week 16 in Infants' Dermatitis Quality of Life Index (IDQOL) (<4 years)

End point description:

IDQOL was a validated questionnaire developed to measure the impact of skin disease on QOL of infants and preschool children <4 years of age. IDQOL was completed by child's parent or caregiver. The questionnaire consisted of 10 questions related to itching and scratching; mood of the child; how long it took for the child to get to sleep; whether the eczema had interfered with the child's playing, swimming or participation in other family activities; problems during mealtimes; problems caused by treatment; level of comfort while dressing or undressing the child; and problems during bathing. Each question asked about the impact over the previous week and was scored on a scale of 0 (minimum impact) to 3 (maximum impact). The higher the score, the greater was the impact on QOL. The baseline value was defined as the last available value before study drug administration. Only participants from ITT population aged <4 years old were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: score on a scale				
least squares mean (standard error)	0.27 (± 3.46)	-9.27 (± 3.46)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 16 in Patient Oriented Eczema Measure (POEM)

End point title	Change from Baseline to Week 16 in Patient Oriented Eczema Measure (POEM)

End point description:

The POEM was a 7-item, validated PRO questionnaire used in clinical practice and clinical trials to assess disease symptoms in children and adults. The format was a response to 7 items (dryness, itching, flaking, cracking, sleep loss, bleeding, and weeping) based on frequency of these disease symptoms during the past week (0 = no days, 1 = 1 to 2 days, 2 = 3 to 4 days, 3 = 5 to 6 days, and 4 = all days) with a scoring system of 0 to 28; the total score reflected disease-related morbidity. Higher scores indicated more severe disease. The baseline value was defined as the last available value before study drug administration. The ITT population included all randomized participants analyzed according to the treatment group allocated by randomization regardless if the treatment kit was used or not. Only those participants with data available were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	29		
Units: score on a scale				
least squares mean (standard error)	-0.89 (± 1.29)	-8.45 (± 1.36)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 16 in Weekly Average of Daily Worst Pruritus Using the Peak Pruritus NRS for Participants Aged ≥12 Years to <18 Years old

End point title	Change from Baseline to Week 16 in Weekly Average of Daily Worst Pruritus Using the Peak Pruritus NRS for Participants Aged ≥12 Years to <18 Years old

End point description:

The peak pruritus NRS was a simple assessment tool used report the intensity of their pruritus (itch) during a 24-hour recall period. Participants were asked the following question: For maximum itch intensity: "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?". Participants answered the question on the scale of 0 (no itch) to 10 (worst itch imaginable), where higher scores indicated greater severity. Baseline pruritus NRS average score for maximum itch intensity was determined based on the average of daily NRS scores for maximum itch intensity during the 7 days immediately preceding randomization. The baseline value was defined as the last available value before study drug administration. Only participants from ITT population aged ≥12 years to <18 years old were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	9		
Units: score on a scale				
least squares mean (standard error)	-1.38 (± 0.46)	-1.32 (± 0.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 16 in Weekly Average of Daily Worst Itch NRS for Participants Aged ≥6 Years to <12 Years old

End point title	Change from Baseline to Week 16 in Weekly Average of Daily Worst Itch NRS for Participants Aged ≥6 Years to <12 Years old

End point description:

The worst itch scale was a simple assessment tool used to report the intensity of their pruritus (itch). This was a 11-point scale (0 to 10) in which 0 indicated no itching while 10 indicated worst itching possible, and higher scores indicated greater severity. Participants were asked the following 2 questions: "What was the worst itch you had today?" and "What was the worst itch you had last night?". The daily worst itch score was calculated as the worse of the scores for the 2 questions. Baseline worst itch average score for maximum itch intensity was determined based on the average of daily worst itch scores for maximum itch intensity during the 7 days immediately preceding randomization. The baseline value was defined as the last available value before study drug administration. Only participants from ITT population aged ≥6 years to <12 years old with data available were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	14		
Units: score on a scale				
least squares mean (standard error)	-0.77 (± 0.68)	-2.95 (± 0.72)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 16 in Weekly Average of Daily Worst Scratch/Itch NRS for Participants Aged ≥6 Months to <6 Years old

End point title	Change from Baseline to Week 16 in Weekly Average of Daily Worst Scratch/Itch NRS for Participants Aged ≥6 Months to <6 Years old

End point description:

The worst scratch/itch scale was an assessment tool that parents/caregivers of children aged ≥6 months to <6 years old used to report intensity of their child pruritus(scratch/itch) on 11-point scale (0-10) in which 0=no scratching/itching while 10=worst scratching/itching possible; higher scores indicated greater severity. Parents/caregivers were asked following instructions: "Answer the question below based on what you observe and what your child tells you (if applicable)", and following question: "How would you rate your child's scratching/itching at its worst in past 24 hours?". Baseline worst itch scratch/itch average score for maximum itch intensity was determined based on average of daily worst scratch/itch scores for maximum itch intensity during 7 days immediately preceding randomization. The baseline value was defined as the last available value before study drug administration. Only participants from ITT population aged ≥6 months to <6 years old were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	4		
Units: score on a scale				
least squares mean (standard error)	-0.80 (± 0.49)	-1.24 (± 0.61)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Skin-Infection TEAEs (Excluding Herpetic Infections) From Baseline to 16 Weeks of Treatment

End point title	Number of Participants With Skin-Infection TEAEs (Excluding Herpetic Infections) From Baseline to 16 Weeks of Treatment

End point description:

AE: Any untoward medical occurrence in a participant or clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. TEAEs: AEs that developed, worsened or became serious during the treatment-emergent period. The baseline value was defined as the last available value before study drug administration. Safety population included all participants randomly assigned to study intervention and who received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	30		
Units: partcipants	2	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-emergent Adverse Events (TEAEs), Treatment-emergent Serious Adverse Events (TESAEs), Serious Adverse Events (SAEs), and Adverse Event of Special Interest (AESI) From Baseline to 16 Weeks of Treatment

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs), Treatment-emergent Serious Adverse Events (TESAEs), Serious Adverse Events (SAEs), and Adverse Event of Special Interest (AESI) From Baseline to 16 Weeks of Treatment

End point description:

Adverse event(AE): Any untoward medical occurrence in participant or clinical study participant, temporally associated with use of study intervention, whether or not considered related to study intervention. SAE: Any untoward medical occurrence that at any dose: resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent disability/incapacity, was congenital anomaly/birth defect, was medically important event. TEAEs: AEs that developed, worsened or became serious during treatment-emergent period. AESI: an AE(serious or nonserious) of scientific and medical concern specific to Sponsor's product or program, for which ongoing monitoring and immediate notification by Investigator to Sponsor was required. Baseline value=as last available value before study drug administration. Safety population=all participants randomly assigned to study intervention and who received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 16

End point values	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	30		
Units: participants				
Any TEAE	19	19		
Any TESAE	1	1		
Any SAE	1	1		
Any AESI	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-emergent Anti-drug Antibody (ADA) to Dupilumab Over Time in Pediatric Participants with AD (Aged ≥6 Months to <18 Years old)

End point title	Number of Participants With Treatment-emergent Anti-drug Antibody (ADA) to Dupilumab Over Time in Pediatric Participants with AD (Aged ≥6 Months to <18 Years old)

End point description:

Treatment-emergent ADA were defined as a positive response in the ADA assay post first dose, when baseline results are negative or missing. ADA population included all participants in the safety population who had at least 1 non-missing result in the ADA assay after first dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 116

End point values	Placebo (Randomization Treatment Period)	Placebo/Dupilumab (Open-label Extension Period)	Dupilumab (Randomization Treatment Period)	Dupilumab/Dupilumab (Open-label Extension Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	32	30	28
Units: participants	2	1	2	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With TEAEs, SAEs, and AESI From Baseline of OLE Through the Last Study Visit

End point title	Number of Participants With TEAEs, SAEs, and AESI From Baseline of OLE Through the Last Study Visit

End point description:

AE: Any untoward medical occurrence in a participant or clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. SAE: Any untoward medical occurrence that at any dose: resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent disability/incapacity, was a congenital anomaly/birth defect, was a medically important event. TEAEs: AEs that developed, worsened or became serious during the treatment-emergent period. AESI: an AE (serious or nonserious) of scientific and medical concern specific to the Sponsor's product or program, for which ongoing monitoring and immediate notification by the Investigator to the Sponsor was required. Safety population included all participants randomly assigned to study intervention and who received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Week 16 to Week 116

End point values	Placebo/Dupilumab (Open-label Extension Period)	Dupilumab/Dupilumab (Open-label Extension Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	28		
Units: participants				
Any TEAE	30	25		
Any SAE	1	2		
Any AESI	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Dupilumab up to Week 116

End point title	Serum Concentration of Dupilumab up to Week 116

End point description:

Serum samples were collected at specified timepoints. The PK population included all participants in the safety population with at least 1 non-missing result for functional dupilumab concentration in serum after first dose of the study treatment. Participants were analyzed according to the intervention actually received. Only those participants with data available were analyzed. Here, n=number of participants analyzed at the specified timepoint. 9999=parameter was not estimable as no participants were analyzed.

End point type	Secondary

End point timeframe:

Pre-dose at Baseline (Day 1), and Weeks 4, 12, 16, 24, 32, 52, 68, 92, and 116

End point values	Placebo/Dupilumab (Dupilumab Exposure Period)	Dupilumab /Dupilumab (Dupilumab Exposure Period)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Baseline (n=0, 30)	9999 (± 9999)	0.000 (± 0.000)		
Week 4 (n=0, 29)	9999 (± 9999)	52439.45 (± 24687.36)		
Week 12 (n=0, 25)	9999 (± 9999)	70160.00 (± 28052.67)		
Week 16 (n=0, 27)	9999 (± 9999)	75525.93 (± 31785.13)		
Week 24 (n=30, 23)	47883.33 (± 15953.99)	86665.22 (± 45997.76)		
Week 32 (n=29, 20)	58496.55 (± 25001.72)	84075.00 (± 49956.25)		
Week 52 (n=23, 22)	61856.52 (± 20717.49)	78286.36 (± 42318.32)		
Week 68 (n=27, 24)	62133.33 (± 18267.44)	77916.67 (± 41003.26)		
Week 92 (n=26, 25)	57373.08 (± 19790.96)	70153.56 (± 31250.06)		
Week 116 (n=17, 17)	51405.88 (± 16209.85)	64294.12 (± 24337.07)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to Week 16 (randomization treatment period) and Week 16 to end of study (EOS) (OLE period), up to approximately 140 weeks

Adverse event reporting additional description:

Analysis was performed on safety population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Placebo (Randomization Treatment Period)

Reporting group description:

Participants received placebo matched to dupilumab SC q2w with placebo loading dose for ≥30 kg body weight at baseline; placebo matched to dupilumab SC q4w for ≥5 to <30 kg body weight at baseline, for up to 16 weeks during the randomization treatment period.

Reporting group title	Dupilumab (Randomization Treatment Period)

Reporting group description:

Participants received dupilumab 300 mg SC q2w with 600 mg loading dose for ≥60 kg body weight at baseline; dupilumab 200 mg SC q2w with 400 mg loading dose for ≥30 to <60 kg body weight at baseline; dupilumab 300 mg SC q4w for ≥15 to <30 kg body weight at baseline; and dupilumab 200 mg SC q4w for ≥5 to <15 kg body weight at baseline, for up to 16 weeks during the randomization treatment period.

Reporting group title	Placebo/Dupilumab (Open-label Extension Period)

Reporting group description:

Participants who received placebo during the randomization treatment period and who entered the OLE period, received dupilumab 300 mg SC q2w with 600 mg loading dose for ≥60 kg body weight; dupilumab 200 mg SC q2w with 400 mg loading dose for ≥30 to <60 kg body weight; dupilumab 300 mg SC q4w for ≥15 to <30 kg body weight; and dupilumab 200 mg SC q4w for ≥5 to <15 kg body weight, for 3 years or until approval of the indication in Japan.

Reporting group title	Dupilumab/Dupilumab (Open-label Extension Period)

Reporting group description:

Participants who received dupilumab during the randomization treatment period and who entered the OLE period, received dupilumab 300 mg SC q2w with 300 mg loading dose for ≥60 kg body weight; dupilumab 200 mg SC q2w with 200 mg loading dose for ≥30 to <60 kg body weight; dupilumab 300 mg SC q4w for ≥15 to <30 kg body weight; and dupilumab 200 mg SC q4w for ≥5 to <15 kg body weight, for 3 years or until approval of the indication in Japan.

Serious adverse events	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)	Placebo/Dupilumab (Open-label Extension Period)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 32 (3.13%)	1 / 30 (3.33%)	1 / 32 (3.13%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Skin Laceration			

subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile Convulsion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Terminal Ileitis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 30 (3.33%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Attention Deficit Hyperactivity Disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Covid-19			
subjects affected / exposed	1 / 32 (3.13%)	0 / 30 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Dupilumab/Dupilumab (Open-label Extension Period)		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 28 (7.14%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			

Skin Laceration			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Febrile Convulsion			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Terminal Ileitis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Attention Deficit Hyperactivity Disorder			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Covid-19			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo (Randomization Treatment Period)	Dupilumab (Randomization Treatment Period)	Placebo/Dupilumab (Open-label Extension Period)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 32 (37.50%)	14 / 30 (46.67%)	28 / 32 (87.50%)

Injury, poisoning and procedural complications			
Wound			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Ligament Sprain			
subjects affected / exposed	1 / 32 (3.13%)	0 / 30 (0.00%)	3 / 32 (9.38%)
occurrences (all)	1	0	3
Hand Fracture			
subjects affected / exposed	0 / 32 (0.00%)	1 / 30 (3.33%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
Foot Fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Arthropod Bite			
subjects affected / exposed	2 / 32 (6.25%)	0 / 30 (0.00%)	2 / 32 (6.25%)
occurrences (all)	2	0	2
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 32 (3.13%)	1 / 30 (3.33%)	1 / 32 (3.13%)
occurrences (all)	1	1	1
Syncope			
subjects affected / exposed	0 / 32 (0.00%)	2 / 30 (6.67%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 32 (0.00%)	3 / 30 (10.00%)	6 / 32 (18.75%)
occurrences (all)	0	3	7
Injection Site Reaction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Eye disorders			

Conjunctivitis Allergic			
subjects affected / exposed	0 / 32 (0.00%)	4 / 30 (13.33%)	6 / 32 (18.75%)
occurrences (all)	0	4	9
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 32 (0.00%)	2 / 30 (6.67%)	0 / 32 (0.00%)
occurrences (all)	0	5	0
Enteritis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Dental Caries			
subjects affected / exposed	2 / 32 (6.25%)	1 / 30 (3.33%)	4 / 32 (12.50%)
occurrences (all)	2	1	8
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis Contact			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	4 / 32 (12.50%)
occurrences (all)	0	0	4
Dermatitis Atopic			
subjects affected / exposed	2 / 32 (6.25%)	0 / 30 (0.00%)	1 / 32 (3.13%)
occurrences (all)	2	0	1
Acne			
subjects affected / exposed	0 / 32 (0.00%)	1 / 30 (3.33%)	4 / 32 (12.50%)
occurrences (all)	0	1	7
Urticaria			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Psychiatric disorders			
Autism Spectrum Disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Myalgia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	3
Back Pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	2
Infections and infestations			
Impetigo			
subjects affected / exposed	1 / 32 (3.13%)	0 / 30 (0.00%)	2 / 32 (6.25%)
occurrences (all)	1	0	3
Hordeolum			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Gastroenteritis			
subjects affected / exposed	1 / 32 (3.13%)	1 / 30 (3.33%)	5 / 32 (15.63%)
occurrences (all)	4	1	5
Covid-19			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	14 / 32 (43.75%)
occurrences (all)	0	0	15
Bronchitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 30 (3.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Oral Herpes			
subjects affected / exposed	0 / 32 (0.00%)	2 / 30 (6.67%)	1 / 32 (3.13%)
occurrences (all)	0	2	1
Nasopharyngitis			
subjects affected / exposed	7 / 32 (21.88%)	3 / 30 (10.00%)	19 / 32 (59.38%)
occurrences (all)	7	3	49
Influenza			

subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	3

Non-serious adverse events	Dupilumab/Dupilumab (Open-label Extension Period)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 28 (82.14%)		
Injury, poisoning and procedural complications			
Wound			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Ligament Sprain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Hand Fracture			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Foot Fracture			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		
Arthropod Bite			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Syncope			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
General disorders and administration site conditions			

Pyrexia subjects affected / exposed occurrences (all) Injection Site Reaction subjects affected / exposed occurrences (all)	11 / 28 (39.29%) 15 2 / 28 (7.14%) 2		
Eye disorders Conjunctivitis Allergic subjects affected / exposed occurrences (all)	4 / 28 (14.29%) 5		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Enteritis subjects affected / exposed occurrences (all) Dental Caries subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2 2 / 28 (7.14%) 3 3 / 28 (10.71%) 3		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 3		
Skin and subcutaneous tissue disorders Dermatitis Contact subjects affected / exposed occurrences (all) Dermatitis Atopic subjects affected / exposed occurrences (all) Acne subjects affected / exposed occurrences (all) Urticaria	0 / 28 (0.00%) 0 0 / 28 (0.00%) 0 2 / 28 (7.14%) 3		

subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	4		
Psychiatric disorders			
Autism Spectrum Disorder			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Back Pain			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Arthralgia			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Infections and infestations			
Impetigo			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Hordeolum			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Gastroenteritis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Covid-19			
subjects affected / exposed	15 / 28 (53.57%)		
occurrences (all)	17		
Bronchitis			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Sinusitis			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	5		
Oral Herpes			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	3		
Nasopharyngitis			
subjects affected / exposed	11 / 28 (39.29%)		
occurrences (all)	18		
Influenza			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		

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