Clinical trial results:
A Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group Study to Evaluate the Efficacy and Safety of Dupilumab in Adult and Adolescent Patients with Moderate-to-Severe Atopic Hand and Foot Dermatitis

Summary

EudraCT number	2019-003088-22
Trial protocol	DE PL
Global end of trial date	23 November 2022

Results information

Result version number	v1 (current)
This version publication date	07 June 2023
First version publication date	07 June 2023

Trial information

Trial identification

Sponsor protocol code	R668-AD-1924

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04417894
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Road, Tarrytown, United States, 10591
Public contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.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	23 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of dupilumab on skin lesions in participants with atopic hand and foot dermatitis

Protection of trial subjects:

It is the responsibility of both the sponsor and the investigator(s) to ensure that this clinical study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the ICH guidelines for GCP and applicable regulatory requirements.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	14 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: 28
Country: Number of subjects enrolled	Japan: 13
Country: Number of subjects enrolled	Poland: 44
Country: Number of subjects enrolled	Germany: 48
Worldwide total number of subjects	133
EEA total number of subjects	92

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)	27
Adults (18-64 years)	102
From 65 to 84 years	4

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 170 participants were screened, 37 participants failed screening, and 133 participants were randomized. Of the 37 screen failures: 2 withdrew consent, 33 did not meet inclusion/exclusion criteria, 1 was lost to follow-up and 1 was for an unknown reason.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Matching Placebo

Arm description:

Administered subcutaneously (SC) once every 2 weeks (Q2W), following a loading dose on Day 1

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered SC Q2W, following a loading dose on Day 1

Arm title	dupilumab

Arm description:

Administered SC Q2W, following a loading dose on Day 1

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

Dosage and administration details:

Administered SC Q2W, following a loading dose on Day 1

Number of subjects in period 1	Matching Placebo	dupilumab
Started	66	67
Completed	53	60
Not completed	13	7
Consent withdrawn by subject	7	6
Lost to follow-up	3	-
Lack of efficacy	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Matching Placebo
Reporting group description:	
Administered subcutaneously (SC) once every 2 weeks (Q2W), following a loading dose on Day 1	
Reporting group title	dupilumab
Reporting group description:	
Administered SC Q2W, following a loading dose on Day 1	

Reporting group values	Matching Placebo	dupilumab	Total
Number of subjects	66	67	133
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	13	14	27
Adults (18-64 years)	52	50	102
From 65-84 years	1	3	4
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	33.4	35.8	
standard deviation	± 14.66	± 17.07	-
Gender Categorical Units: Subjects			
Female	38	45	83
Male	28	22	50
Race (NIH/OMB Units: Subjects			
White	53	53	106
Black or African American	4	3	7
Asian	8	9	17
American Indian or Alaska Native	0	1	1
Other	1	1	2
Ethnicity (NIH/OMB) Units: Subjects			
Not Hispanic or Latino	63	64	127
Hispanic or Latino	2	3	5
Unknown	1	0	1

End points

End points reporting groups

Reporting group title	Matching Placebo
Reporting group description:	
Administered subcutaneously (SC) once every 2 weeks (Q2W), following a loading dose on Day 1	
Reporting group title	dupilumab
Reporting group description:	
Administered SC Q2W, following a loading dose on Day 1	
Subject analysis set title	Matching Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The ADA analysis set (AAS) includes all treated participants who received any amount of study drug (active or placebo [safety analysis set]) and had at least one non-missing ADA result following the first dose of study drug or placebo. The ADA analysis set is based on the actual treatment received (as treated) rather than as randomized.	
Subject analysis set title	Dupilumab 300 mg - Adult Participants
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Adult participants were administered 300 mg SC Q2W, following a loading dose on Day 1	
Subject analysis set title	Dupilumab 200 mg - Adolescent Participants
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Adolescent participants were administered 200 mg SC Q2W, following a loading dose on Day 1	
Subject analysis set title	Dupilumab 300 mg - Adolescent Participants
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Adolescent participants were administered 300 mg SC Q2W, following a loading dose on Day 1	

Primary: Percentage of Participants with Hand and Foot IGA 0 or 1 at Week 16

End point title	Percentage of Participants with Hand and Foot IGA 0 or 1 at Week 16
End point description:	
IGA is an assessment scale used to determine severity of hand and foot AD and clinical response to treatment on a 5-point scale (0 = clear; 1 = almost clear; 2 = mild; 3 = moderate; 4 = severe) based on erythema and papulation/infiltration. The full analysis set (FAS) includes all randomized participants. Efficacy analyses will be based on the treatment allocated at randomization (as randomized). Here 'n' = number of evaluable participants at a specified point in time.	
End point type	Primary
End point timeframe:	
Week 16	

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	67		
Units: Percentage of participants				
number (not applicable)	16.7	40.3		

Statistical analyses

Statistical analysis title	Matching placebo vs. dupilumab
Comparison groups	Matching Placebo v dupilumab
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Mantel-Haenszel

Secondary: Percent Change from Baseline to Week 16 in Weekly Average of Daily Hand and Foot Peak Pruritus NRS

End point title	Percent Change from Baseline to Week 16 in Weekly Average of Daily Hand and Foot Peak Pruritus NRS

End point description:

Pruritus NRS is an assessment tool that is used to report the intensity of a patient's pruritus (itch), both maximum and average intensity, during a 24-hour recall period; maximum itch intensity on a scale of 0 - 10 (0 = no itch; 10 = worst itch imaginable). The full analysis set (FAS) includes all randomized participants. Efficacy analyses will be based on the treatment allocated at randomization (as randomized). Here 'n' = number of evaluable participants at a specified point in time.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	67		
Units: Percentage of change				
arithmetic mean (standard deviation)	-19.3 (± 32.91)	-56.5 (± 35.28)		

Statistical analyses

Statistical analysis title	Matching Placebo vs. dupilumab
Comparison groups	Matching Placebo v dupilumab

Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-36.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-48.8
upper limit	-24.61

Secondary: Percentage of Participants With Improvement (Reduction) of Weekly Average of Daily Hand and Foot Peak Pruritus NRS of ≥4 Points from Baseline to Week 16

End point title	Percentage of Participants With Improvement (Reduction) of Weekly Average of Daily Hand and Foot Peak Pruritus NRS of ≥4 Points from Baseline to Week 16

End point description:

Pruritus NRS is an assessment tool that is used to report the intensity of a patient's pruritus (itch), both maximum and average intensity, during a 24-hour recall period; maximum itch intensity on a scale of 0 - 10 (0 = no itch; 10 = worst itch imaginable). The full analysis set (FAS) includes all randomized participants. Efficacy analyses will be based on the treatment allocated at randomization (as randomized). Here 'n' = number of evaluable participants at a specified point in time.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	67		
Units: Percentage of participants				
number (not applicable)	13.6	52.2		

Statistical analyses

Statistical analysis title	Matching placebo vs. dupilumab
Comparison groups	Matching Placebo v dupilumab

Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	38.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	24.06
upper limit	53.15

Secondary: Percentage of Participants with Improvement (Reduction) of Weekly Average of Daily Hand and Foot Peak Pruritus NRS ≥3 from Baseline to Week 16

End point title	Percentage of Participants with Improvement (Reduction) of Weekly Average of Daily Hand and Foot Peak Pruritus NRS ≥3 from Baseline to Week 16

End point description:

Pruritus NRS is an assessment tool that is used to report the intensity of a patient's pruritus (itch), both maximum and average intensity, during a 24-hour recall period; maximum itch intensity on a scale of 0 - 10 (0 = no itch; 10 = worst itch imaginable). The full analysis set (FAS) includes all randomized participants. Efficacy analyses will be based on the treatment allocated at randomization (as randomized). Here 'n' = number of evaluable participants at a specified point in time.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	67		
Units: Percentage of participants				
number (not applicable)	16.7	61.2		

Statistical analyses

Statistical analysis title	Matching Placebo vs. dupilumab
Comparison groups	Matching Placebo v dupilumab
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Secondary: Mean Change from Baseline to Week 16 in Percent Surface Area of Hand and Foot Involvement with AD

End point title	Mean Change from Baseline to Week 16 in Percent Surface Area of Hand and Foot Involvement with AD

End point description:

The full analysis set (FAS) includes all randomized participants. Efficacy analyses will be based on the treatment allocated at randomization (as randomized). Here 'n' = number of evaluable participants at a specified point in time.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	67		
Units: Percent surface area				
least squares mean (standard error)	-10.01 (± 2.388)	-16.70 (± 2.375)		

Statistical analyses

Statistical analysis title	Matching Placebo vs dupilumab
Comparison groups	Matching Placebo v dupilumab
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0067
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-6.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.526
upper limit	-1.852

Secondary: Mean Change from Baseline to Week 16 in Weekly Average of Daily Sleep NRS

End point title	Mean Change from Baseline to Week 16 in Weekly Average of Daily Sleep NRS

End point description:

Sleep NRS is an 11-point scale (0 to 10) in which 0 indicates worst possible sleep while 10 indicates best possible sleep. The full analysis set (FAS) includes all randomized participants. Efficacy analyses will be based on the treatment allocated at randomization (as randomized). Here 'n' = number of evaluable participants at a specified point in time.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	67		
Units: Score on a scale				
least squares mean (standard error)	-0.00 (± 0.335)	0.88 (± 0.334)		

Statistical analyses

Statistical analysis title	Matching Placebo vs dupilumab
Comparison groups	Matching Placebo v dupilumab
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0115
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.199
upper limit	1.576

Secondary: Percent Change from Baseline to Week 16 in Weekly Average of Daily Hand and Foot Peak Pain NRS

End point title	Percent Change from Baseline to Week 16 in Weekly Average of Daily Hand and Foot Peak Pain NRS

End point description:

Pain NRS Scale is an assessment tool used to report the intensity of a participant's pain. Participants will select the number between 0 and 10 that fits best to their worst pain intensity over the past 24 hours (0 = no pain and 10 = the worst pain possible). The full analysis set (FAS) includes all randomized participants. Efficacy analyses will be based on the treatment allocated at randomization (as randomized). Here 'n' = number of evaluable participants at a specified point in time.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	67		
Units: Percentage of change				
least squares mean (standard error)	-1.93 (± 0.432)	-4.66 (± 0.426)		

Statistical analyses

Statistical analysis title	Matching Placebo vs dupilumab
Comparison groups	Matching Placebo v dupilumab
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.614
upper limit	-1.844

Secondary: Percent Change in mTLSS for Hand/Foot Lesions from Baseline to Week 16

End point title	Percent Change in mTLSS for Hand/Foot Lesions from Baseline to Week 16

End point description:

mTLSS combines an evaluation of hand and foot eczema lesions severity; scores are summed, extending from a base estimation of 0 (no signs or symptoms) to the most extreme of 18 (more serious disease). The full analysis set (FAS) includes all randomized participants. Efficacy analyses will be based on the treatment allocated at randomization (as randomized).

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	67		
Units: Percentage of change				
arithmetic mean (standard deviation)	-24.9 (± 40.01)	-63.8 (± 25.68)		

Statistical analyses

Statistical analysis title	Matching Placebo vs Dupilumab
Comparison groups	Matching Placebo v dupilumab
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA

Secondary: Proportion of Participants with Improvement (Reduction) of Weekly Average of Daily Hand and Foot Peak Pruritus NRS ≥4 from Baseline to Week 4

End point title	Proportion of Participants with Improvement (Reduction) of Weekly Average of Daily Hand and Foot Peak Pruritus NRS ≥4 from Baseline to Week 4

End point description:

Pruritus NRS is an assessment tool that is used to report the intensity of a participant's pruritus (itch), both maximum and average intensity, during a 24-hour recall period; maximum itch intensity on a scale of 0 - 10 (0 = no itch; 10 = worst itch imaginable). The full analysis set (FAS) includes all randomized participants. Efficacy analyses will be based on the treatment allocated at randomization (as randomized). Here 'n' = number of evaluable participants at a specified point in time.

End point type	Secondary

End point timeframe:

Baseline to Week 4

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	67		
Units: Percentage of participants				
number (not applicable)	9.1	34.3		

Statistical analyses

Statistical analysis title	Matching Placebo vs dupilumab
Comparison groups	Matching Placebo v dupilumab

Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.78
upper limit	11.98

Secondary: Percent change from baseline to week 4 in weekly average of daily hand and foot peak Pruritus NRS

End point title	Percent change from baseline to week 4 in weekly average of daily hand and foot peak Pruritus NRS

End point description:

Pruritus NRS is an assessment tool that is used to report the intensity of a participant's pruritus (itch), both maximum and average intensity, during a 24-hour recall period; maximum itch intensity on a scale of 0 - 10 (0 = no itch; 10 = worst itch imaginable). The full analysis set (FAS) includes all randomized participants. Efficacy analyses will be based on the treatment allocated at randomization (as randomized). Here 'n' = number of evaluable participants at a specified point in time.

End point type	Secondary

End point timeframe:

Baseline to Week 4

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	67		
Units: Percentage of change				
least squares mean (standard error)	-25.6 (± 5.42)	-47.2 (± 5.37)		

Statistical analyses

Statistical analysis title	Matching Placebo vs dupilumab
Comparison groups	Matching Placebo v dupilumab
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-21.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.43
upper limit	-10.64

Secondary: Percent Change from Baseline to Week 16 in Hand Eczema Severity Index (HECSI) Score in Participants with Hand Dermatitis

End point title	Percent Change from Baseline to Week 16 in Hand Eczema Severity Index (HECSI) Score in Participants with Hand Dermatitis

End point description:

For participants with hand dermatitis HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 hand areas by use of standard scales. The total HECSI score is based on a 4-point severity scale ranging from 0 (none/absent) to 3 (severe) and a 5-point scale rating the affected area(s) ranging from 0 (0% affected area) to 4 (76% to 100% affected area). Here 'n' = number of evaluable participants at a specified point in time.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	64		
Units: Percentage of change				
arithmetic mean (standard deviation)	-33.8 (± 42.21)	-68.2 (± 25.56)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HECSI-90 at Week 16

End point title	Percentage of Participants with HECSI-90 at Week 16

End point description:

HECSI-90 is defined as HECSI score has ≥90% improvement from baseline for participants with hand dermatitis. The full analysis set (FAS) includes all randomized participants. Efficacy analyses will be based on the treatment allocated at randomization (as randomized). Here 'n' = number of evaluable participants at a specified point in time.

End point type	Secondary

End point timeframe:

Week 16

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	64		
Units: Percentage of participants				
number (not applicable)	9.2	18.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants with HECSI-75 at Week 16

End point title	Proportion of Participants with HECSI-75 at Week 16

End point description:

HECSI-75 is defined as HECSI score has ≥75% improvement from baseline for participants with hand dermatitis. The full analysis set (FAS) includes all randomized participants. Efficacy analyses will be based on the treatment allocated at randomization (as randomized). Here 'n' = number of evaluable participants at a specified point in time.

End point type	Secondary

End point timeframe:

Week 16

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	64		
Units: Percentage of participants				
number (not applicable)	21.5	46.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HECSI-50 at Week 16

End point title	Percentage of Participants with HECSI-50 at Week 16

End point description:

HECSI-50 is defined as HECSI score has ≥50% improvement from baseline, for participants with hand dermatitis. The full analysis set (FAS) includes all randomized participants. Efficacy analyses will be based on the treatment allocated at randomization (as randomized). Here 'n' = number of evaluable participants at a specified point in time.

End point type	Secondary

End point timeframe:

Week 16

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	64		
Units: Percentage of participants				
number (not applicable)	30.8	75.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 16 in Quality of Life in Hand Eczema Questionnaire (QOLHEQ)

End point title	Change from Baseline to Week 16 in Quality of Life in Hand Eczema Questionnaire (QOLHEQ)

End point description:

For participants with hand dermatitis QOLHEQ is an instrument to assess disease specific Health Related Quality of Life (HRQOL) in participants suffering from hand eczema. It consists out of 30 items which can be summarized according to four domains of HRQOL: Impairments because of (1) symptoms, (2) emotions, (3) limitations in functioning or (4) because of treatment and prevention. The full analysis set (FAS) includes all randomized participants. Efficacy analyses will be based on the treatment allocated at randomization (as randomized). Here 'n' = number of evaluable participants at a specified point in time.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	64		
Units: Score on a scale				
arithmetic mean (standard error)	-13.36 (± 21.222)	-38.70 (± 23.920)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline to Week 16 in Work Productivity and Impairment (WPAI) and Classroom Impairment Questionnaire (CIQ)

End point title	Mean Change from Baseline to Week 16 in Work Productivity and Impairment (WPAI) and Classroom Impairment Questionnaire (CIQ)

End point description:

WPAI + CIQ is a self-administered instrument used to capture the impairment to work productivity/classroom impairment and activity due to atopic hand and foot dermatitis. The WPAI+CIQ yields 4 types of scores: absenteeism, presenteeism, work/classroom productivity loss and activity impairment. All scores range from 0 to 100% with 100% indicating total work/classroom productivity impairment and 0 no impairment at all. Here 'n' = number of evaluable participants at a specified point in time.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	67		
Units: Score on a scale				
least squares mean (standard error)	-21.26 (± 3.761)	-36.39 (± 3.649)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Treatment-Emergent Anti-Drug Antibody (ADA)

End point title	Percentage of Participants with Treatment-Emergent Anti-Drug Antibody (ADA)

End point description:

The ADA analysis set (AAS) includes all treated participants who received any amount of study drug (active or placebo [safety analysis set]) and had at least one non-missing ADA result following the first dose of study drug or placebo. The ADA analysis set is based on the actual treatment received (as treated) rather than as randomized. Here 'n' = number of evaluable participants at a specified point in time.

End point type	Secondary

End point timeframe:

Up to Week 28

End point values	Matching Placebo	Dupilumab 300 mg - Adult Participants	Dupilumab 200 mg - Adolescent Participants	Dupilumab 300 mg - Adolescent Participants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	55	49	6	6
Units: Percentage				
number (not applicable)				
Persistent TE Response (n = 55, 49, 6, 6)	0.0	4.1	0.0	0.0
Transient TE Response (n = 55, 49, 6, 6)	1.8	0.0	0.0	0.0

Indeterminate TE Response (n = 55, 49, 6, 6)	0.0	10.2	0.0	16.7

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Concentration of Functional Dupilumab in Serum at Various Time Points

End point title	Trough Concentration of Functional Dupilumab in Serum at Various Time Points
End point description:	
End point type	Secondary
End point timeframe: Up to Week 28	

End point values	Dupilumab 300 mg - Adult Participants	Dupilumab 200 mg - Adolescent Participants	Dupilumab 300 mg - Adolescent Participants	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	49	6	6	
Units: Milligrams per Liter (mg/L)				
arithmetic mean (standard deviation)				
Week 0; (n = 43, 6, 6)	0 (± 0)	0 (± 0)	0 (± 0)	
Week 16; (n = 48, 6, 4)	51.2 (± 22.0)	34.0 (± 10.7)	37.1 (± 15.9)	
Week 28; (n = 43, 2, 5)	7.37 (± 25.0)	60.0 (± 84.9)	7.54 (± 16.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Treatment-Emergent Adverse Events (TEAEs) Through Week 16

End point title	Percentage of Participants with Treatment-Emergent Adverse Events (TEAEs) Through Week 16
End point description:	
End point type	Secondary
End point timeframe: Through Week 16	

End point values	Matching Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	67		
Units: Percentage of participants				
number (not applicable)	74.2	65.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Treatment-Emergent ADA by Maximum Titer Category

End point title	Percentage of Participants with Treatment-Emergent ADA by Maximum Titer Category

End point description:

The ADA analysis set (AAS) includes all treated participants who received any amount of study drug (active or placebo [safety analysis set]) and had at least one non-missing ADA result following the first dose of study drug or placebo. The ADA analysis set is based on the actual treatment received (as treated) rather than as randomized. Here 'n' = number of evaluable participants at a specified point in time.

End point type	Secondary

End point timeframe:

Up to Week 28

End point values	Matching Placebo	Dupilumab 300 mg - Adult Participants	Dupilumab 200 mg - Adolescent Participants	Dupilumab 300 mg - Adolescent Participants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	55	49	6	6
Units: Percentage				
number (not applicable)				
Low (<1,000)	1.8	14.3	0.0	16.7
Moderate (1,000 to 10,000)	0.0	0.0	0.0	0.0
High (>10,000)	0.0	0.0	0.0	0.0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose to week 28	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups	
Reporting group title	Matching Placebo
Reporting group description:	
Administered subcutaneously (SC) once every 2 weeks (Q2W), following a loading dose on Day 1	
Reporting group title	Dupilumab
Reporting group description:	
Administered SC Q2W, following a loading dose on Day 1	

Serious adverse events	Matching Placebo	Dupilumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 66 (1.52%)	3 / 67 (4.48%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to lung			
subjects affected / exposed	0 / 66 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	0 / 66 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 66 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			

subjects affected / exposed	0 / 66 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 66 (0.00%)	1 / 67 (1.49%)	
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: 5 %

Non-serious adverse events	Matching Placebo	Dupilumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 66 (51.52%)	33 / 67 (49.25%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 66 (1.52%)	4 / 67 (5.97%)	
occurrences (all)	1	4	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	16 / 66 (24.24%)	6 / 67 (8.96%)	
occurrences (all)	18	6	
Infections and infestations			
COVID-19			
subjects affected / exposed	14 / 66 (21.21%)	11 / 67 (16.42%)	
occurrences (all)	14	11	
Nasopharyngitis			
subjects affected / exposed	8 / 66 (12.12%)	16 / 67 (23.88%)	
occurrences (all)	13	18	
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	3 / 66 (4.55%) 3	7 / 67 (10.45%) 9	

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