



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 (\pm 2.388) | -16.70 (\pm 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 (\pm 0.335) | 0.88 (\pm 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 (\pm 0.432) | -4.66 (\pm 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 $\geq 75\%$ 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 $\geq 50\%$ 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 (\pm 3.761) | -36.39 (\pm 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 | 3 / 66 (4.55%) | 7 / 67 (10.45%) | |
| occurrences (all) | 3 | 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