

**Clinical trial results:****A Phase 2A Study Investigating the Safety, Pharmacokinetics, Immunogenicity, and Exploratory Efficacy of Dupilumab in Patients Aged 6 to <18 Years With Atopic Dermatitis****Summary**

| | |
|--------------------------|-------------------------------|
| EudraCT number | 2014-003263-37 |
| Trial protocol | HU DE CZ PL GB Outside EU/EEA |
| Global end of trial date | 14 March 2016 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 |
| This version publication date | 30 March 2017 |
| First version publication date | 30 March 2017 |

Trial information**Trial identification**

| | |
|-----------------------|--------------|
| Sponsor protocol code | R668-AD-1412 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02407756 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Regeneron Pharmaceuticals, Inc. |
| Sponsor organisation address | 777 Old Saw Mill River Rd., Tarrytown, United States, 10591 |
| Public contact | Clinical Trial Management, Regeneron Pharmaceuticals, Inc., clinicaltrials@regeneron.com |
| Scientific contact | Clinical Trial Management, Regeneron Pharmaceuticals, Inc., clinicaltrials@regeneron.com |

Notes:

Paediatric regulatory details

| | |
|--|----------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-001501-PIP01-13 |
| 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 | 12 April 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 March 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To characterize the safety and pharmacokinetics (PK) of Dupilumab in pediatric subjects with moderate-to-severe atopic dermatitis (AD) (for adolescents ≥ 12 to < 18 years of age) or severe AD (for children ≥ 6 to < 12 years of age).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the International Conference on Harmonisation (ICH) guidelines for Good Clinical Practice (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 17 March 2015 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Poland: 25 |
| Country: Number of subjects enrolled | United Kingdom: 10 |
| Country: Number of subjects enrolled | Czech Republic: 3 |
| Country: Number of subjects enrolled | Germany: 18 |
| Country: Number of subjects enrolled | Hungary: 10 |
| Country: Number of subjects enrolled | Canada: 12 |
| Worldwide total number of subjects | 78 |
| EEA total number of subjects | 66 |

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) | 38 |

| | |
|---------------------------|----|
| Adolescents (12-17 years) | 40 |
| 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 25 sites in 6 countries. A total of 88 subjects were screened between 17 Mar 2015 & 25 Sep 2015 of whom 78 subjects were randomized and 77 were treated. Ten subjects were screen failures as 5 were due to exclusion criteria met & inclusion criteria not met, 4 subjects withdrew consent and 1 subject was lost to follow-up.

Pre-assignment

Screening details:

A total of 40 adolescents (aged ≥ 12 to < 18 years) and 38 children (aged ≥ 6 to < 12 years) were enrolled and randomized to 2 sequential ascending dose cohorts: Cohort 1 (2 mg/kg) and Cohort 2 (4 mg/kg). Dosing started with cohort 1. Proceeding to the next cohort occurred once all initial 8 patients enrolled had been observed for at least 2 weeks.

Period 1

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

Arms

| | |
|------------------------------|-------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Dupilumab 2mg/kg: Adolescents |

Arm description:

Dupilumab 2 mg/kg as a single dose on Day 1 followed by 8-week PK sampling period then 4 repeated doses weekly in subjects aged between ≥ 12 to < 18 years.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dupilumab |
| Investigational medicinal product code | REGN668, SAR231893 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subcutaneous injection in the different quadrants of the abdomen (avoiding navel and waist areas), upper thighs and upper arms.

| | |
|------------------|----------------------------|
| Arm title | Dupilumab 2mg/kg: Children |
|------------------|----------------------------|

Arm description:

Dupilumab 2 mg/kg as a single dose on Day 1 followed by 8-week PK sampling period then 4 repeated doses weekly in subjects aged between ≥ 6 to < 12 years.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dupilumab |
| Investigational medicinal product code | REGN668, SAR231893 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subcutaneous injection in the different quadrants of the abdomen (avoiding navel and waist areas), upper thighs and upper arms.

| | |
|------------------|-------------------------------|
| Arm title | Dupilumab 4mg/kg: Adolescents |
|------------------|-------------------------------|

Arm description:

Dupilumab 4 mg/kg as a single dose on Day 1 followed by 8-week PK sampling period then 4 repeated doses weekly in subjects aged between ≥ 12 to < 18 years.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|------------------------|
| Investigational medicinal product name | Dupilumab |
| Investigational medicinal product code | REGN668, SAR231893 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subcutaneous injection in the different quadrants of the abdomen (avoiding navel and waist areas), upper thighs and upper arms.

| | |
|------------------|----------------------------|
| Arm title | Dupilumab 4mg/kg: Children |
|------------------|----------------------------|

Arm description:

Dupilumab 4 mg/kg as a single dose on Day 1 followed by 8-week PK sampling period then 4 repeated doses weekly in subjects aged between ≥6 to <12 years.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dupilumab |
| Investigational medicinal product code | REGN668, SAR231893 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subcutaneous injection in the different quadrants of the abdomen (avoiding navel and waist areas), upper thighs and upper arms.

| Number of subjects in period 1^[1] | Dupilumab 2mg/kg: Adolescents | Dupilumab 2mg/kg: Children | Dupilumab 4mg/kg: Adolescents |
|---|-------------------------------|----------------------------|-------------------------------|
| Started | 20 | 18 | 20 |
| Treated | 20 | 18 | 20 |
| Completed | 20 | 18 | 20 |

| Number of subjects in period 1^[1] | Dupilumab 4mg/kg: Children |
|---|----------------------------|
| Started | 19 |
| Treated | 19 |
| Completed | 19 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: One subject in the 4 mg/kg (Cohort 2b) arm did not receive study drug and was withdrawn from the study on study day 1 during Part A period due to withdrawal of consent (fear of study drug injection) and was not included in the analysis. Analysis was performed on safety analysis set (SAF) that included all subjects who received any study drug.

Baseline characteristics

Reporting groups

| | |
|--|-------------------------------|
| Reporting group title | Dupilumab 2mg/kg: Adolescents |
| Reporting group description: Dupilumab 2 mg/kg as a single dose on Day 1 followed by 8-week PK sampling period then 4 repeated doses weekly in subjects aged between ≥ 12 to < 18 years. | |
| Reporting group title | Dupilumab 2mg/kg: Children |
| Reporting group description: Dupilumab 2 mg/kg as a single dose on Day 1 followed by 8-week PK sampling period then 4 repeated doses weekly in subjects aged between ≥ 6 to < 12 years. | |
| Reporting group title | Dupilumab 4mg/kg: Adolescents |
| Reporting group description: Dupilumab 4 mg/kg as a single dose on Day 1 followed by 8-week PK sampling period then 4 repeated doses weekly in subjects aged between ≥ 12 to < 18 years. | |
| Reporting group title | Dupilumab 4mg/kg: Children |
| Reporting group description: Dupilumab 4 mg/kg as a single dose on Day 1 followed by 8-week PK sampling period then 4 repeated doses weekly in subjects aged between ≥ 6 to < 12 years. | |

| Reporting group values | Dupilumab 2mg/kg: Adolescents | Dupilumab 2mg/kg: Children | Dupilumab 4mg/kg: Adolescents |
|------------------------------------|-------------------------------|----------------------------|-------------------------------|
| Number of subjects | 20 | 18 | 20 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|--------------------|-------------------|--------------------|
| Age continuous Units: years arithmetic mean standard deviation | 14.7 ± 2.01 | 8.2 ± 1.62 | 14.3 ± 1.66 |
| Gender categorical Units: Subjects | | | |
| Female | 11 | 9 | 11 |
| Male | 9 | 9 | 9 |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | 0 |
| Not Hispanic or Latino | 20 | 18 | 20 |
| Race Units: Subjects | | | |
| White | 17 | 17 | 15 |
| Black or African American | 0 | 0 | 1 |
| Asian | 2 | 0 | 3 |
| Other | 1 | 1 | 1 |
| Number of Subjects with Investigator Global Assessment (IGA) score of 3 or 4 | | | |
| IGA is an assessment scale used to determine severity of 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. Therapeutic response is an IGA score of 0 (clear) or 1 (almost clear). Analysis was performed on SAF. | | | |
| Units: Subjects | | | |
| IGA score of 3 | 8 | 1 | 11 |

| | | | |
|----------------|----|----|---|
| IGA score of 4 | 12 | 17 | 9 |
|----------------|----|----|---|

| | | | |
|---|--|--|--|
| Eczema Area and Severity Index (EASI) score | | | |
|---|--|--|--|

The EASI score was used to measure the severity and extent of atopic dermatitis (AD) and measures erythema, infiltration, excoriation and lichenification on 4 anatomic regions of the body: head, trunk, upper and lower extremities. The total EASI score ranges from 0 to 72 points, with the higher scores reflecting the worse severity of AD. Analysis was performed on Safety Analysis set (SAF).

| | | | |
|-------------------------|------|---------|--------|
| Units: Score on a scale | | | |
| arithmetic mean | 34.8 | 32.9 | 28.6 |
| standard deviation | ± 17 | ± 15.53 | ± 14.7 |

| | | | |
|---------------------------------------|--|--|--|
| Pruritus Numerical Rating Scale (NRS) | | | |
|---------------------------------------|--|--|--|

Pruritus NRS scale is an assessment tool that is used to report the intensity of subject's pruritus (itch), both maximum and average intensity, during a 24-hour recall period. Subjects were asked the following question: how would a subject rate his itch at the worst moment during the previous 24 hours (for maximum itch intensity on a scale of 0 – 10 [0 = no itch; 10 = worst itch imaginable]). Weekly average obtained in the 7-day period prior to the baseline visit. Analysis was performed on SAF.

| | | | |
|-------------------------|--------|--------|--------|
| Units: Score on a scale | | | |
| arithmetic mean | 6.1 | 6.4 | 6.9 |
| standard deviation | ± 2.47 | ± 2.23 | ± 2.21 |

| | | | |
|---|--|--|--|
| Body Surface Area (BSA) Involvement with Atopic Dermatitis (AD) | | | |
|---|--|--|--|

BSA affected by AD was assessed for each section of the body (the possible highest score for each region was: head and neck [9%], anterior trunk [18%], back [18%], upper limbs [18%], lower limbs [36%], and genitals [1%]). It was reported as a percentage of all major body sections combined. Analysis was performed on SAF.

| | | | |
|--|---------|---------|---------|
| Units: Percentage of body surface area | | | |
| arithmetic mean | 52.2 | 59 | 45.9 |
| standard deviation | ± 24.78 | ± 22.49 | ± 25.34 |

| | | | |
|--|--|--|--|
| SCORing Atopic Dermatitis (SCORAD) Score | | | |
|--|--|--|--|

SCORAD is a clinical tool for assessing the severity of atopic dermatitis developed by the European Task Force on Atopic Dermatitis ("Severity scoring of atopic dermatitis: the SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis". *Dermatology (Basel)* 186 (1): 23–31. 1993). Extent and intensity of eczema as well as subjective signs (insomnia, etc.) are assessed and scored. Total score ranges from 0 [absent disease] to 103 [severe disease]). Analysis was performed on SAF.

| | | | |
|-------------------------|---------|---------|---------|
| Units: Score on a scale | | | |
| arithmetic mean | 68 | 66.4 | 63 |
| standard deviation | ± 13.19 | ± 13.06 | ± 14.43 |

| | | | |
|-------------------------------|----------------------------|-------|--|
| Reporting group values | Dupilumab 4mg/kg: Children | Total | |
|-------------------------------|----------------------------|-------|--|

| | | | |
|--------------------|----|----|--|
| Number of subjects | 19 | 77 | |
|--------------------|----|----|--|

| | | | |
|-----------------|--|--|--|
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--------------------|--------|---|--|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 8.2 | - | |
| standard deviation | ± 1.99 | | |

| | | | |
|--------------------|--|--|--|
| Gender categorical | | | |
| Units: Subjects | | | |

| | | | |
|--------|----|----|--|
| Female | 8 | 39 | |
| Male | 11 | 38 | |

| | | | |
|---|---------|----|--|
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 1 | 1 | |
| Not Hispanic or Latino | 18 | 76 | |
| Race | | | |
| Units: Subjects | | | |
| White | 18 | 67 | |
| Black or African American | 1 | 2 | |
| Asian | 0 | 5 | |
| Other | 0 | 3 | |
| Number of Subjects with Investigator Global Assessment (IGA) score of 3 or 4 | | | |
| IGA is an assessment scale used to determine severity of 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. Therapeutic response is an IGA score of 0 (clear) or 1 (almost clear). Analysis was performed on SAF. | | | |
| Units: Subjects | | | |
| IGA score of 3 | 0 | 20 | |
| IGA score of 4 | 19 | 57 | |
| Eczema Area and Severity Index (EASI) score | | | |
| The EASI score was used to measure the severity and extent of atopic dermatitis (AD) and measures erythema, infiltration, excoriation and lichenification on 4 anatomic regions of the body: head, trunk, upper and lower extremities. The total EASI score ranges from 0 to 72 points, with the higher scores reflecting the worse severity of AD. Analysis was performed on Safety Analysis set (SAF). | | | |
| Units: Score on a scale | | | |
| arithmetic mean | 38.8 | - | |
| standard deviation | ± 18.64 | - | |
| Pruritus Numerical Rating Scale (NRS) | | | |
| Pruritus NRS scale is an assessment tool that is used to report the intensity of subject's pruritus (itch), both maximum and average intensity, during a 24-hour recall period. Subjects were asked the following question: how would a subject rate his itch at the worst moment during the previous 24 hours (for maximum itch intensity on a scale of 0 – 10 [0 = no itch; 10 = worst itch imaginable]). Weekly average obtained in the 7-day period prior to the baseline visit. Analysis was performed on SAF. | | | |
| Units: Score on a scale | | | |
| arithmetic mean | 6.7 | - | |
| standard deviation | ± 2.35 | - | |
| Body Surface Area (BSA) Involvement with Atopic Dermatitis (AD) | | | |
| BSA affected by AD was assessed for each section of the body (the possible highest score for each region was: head and neck [9%], anterior trunk [18%], back [18%], upper limbs [18%], lower limbs [36%], and genitals [1%]). It was reported as a percentage of all major body sections combined. Analysis was performed on SAF. | | | |
| Units: Percentage of body surface area | | | |
| arithmetic mean | 62.3 | - | |
| standard deviation | ± 30.34 | - | |
| SCORing Atopic Dermatitis (SCORAD) Score | | | |
| SCORAD is a clinical tool for assessing the severity of atopic dermatitis developed by the European Task Force on Atopic Dermatitis ("Severity scoring of atopic dermatitis: the SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis". Dermatology (Basel) 186 (1): 23–31. 1993). Extent and intensity of eczema as well as subjective signs (insomnia, etc.) are assessed and scored. Total score ranges from 0 [absent disease] to 103 [severe disease]). Analysis was performed on SAF. | | | |
| Units: Score on a scale | | | |
| arithmetic mean | 72.7 | - | |
| standard deviation | ± 12.96 | - | |

End points

End points reporting groups

| | |
|------------------------------|--|
| Reporting group title | Dupilumab 2mg/kg: Adolescents |
| Reporting group description: | Dupilumab 2 mg/kg as a single dose on Day 1 followed by 8-week PK sampling period then 4 repeated doses weekly in subjects aged between ≥ 12 to < 18 years. |
| Reporting group title | Dupilumab 2mg/kg: Children |
| Reporting group description: | Dupilumab 2 mg/kg as a single dose on Day 1 followed by 8-week PK sampling period then 4 repeated doses weekly in subjects aged between ≥ 6 to < 12 years. |
| Reporting group title | Dupilumab 4mg/kg: Adolescents |
| Reporting group description: | Dupilumab 4 mg/kg as a single dose on Day 1 followed by 8-week PK sampling period then 4 repeated doses weekly in subjects aged between ≥ 12 to < 18 years. |
| Reporting group title | Dupilumab 4mg/kg: Children |
| Reporting group description: | Dupilumab 4 mg/kg as a single dose on Day 1 followed by 8-week PK sampling period then 4 repeated doses weekly in subjects aged between ≥ 6 to < 12 years. |

Primary: Pharmacokinetics (PK) of dupilumab: Maximum plasma concentration observed (C_{max}) after single administration

| | |
|------------------------|---|
| End point title | Pharmacokinetics (PK) of dupilumab: Maximum plasma concentration observed (C _{max}) after single administration ^[1] |
| End point description: | Peak dupilumab concentration in serum following single dose administration. Analysis was performed on PK analysis set that included all treated subjects who received the study medication and had at least 1 quantified (non-missing) result for dupilumab concentration following the first dose of the study drug. |
| End point type | Primary |
| End point timeframe: | Day 2, 4, 8, 15, 22, 29, 36, 43, and 50 |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis is descriptive only. No formal statistical comparison was performed.

| End point values | Dupilumab 2mg/kg: Adolescents | Dupilumab 2mg/kg: Children | Dupilumab 4mg/kg: Adolescents | Dupilumab 4mg/kg: Children |
|--------------------------------------|-------------------------------|----------------------------|-------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 18 | 20 | 19 |
| Units: mg/L | | | | |
| arithmetic mean (standard deviation) | 9.91 (\pm 2.15) | 14.3 (\pm 5.9) | 23.1 (\pm 8.71) | 32.4 (\pm 7.04) |

Statistical analyses

No statistical analyses for this end point

Primary: PK of dupilumab: Area under the plasma concentration versus time curve

(AUClast) after single administration

| | |
|-----------------|---|
| End point title | PK of dupilumab: Area under the plasma concentration versus time curve (AUClast) after single administration ^[2] |
|-----------------|---|

End point description:

Mean AUC estimates were calculated using mean concentration data at each time point, using a non-compartmental approach (NCA). Calculated AUClast (computed from time zero to the time of the last positive concentration) are presented. Analysis was performed on PK analysis set that included all treated subjects who received the study medication and had at least 1 quantified (non-missing) result for dupilumab concentration following the first dose of the study drug.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 2, 4, 8, 15, 22, 29, 36, 43, and 50

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis is descriptive only. No formal statistical comparison was performed.

| End point values | Dupilumab 2mg/kg: Adolescents | Dupilumab 2mg/kg: Children | Dupilumab 4mg/kg: Adolescents | Dupilumab 4mg/kg: Children |
|--------------------------------------|-------------------------------------|----------------------------------|-------------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 18 | 20 | 19 |
| Units: Day*mg/L | | | | |
| arithmetic mean (standard deviation) | 104 (± 0) | 160 (± 0) | 362 (± 0) | 330 (± 0) |

Statistical analyses

No statistical analyses for this end point

Primary: PK of dupilumab: Trough dupilumab concentration in serum (Ctrough) before 3rd and 4th repeated dose

| | |
|-----------------|--|
| End point title | PK of dupilumab: Trough dupilumab concentration in serum (Ctrough) before 3rd and 4th repeated dose ^[3] |
|-----------------|--|

End point description:

Analysis was performed on PK analysis set that included all treated subjects who received the study medication and had at least 1 quantified (non-missing) result for dupilumab concentration following the first dose of study drug.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Pre-dose on Day 71 and Day 85

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis is descriptive only. No formal statistical comparison was performed.

| End point values | Dupilumab 2mg/kg: Adolescents | Dupilumab 2mg/kg: Children | Dupilumab 4mg/kg: Adolescents | Dupilumab 4mg/kg: Children |
|--------------------------------------|-------------------------------------|----------------------------------|-------------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 18 | 20 | 19 |
| Units: mg/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 71 | 10.4 (± 7.16) | 17.2 (± 8.44) | 32.8 (± 18.9) | 42.1 (± 19.4) |

| | | | | |
|--------|---------------|-------------|---------------|---------------|
| Day 85 | 18.5 (± 12.4) | 28 (± 12.9) | 58.5 (± 24.4) | 60.3 (± 36.3) |
|--------|---------------|-------------|---------------|---------------|

Statistical analyses

No statistical analyses for this end point

Secondary: Percent reduction from baseline in Eczema Area and Severity Index (EASI) at Week 12

| | |
|-----------------|---|
| End point title | Percent reduction from baseline in Eczema Area and Severity Index (EASI) at Week 12 |
|-----------------|---|

End point description:

The EASI score was used to measure the severity and extent of atopic dermatitis (AD) and measures erythema, infiltration, excoriation and lichenification on 4 anatomic regions of the body: head, trunk, upper and lower extremities. The total EASI score ranges from 0 to 72 points, with the higher scores reflecting the worse severity of AD. Analysis was performed on safety analysis set (SAF) that included all subjects who received any study drug. Data after rescue treatment use during the Part B period were set to missing, then missing values were imputed by last observation carried forward (LOCF).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 12 (one week after last dose)

| End point values | Dupilumab 2mg/kg: Adolescents | Dupilumab 2mg/kg: Children | Dupilumab 4mg/kg: Adolescents | Dupilumab 4mg/kg: Children |
|--------------------------------------|-------------------------------------|----------------------------------|-------------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 18 | 20 | 19 |
| Units: percent change | | | | |
| arithmetic mean (standard deviation) | -66.4 (± 29.25) | -76.2 (± 25.48) | -69.7 (± 24.48) | -63.4 (± 25.37) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent reduction from baseline in SCORing Atopic Dermatitis (SCORAD) Score at Week 12

| | |
|-----------------|--|
| End point title | Percent reduction from baseline in SCORing Atopic Dermatitis (SCORAD) Score at Week 12 |
|-----------------|--|

End point description:

SCORAD is a clinical tool for assessing the severity of atopic dermatitis developed by the European Task Force on Atopic Dermatitis ("Severity scoring of atopic dermatitis: the SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis". Dermatology (Basel) 186 (1): 23–31. 1993). Extent and intensity of eczema as well as subjective signs (insomnia, etc.) are assessed and scored. Total score ranges from 0 [absent disease] to 103 [severe disease]. Analysis was performed on SAF. Data after rescue treatment use during the Part B period were set to missing, then missing values were imputed by LOCF.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline to Week 12 (one week after last dose) | |

| End point values | Dupilumab 2mg/kg: Adolescents | Dupilumab 2mg/kg: Children | Dupilumab 4mg/kg: Adolescents | Dupilumab 4mg/kg: Children |
|--------------------------------------|-------------------------------------|----------------------------------|-------------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 18 | 20 | 19 |
| Units: percent change | | | | |
| arithmetic mean (standard deviation) | -47.7 (± 27.27) | -57.5 (± 23.1) | -43.4 (± 25.38) | -46.9 (± 24.31) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent reduction from baseline in Pruritus Numerical Rating Scale (NRS) at Week 12

| | |
|-----------------|---|
| End point title | Percent reduction from baseline in Pruritus Numerical Rating Scale (NRS) at Week 12 |
|-----------------|---|

End point description:

Pruritus NRS scale is an assessment tool that is used to report the intensity of subject's pruritus (itch), both maximum and average intensity, during a 24-hour recall period. Subjects were asked the following question: how would a subject rate his itch at the worst moment during the previous 24 hours (for maximum itch intensity on a scale of 0 – 10 [0 = no itch; 10 = worst itch imaginable]). Analysis was performed on SAF. Data after rescue treatment use during the Part B period were set to missing, then missing values were imputed by LOCF.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline to Week 12 (one week after last dose) | |

| End point values | Dupilumab 2mg/kg: Adolescents | Dupilumab 2mg/kg: Children | Dupilumab 4mg/kg: Adolescents | Dupilumab 4mg/kg: Children |
|--------------------------------------|-------------------------------------|----------------------------------|-------------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 18 | 20 | 19 |
| Units: Percent change | | | | |
| arithmetic mean (standard deviation) | -30.8 (± 68.35) | -41.6 (± 35.32) | -37.6 (± 34.42) | -39.6 (± 40.88) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with Investigator Global Assessment (IGA) score of "0" or "1" (clear or almost clear) at Week 12

End point title | Percentage of subjects with Investigator Global Assessment (IGA) score of "0" or "1" (clear or almost clear) at Week 12

End point description:

IGA is an assessment scale used to determine severity of 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. Therapeutic response is an IGA score of 0 (clear) or 1 (almost clear). Analysis was performed on SAF. Subjects with rescue treatment usage during the Part B period were specified as non-responders from the time the rescue was used.

End point type | Secondary

End point timeframe:

Week 12

| End point values | Dupilumab 2mg/kg: Adolescents | Dupilumab 2mg/kg: Children | Dupilumab 4mg/kg: Adolescents | Dupilumab 4mg/kg: Children |
|-------------------------------|-------------------------------------|----------------------------------|-------------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 18 | 20 | 19 |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 10 | 16.7 | 35 | 21.1 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent reduction from baseline in Body Surface Area (BSA) at week 12

End point title | Percent reduction from baseline in Body Surface Area (BSA) at week 12

End point description:

Body surface area affected by AD was assessed for each section of the body (the possible highest score for each region was: head and neck [9%], anterior trunk [18%], back [18%], upper limbs [18%], lower limbs [36%], and genitals [1%]). It was reported as a percentage of all major body sections combined. Analysis was performed on SAF.

End point type | Secondary

End point timeframe:

Baseline to Week 12

| End point values | Dupilumab 2mg/kg: Adolescents | Dupilumab 2mg/kg: Children | Dupilumab 4mg/kg: Adolescents | Dupilumab 4mg/kg: Children |
|--|-------------------------------------|----------------------------------|-------------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 19 | 16 | 19 | 19 |
| Units: Percentage of body surface area | | | | |
| arithmetic mean (standard deviation) | -61 (± 31.08) | -70 (± 31.93) | -60.4 (± | -50 (± 30.8) |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AEs) were collected from signature of the informed consent form up to the final visit (Week 20) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Treatment Emergent Adverse Events (TEAEs) that developed/ worsened during the treatment and follow-up period (time period from the administration of first dose of study drug to End of Study (EOS) visit [8 weeks after the last dose]). Analysis was performed on SAF.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 18.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------------------|
| Reporting group title | Dupilumab 2mg/kg: Adolescents |
|-----------------------|-------------------------------|

Reporting group description:

Dupilumab 2 mg/kg as a single dose on Day 1 followed by 8-week PK sampling period, then 4 repeated doses weekly in subjects aged between ≥ 12 to < 18 years.

| | |
|-----------------------|----------------------------|
| Reporting group title | Dupilumab 2mg/kg: Children |
|-----------------------|----------------------------|

Reporting group description:

Dupilumab 2 mg/kg as a single dose on Day 1 followed by 8-week PK sampling period, then 4 repeated doses weekly in subjects aged between ≥ 6 to < 12 years.

| | |
|-----------------------|--------------------------------|
| Reporting group title | Dupilumab 4 mg/kg: Adolescents |
|-----------------------|--------------------------------|

Reporting group description:

Dupilumab 4 mg/kg as a single dose on Day 1 followed by 8-week PK sampling period, then 4 repeated doses weekly in subjects aged between ≥ 12 to < 18 years.

| | |
|-----------------------|-----------------------------|
| Reporting group title | Dupilumab 4 mg/kg: Children |
|-----------------------|-----------------------------|

Reporting group description:

Dupilumab 4 mg/kg as a single dose on Day 1 followed by 8-week PK sampling period), then 4 repeated doses weekly in subjects aged between ≥ 6 to < 12 years.

| Serious adverse events | Dupilumab 2mg/kg: Adolescents | Dupilumab 2mg/kg: Children | Dupilumab 4 mg/kg: Adolescents |
|---|-------------------------------|----------------------------|--------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Cardiac disorders | | | |
| Palpitations | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |

| | | |
|---|---|---|
| <p> Dermatitis atopic alternative assessment type: Systematic subjects affected / exposed 0 / 20 (0.00%) occurrences causally related to treatment / all 0 / 0 deaths causally related to treatment / all 0 / 0 </p> | <p> 0 / 18 (0.00%) 0 / 0 0 / 0 </p> | <p> 0 / 20 (0.00%) 0 / 0 0 / 0 </p> |
| <p> Infections and infestations Staphylococcal skin infection alternative assessment type: Systematic subjects affected / exposed 0 / 20 (0.00%) occurrences causally related to treatment / all 0 / 0 deaths causally related to treatment / all 0 / 0 </p> | <p> 0 / 18 (0.00%) 0 / 0 0 / 0 </p> | <p> 1 / 20 (5.00%) 1 / 1 0 / 0 </p> |
| <p> Arthritis bacterial alternative assessment type: Systematic subjects affected / exposed 0 / 20 (0.00%) occurrences causally related to treatment / all 0 / 0 deaths causally related to treatment / all 0 / 0 </p> | <p> 0 / 18 (0.00%) 0 / 0 0 / 0 </p> | <p> 0 / 20 (0.00%) 0 / 0 0 / 0 </p> |
| <p> Dermatitis infected alternative assessment type: Systematic subjects affected / exposed 1 / 20 (5.00%) occurrences causally related to treatment / all 1 / 1 deaths causally related to treatment / all 0 / 0 </p> | <p> 0 / 18 (0.00%) 0 / 0 0 / 0 </p> | <p> 1 / 20 (5.00%) 1 / 1 0 / 0 </p> |

| | | | |
|--|--------------------------------|--|--|
| Serious adverse events | Dupilumab 4 mg/kg: Children | | |
| Total subjects affected by serious adverse events | | | |
| <p> subjects affected / exposed 2 / 19 (10.53%) number of deaths (all causes) 0 number of deaths resulting from adverse events </p> | | | |
| <p> Cardiac disorders Palpitations alternative assessment type: Systematic subjects affected / exposed 0 / 19 (0.00%) occurrences causally related to treatment / all 0 / 0 deaths causally related to treatment / all 0 / 0 </p> | | | |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|---|--|--|
| <p> Dermatitis atopic alternative assessment type: Systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all </p> | <p> 1 / 19 (5.26%) 1 / 1 0 / 0 </p> | | |
| <p> Infections and infestations Staphylococcal skin infection alternative assessment type: Systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all </p> | <p> 0 / 19 (0.00%) 0 / 0 0 / 0 </p> | | |
| <p> Arthritis bacterial alternative assessment type: Systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all </p> | <p> 1 / 19 (5.26%) 1 / 1 0 / 0 </p> | | |
| <p> Dermatitis infected alternative assessment type: Systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all </p> | <p> 1 / 19 (5.26%) 1 / 1 0 / 0 </p> | | |

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

| Non-serious adverse events | Dupilumab 2mg/kg: Adolescents | Dupilumab 2mg/kg: Children | Dupilumab 4 mg/kg: Adolescents |
|---|----------------------------------|-------------------------------|-----------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 11 / 20 (55.00%) | 11 / 18 (61.11%) | 16 / 20 (80.00%) |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Chills | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chest pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pyrexia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Injection site urticaria | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Injection site irritation | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Injection site erythema | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Feeling of body temperature change | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Immune system disorders | | | |
| Food allergy | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 18 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Hypersensitivity alternative assessment type: Systematic | | | |
| subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 18 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Allergic oedema alternative assessment type: Systematic | | | |
| subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 18 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| Reproductive system and breast disorders | | | |
| Vaginal haemorrhage alternative assessment type: Systematic | | | |
| subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 18 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dysphonia alternative assessment type: Systematic | | | |
| subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 18 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Asthma alternative assessment type: Systematic | | | |
| subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 | 0 / 18 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Cough alternative assessment type: Systematic | | | |
| subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 18 (5.56%) 2 | 1 / 20 (5.00%) 2 |
| Dyspnoea alternative assessment type: Systematic | | | |
| subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 18 (5.56%) 1 | 0 / 20 (0.00%) 0 |
| Epistaxis alternative assessment type: Systematic | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Rhinitis allergic | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Oropharyngeal pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasal disorder | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Psychiatric disorders | | | |
| Depressed mood | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Anxiety | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Investigations | | | |
| Protein urine present | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injury, poisoning and procedural complications | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| Animal bite alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 | 0 / 18 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Ligament sprain alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 18 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Contusion alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 18 (5.56%) 1 | 0 / 20 (0.00%) 0 |
| Hand fracture alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 18 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| Bone contusion alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 18 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Muscle strain alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 18 (5.56%) 1 | 0 / 20 (0.00%) 0 |
| Post procedural inflammation alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 | 0 / 18 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Congenital, familial and genetic disorders Dermoid cyst alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 18 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| Cardiac disorders | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| Cyanosis alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 18 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| Nervous system disorders | | | |
| Dizziness alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 18 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Akathisia alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 18 (0.00%) 0 | 1 / 20 (5.00%) 2 |
| Headache alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 2 | 1 / 18 (5.56%) 1 | 1 / 20 (5.00%) 1 |
| Lethargy alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 | 0 / 18 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Syncope alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 | 0 / 18 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Paraesthesia alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 18 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Iron deficiency anaemia alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 | 0 / 18 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| Eosinophilia | | | |

| | | | |
|--|--|---|--|
| alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 18 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Eye disorders Conjunctivitis allergic alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 18 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Gastrointestinal disorders Apthous stomatitis alternative assessment type: Systematic subjects affected / exposed occurrences (all) Cheilitis alternative assessment type: Systematic subjects affected / exposed occurrences (all) Constipation alternative assessment type: Systematic subjects affected / exposed occurrences (all) Diarrhoea alternative assessment type: Systematic subjects affected / exposed occurrences (all) Abdominal pain upper alternative assessment type: Systematic subjects affected / exposed occurrences (all) Vomiting alternative assessment type: Systematic subjects affected / exposed occurrences (all) Mouth ulceration alternative assessment type: Systematic | 0 / 20 (0.00%) 0 0 / 20 (0.00%) 0 1 / 20 (5.00%) 1 | 0 / 18 (0.00%) 0 1 / 18 (5.56%) 1 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 | 0 / 20 (0.00%) 0 0 / 20 (0.00%) 0 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 2 / 20 (10.00%) 2 2 / 20 (10.00%) 2 |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Nausea | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermatitis contact | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Alopecia areata | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermatitis atopic | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 5 / 18 (27.78%) | 3 / 20 (15.00%) |
| occurrences (all) | 2 | 11 | 6 |
| Alopecia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Dry skin | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Erythema | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin erosion | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Psoriasis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Rash | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pain of skin | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Solar dermatitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vitiligo | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Urticaria | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Haematuria | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Arthralgia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bone pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epiphysiolysis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pain in extremity | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Bacterial disease carrier | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Acute tonsillitis | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|--|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Croup infectious | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dermatitis infected | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 18 (5.56%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 1 | 4 |
| Ear infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Folliculitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Gingivitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Herpes simplex | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 3 |

| | | | |
|------------------------------|-----------------|-----------------|-----------------|
| Molluscum contagiosum | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Laryngitis | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Herpes virus infection | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasopharyngitis | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 5 / 18 (27.78%) | 8 / 20 (40.00%) |
| occurrences (all) | 3 | 9 | 11 |
| Oral herpes | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Pharyngitis bacterial | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pharyngitis streptococcal | | | |
| alternative assessment type: | | | |
| Systematic | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Paronychia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin bacterial infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin candida | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Upper respiratory tract infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 1 / 18 (5.56%) | 1 / 20 (5.00%) |
| occurrences (all) | 2 | 1 | 1 |
| Tonsillitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Increased appetite | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |

| Non-serious adverse events | Dupilumab 4 mg/kg: Children | | |
|---|--------------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 18 / 19 (94.74%) | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Chills | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Chest pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pyrexia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 19 (10.53%) | | |
| occurrences (all) | 2 | | |
| Injection site urticaria | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 3 | | |
| Injection site swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injection site irritation | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|--|--|--|
| <p>subjects affected / exposed occurrences (all)</p> <p>0 / 19 (0.00%) 0</p> <p>Injection site erythema alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>1 / 19 (5.26%) 1</p> <p>Feeling of body temperature change alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>0 / 19 (0.00%) 0</p> | | | |
| <p>Immune system disorders</p> <p>Food allergy alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>1 / 19 (5.26%) 1</p> <p>Hypersensitivity alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>1 / 19 (5.26%) 1</p> <p>Allergic oedema alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>0 / 19 (0.00%) 0</p> | | | |
| <p>Reproductive system and breast disorders</p> <p>Vaginal haemorrhage alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>0 / 19 (0.00%) 0</p> | | | |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Dysphonia alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>1 / 19 (5.26%) 1</p> <p>Asthma alternative assessment type:</p> | | | |

| | | | |
|--|-----------------|--|--|
| Systematic | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Cough | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 7 / 19 (36.84%) | | |
| occurrences (all) | 8 | | |
| Dyspnoea | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Epistaxis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Rhinitis allergic | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oropharyngeal pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 2 | | |
| Nasal disorder | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Rhinorrhoea | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders | | | |
| Depressed mood | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|--|---|--|--|
| <p>subjects affected / exposed occurrences (all)</p> <p>Anxiety alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> | <p>0 / 19 (0.00%) 0</p> <p>0 / 19 (0.00%) 0</p> | | |
| <p>Investigations Protein urine present alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> | <p>0 / 19 (0.00%) 0</p> | | |
| <p>Injury, poisoning and procedural complications</p> <p>Animal bite alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>Ligament sprain alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>Contusion alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>Hand fracture alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>Bone contusion alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>Muscle strain alternative assessment type: Systematic</p> | <p>0 / 19 (0.00%) 0</p> <p>1 / 19 (5.26%) 1</p> <p>0 / 19 (0.00%) 0</p> <p>0 / 19 (0.00%) 0</p> <p>1 / 19 (5.26%) 1</p> | | |

| | | | |
|--|---|--|--|
| <p>subjects affected / exposed occurrences (all)</p> <p>Post procedural inflammation alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> | <p>0 / 19 (0.00%) 0</p> <p>0 / 19 (0.00%) 0</p> | | |
| <p>Congenital, familial and genetic disorders</p> <p>Dermoid cyst alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> | <p>0 / 19 (0.00%) 0</p> | | |
| <p>Cardiac disorders</p> <p>Cyanosis alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> | <p>0 / 19 (0.00%) 0</p> | | |
| <p>Nervous system disorders</p> <p>Dizziness alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>Akathisia alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>Headache alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>Lethargy alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>Syncope alternative assessment type: Systematic</p> | <p>2 / 19 (10.53%) 3</p> <p>0 / 19 (0.00%) 0</p> <p>2 / 19 (10.53%) 3</p> <p>1 / 19 (5.26%) 1</p> | | |

| | | | |
|--|---|--|--|
| <p>subjects affected / exposed occurrences (all)</p> <p>Paraesthesia alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> | <p>0 / 19 (0.00%) 0</p> <p>1 / 19 (5.26%) 1</p> | | |
| <p>Blood and lymphatic system disorders</p> <p>Iron deficiency anaemia alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>Eosinophilia alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> | <p>0 / 19 (0.00%) 0</p> <p>1 / 19 (5.26%) 1</p> | | |
| <p>Eye disorders</p> <p>Conjunctivitis allergic alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> | <p>1 / 19 (5.26%) 3</p> | | |
| <p>Gastrointestinal disorders</p> <p>Aphthous stomatitis alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>Cheilitis alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>Constipation alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>Diarrhoea alternative assessment type: Systematic</p> | <p>1 / 19 (5.26%) 1</p> <p>0 / 19 (0.00%) 0</p> <p>0 / 19 (0.00%) 0</p> | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain upper | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 19 (15.79%) | | |
| occurrences (all) | 3 | | |
| Vomiting | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Mouth ulceration | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nausea | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 19 (10.53%) | | |
| occurrences (all) | 2 | | |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dermatitis contact | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Alopecia areata | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dermatitis atopic | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|------------------------------|-----------------|--|--|
| subjects affected / exposed | 5 / 19 (26.32%) | | |
| occurrences (all) | 10 | | |
| Alopecia | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dry skin | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Erythema | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin erosion | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psoriasis | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain of skin | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Solar dermatitis | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|--|--|--|
| <p>Vitiligo</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed 0 / 19 (0.00%)</p> <p>occurrences (all) 0</p> <p>Urticaria</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed 1 / 19 (5.26%)</p> <p>occurrences (all) 2</p> | | | |
| <p>Renal and urinary disorders</p> <p>Dysuria</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed 0 / 19 (0.00%)</p> <p>occurrences (all) 0</p> <p>Haematuria</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed 0 / 19 (0.00%)</p> <p>occurrences (all) 0</p> | | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Back pain</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed 0 / 19 (0.00%)</p> <p>occurrences (all) 0</p> <p>Arthralgia</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed 1 / 19 (5.26%)</p> <p>occurrences (all) 1</p> <p>Bone pain</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed 1 / 19 (5.26%)</p> <p>occurrences (all) 1</p> <p>Epiphysiolysis</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed 0 / 19 (0.00%)</p> <p>occurrences (all) 0</p> <p>Pain in extremity</p> | | | |

| | | | |
|--|----------------------|--|--|
| alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | | |
| Infections and infestations | | | |
| Bacterial disease carrier | | | |
| alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | | |
| Acute tonsillitis | | | |
| alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 2 | | |
| Gastrointestinal infection | | | |
| alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | | |
| Conjunctivitis | | | |
| alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 2 | | |
| Croup infectious | | | |
| alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | | |
| Dermatitis infected | | | |
| alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 2 / 19 (10.53%) 5 | | |
| Ear infection | | | |
| alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | | |
| Folliculitis | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|-------------------------------|------------------|--|--|
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gingivitis | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Herpes simplex | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Molluscum contagiosum | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Influenza | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Laryngitis | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Herpes virus infection | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasopharyngitis | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 10 / 19 (52.63%) | | |
| occurrences (all) | 11 | | |
| Oral herpes | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |

| | | | |
|-----------------------------------|-----------------|--|--|
| Rhinitis | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 2 / 19 (10.53%) | | |
| occurrences (all) | 2 | | |
| Pharyngitis bacterial | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pharyngitis streptococcal | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Paronychia | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Skin bacterial infection | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 2 | | |
| Skin candida | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Urinary tract infection | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | | |
| occurrences (all) | 0 | | |
| Upper respiratory tract infection | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Tonsillitis | | | |
| alternative assessment type: | | | |
| Systematic | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | | |
| Viral upper respiratory tract infection alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | | |
| Metabolism and nutrition disorders Increased appetite alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|--|
| 24 June 2015 | Following changes were made: •Changes were made regarding the use of topical corticosteroids (TCS) and topical calcineurin inhibitors (TCI) were permitted during the study to avoid subjects being unnecessarily deprived of topical medication. •Clarified the use of prescription moisturizers started prior to the study were permitted to continue during the study, but initiation of prescription moisturizers during the study was not allowed. •Clarified the definition of "childbearing potential" for the purpose of the study, and added a note regarding additional requirement for adequate contraceptive methods in certain countries to avoid ambiguity in the interpretation of the relevant exclusion criterion. •Added assessment of body surface area (BSA) affected by AD, at the same time points other efficacy assessments were being performed; added BSA related secondary endpoint. •Clarified that only subjects with a history of active infection with hepatitis B or C or evidence of active disease at screening were excluded from the study. •Clarified the duration of close monitoring required after study drug administration and assessments performed during the monitoring period. • Added text regarding opportunity for subjects who completed the study to enroll into an open-label extension study to continue Dupilumab treatment. •Reduced the amount of information gathered from subjects on pruritus based on NRS. •Clarified cheek swab sample taken for DNA extraction (removed the options of taking whole blood or saliva sample). |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported