



## Clinical trial results:

### A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Nemolizumab (CD14152) in Subjects with Moderate-to-Severe Atopic Dermatitis

#### Summary

|                          |                         |
|--------------------------|-------------------------|
| EudraCT number           | 2019-001887-31          |
| Trial protocol           | LV GB DE LT NL AT CZ PL |
| Global end of trial date | 11 August 2022          |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 02 October 2024 |
| First version publication date | 02 October 2024 |

#### Trial information

##### Trial identification

|                       |                  |
|-----------------------|------------------|
| Sponsor protocol code | RD.06.SPR.118161 |
|-----------------------|------------------|

##### Additional study identifiers

|                                    |                    |
|------------------------------------|--------------------|
| ISRCTN number                      | -                  |
| ClinicalTrials.gov id (NCT number) | NCT03985943        |
| WHO universal trial number (UTN)   | -                  |
| Other trial identifiers            | IND number: 117122 |

Notes:

##### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Galderma S.A.   |
| Sponsor organisation address | Zahlerweg 10, ZUG, Switzerland, 6300  |
| Public contact               | Clinical Trial Information Desk, Galderma S.A.,<br>CTA.Coordinator@galderma.com |
| Scientific contact           | Clinical Trial Information Desk, Galderma S.A.,<br>CTA.Coordinator@galderma.com |

Notes:

##### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-001624-PIP01-14 |
| 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                       | 11 August 2022 |
| Is this the analysis of the primary completion data? | No             |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 11 August 2022 |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective is to assess the efficacy and safety of Nemolizumab (CD14152) after a 16-week treatment period in adult and adolescent subjects with moderate-to-severe atopic dermatitis (AD) not adequately controlled with topical treatments.

Protection of trial subjects:

Subject protection was ensured by following high medical and ethical standards in accordance with the principles laid down in the Declaration of Helsinki, and that are consistent with Good Clinical Practice and applicable regulation.

Background therapy:

Subjects received topical corticosteroids (TCS) and topical calcineurin inhibitors (TCI) as background therapy.

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 27 June 2019 |
| 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 | Netherlands: 7                             |
| Country: Number of subjects enrolled | Poland: 190                                |
| Country: Number of subjects enrolled | Spain: 46                                  |
| Country: Number of subjects enrolled | United Kingdom: 16                         |
| Country: Number of subjects enrolled | Austria: 29                                |
| Country: Number of subjects enrolled | Czechia: 64                                |
| Country: Number of subjects enrolled | Germany: 90                                |
| Country: Number of subjects enrolled | Latvia: 28                                 |
| Country: Number of subjects enrolled | Lithuania: 10                              |
| Country: Number of subjects enrolled | Australia: 54                              |
| Country: Number of subjects enrolled | Canada: 102                                |
| Country: Number of subjects enrolled | New Zealand: 13                            |
| Country: Number of subjects enrolled | Korea, Democratic People's Republic of: 83 |
| Country: Number of subjects enrolled | United States: 209                         |
| Worldwide total number of subjects   | 941  |
| EEA total number of subjects         | 464  |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| 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)                 | 134 |
| Adults (18-64 years)                      | 768 |
| From 65 to 84 years                       | 39  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 177 active sites in Australia, Austria, Canada, Czech Republic, Germany, Great Britain, Korea, Latvia, Lithuania, Netherlands, New Zealand, Poland, Spain and the United States from 27 June 2019 to 11 August 2022.

### Pre-assignment

Screening details:

Total of 941 randomized 2:1 to receive either nemolizumab or placebo. At Week 16, 272 nemolizumab responders re-randomized to receive nemolizumab Q4W, nemolizumab Q8W, or placebo during Maintenance Period. 100 subjects received placebo in Initial Treatment, responded to placebo at Week 16, re-assigned to placebo and continued to receive placebo Q4W.

### Period 1

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

### Arms

|                              |                                   |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes                               |
| <b>Arm title</b>             | Initial Treatment Period: Placebo |

Arm description:

Subjects received placebo via 2 subcutaneous (SC) injections at Day 1, thereafter, every 4 weeks (Q4W) at Weeks 4, 8, and 12 by a single SC injection during Initial Treatment Period.

|  |                  |
|--|------------------|
| Arm type                               | Placebo          |
| Investigational medicinal product name | Placebo          |
| Investigational medicinal product code |                  |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Nemolizumab matched Placebo

|                  |   |
|------------------|---|
| <b>Arm title</b> | Initial Treatment Period: Nemolizumab 30 mg |
|------------------|---|

Arm description:

Subjects received nemolizumab 30 mg via 2 SC injections at Day 1, thereafter, Q4W at Weeks 4, 8, and 12 by a single SC injection during Initial Treatment Period.

|  |                  |
|--|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Nemolizumab      |
| Investigational medicinal product code |                  |
| Other name                             | CD14152          |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Nemolizumab 30 mg via 2 SC injections on Day 1 followed by single SC injection.

| Number of subjects in period 1 | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |
|--------------------------------|-----------------------------------|---|
|                                |                                   |   |
| Started                        | 321                               | 620   |
| Treated                        | 321                               | 620   |
| Completed                      | 296                               | 560   |
| Not completed                  | 25                                | 60  |
| Physician decision             | -                                 | 1   |
| Subjects request               | 11                                | 25  |
| Adverse event, non-fatal       | 9                                 | 9   |
| Randomized but not treated     | -                                 | 4   |
| Pregnancy                      | -                                 | 2   |
| Lost to follow-up              | -                                 | 10  |
| Lack of efficacy               | 2                                 | 5   |
| Protocol deviation             | 3                                 | 4   |

## Period 2

|                              |  |
|------------------------------|--|
| Period 2 title               | Maintenance Period (Week 16-Week 48)   |
| Is this the baseline period? | No                                     |
| Allocation method            | Randomised - controlled                |
| Blinding used                | Double blind                           |
| Roles blinded                | Subject, Investigator, Carer, Assessor |

## Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | Yes  |
| <b>Arm title</b>             | Maintenance Period: Nemolizumab 30 mg Q4W to Q4W |

### Arm description:

Subjects who received nemolizumab, Q4W during Initial Treatment Period and were clinical responders (defined as subjects with an IGA of 0 (clear) or 1 (almost clear) or a  $\geq 75\%$  improvement in EASI from Baseline) at Week 16 received nemolizumab 30 mg, every 4 weeks (Q4W) at Weeks 16, 20, 24, 28, 32, 36, 40, and 44 by a single SC injection during Maintenance Period.

|  |                  |
|--|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Nemolizumab      |
| Investigational medicinal product code |                  |
| Other name                             | CD14152          |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

### Dosage and administration details:

Nemolizumab 30 mg

|                  |  |
|------------------|--|
| <b>Arm title</b> | Maintenance Period: Nemolizumab 30 mg Q4W to Q8W |
|------------------|--|

### Arm description:

Subjects who received nemolizumab, Q4W during Initial Treatment Period and were clinical responders (defined as subjects with an IGA of 0 (clear) or 1 (almost clear) or a  $\geq 75\%$  improvement in EASI from Baseline) at Week 16 received nemolizumab 30 mg, Q8W at Weeks 16, 24, 32, and 40 by a single SC injection during Maintenance Period.

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

|  |  |
|--|--|
| Investigational medicinal product name | Nemolizumab  |
| Investigational medicinal product code |  |
| Other name                             | CD14152  |
| Pharmaceutical forms                   | Injection  |
| Routes of administration               | Subcutaneous use   |
| Dosage and administration details:     |  |
| Nemolizumab 30 mg                      |  |
| <b>Arm title</b>                       | Maintenance Period: Nemolizumab 30 mg Q4W to Placebo Q4W |

Arm description:

Subjects who received nemolizumab, Q4W during Initial Treatment Period and were clinical responders (defined as subjects with an IGA of 0 [clear] or 1 [almost clear] or a  $\geq 75\%$  improvement in EASI from Baseline) at Week 16 received placebo, Q4W at Weeks 16, 20, 24, 28, 32, 36, 40, and 44 by a single SC injection during Maintenance Period.

|  |                  |
|--|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Placebo          |
| Investigational medicinal product code |                  |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Nemolizumab matched Placebo

|                  |  |
|------------------|--|
| <b>Arm title</b> | Maintenance Period: Placebo Q4W Re-assigned to Placebo Q4W |
|------------------|--|

Arm description:

Subjects who received placebo, Q4W during Initial Treatment Period and were clinical responders (defined as subjects with an IGA of 0 [clear] or 1 [almost clear] or a  $\geq 75\%$  improvement in EASI from Baseline) at Week 16 received placebo, Q4W at Weeks 16, 20, 24, 28, 32, 36, 40, and 44 by a single SC injection during Maintenance Period.

|  |                  |
|--|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Placebo          |
| Investigational medicinal product code |                  |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Nemolizumab matched Placebo

| Number of subjects in period 2 <sup>[1]</sup> | Maintenance Period: Nemolizumab 30 mg Q4W to Q4W | Maintenance Period: Nemolizumab 30 mg Q4W to Q8W | Maintenance Period: Nemolizumab 30 mg Q4W to Placebo Q4W |
|---|--|--|--|
|   |  |  |  |
| Started                                       | 90   | 91   | 91   |
| Completed                                     | 76   | 79   | 69   |
| Not completed                                 | 14   | 12   | 22   |
| Consent withdrawn by subject                  | 6  | 4  | 5  |
| Physician decision                            | 2  | 1  | 1  |
| Adverse event, non-fatal                      | 1  | 3  | 1  |
| Not specified                                 | -  | -  | 1  |
| Lost to follow-up                             | -  | 1  | 1  |

|                    |   |   |    |
|--------------------|---|---|----|
| Lack of efficacy   | 4 | 3 | 12 |
| Protocol deviation | 1 | - | 1  |

| <b>Number of subjects in period 2<sup>[1]</sup></b> | Maintenance Period:<br>Placebo Q4W Re-<br>assigned to Placebo<br>Q4W |
|---|--|
| Started   | 100  |
| Completed   | 82   |
| Not completed                                       | 18   |
| Consent withdrawn by subject                        | 9  |
| Physician decision                                  | 2  |
| Adverse event, non-fatal                            | 1  |
| Not specified                                       | 1  |
| Lost to follow-up                                   | 1  |
| Lack of efficacy                                    | 4  |
| Protocol deviation                                  | -  |

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Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Subjects who received nemolizumab, Q4W during Initial Treatment Period and were clinical responders at Week 16 were rerandomized during Maintenance Period. Subjects who received placebo, Q4W during Initial Treatment Period and were clinical responders at Week 16, were re-assigned during Maintenance Period.

## Baseline characteristics

### Reporting groups

|  |   |
|--|---|
| Reporting group title  | Initial Treatment Period: Placebo           |
| Reporting group description:   |   |
| Subjects received placebo via 2 subcutaneous (SC) injections at Day 1, thereafter, every 4 weeks (Q4W) at Weeks 4, 8, and 12 by a single SC injection during Initial Treatment Period. |   |
| Reporting group title  | Initial Treatment Period: Nemolizumab 30 mg |
| Reporting group description:   |   |
| Subjects received nemolizumab 30 mg via 2 SC injections at Day 1, thereafter, Q4W at Weeks 4, 8, and 12 by a single SC injection during Initial Treatment Period.                      |   |

| Reporting group values                    | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg | Total |
|---|-----------------------------------|---|-------|
| Number of subjects                        | 321                               | 620   | 941   |
| Age categorical<br>Units: Subjects        |                                   |   |       |
| Age continuous<br>Units: years            |                                   |   |       |
| arithmetic mean                           | 33.3                              | 33.5  |       |
| standard deviation                        | ± 15.61                           | ± 15.93                                     | -     |
| Gender categorical<br>Units: Subjects     |                                   |   |       |
| Female                                    | 144                               | 297   | 441   |
| Male                                      | 177                               | 323   | 500   |
| Ethnicity<br>Units: Subjects              |                                   |   |       |
| Hispanic or Latino                        | 32                                | 64  | 96    |
| Not Hispanic or Latino                    | 288                               | 552   | 840   |
| Unknown or Not Reported                   | 1                                 | 4   | 5     |
| Race<br>Units: Subjects                   |                                   |   |       |
| Asian                                     | 51                                | 117   | 168   |
| Native Hawaiian or Other Pacific Islander | 0                                 | 1   | 1     |
| Black or African American                 | 18                                | 36  | 54    |
| White                                     | 244                               | 451   | 695   |
| More than one race                        | 4                                 | 10  | 14    |
| Unknown or Not Reported                   | 1                                 | 3   | 4     |
| American Indian or Alaska Native          | 3                                 | 2   | 5     |



## End points

### End points reporting groups

|  |  |
|--|--|
| Reporting group title  | Initial Treatment Period: Placebo                          |
| Reporting group description:<br>Subjects received placebo via 2 subcutaneous (SC) injections at Day 1, thereafter, every 4 weeks (Q4W) at Weeks 4, 8, and 12 by a single SC injection during Initial Treatment Period.   |  |
| Reporting group title  | Initial Treatment Period: Nemolizumab 30 mg                |
| Reporting group description:<br>Subjects received nemolizumab 30 mg via 2 SC injections at Day 1, thereafter, Q4W at Weeks 4, 8, and 12 by a single SC injection during Initial Treatment Period.  |  |
| Reporting group title  | Maintenance Period: Nemolizumab 30 mg Q4W to Q4W           |
| Reporting group description:<br>Subjects who received nemolizumab, Q4W during Initial Treatment Period and were clinical responders (defined as subjects with an IGA of 0 (clear) or 1 (almost clear) or a $\geq 75\%$ improvement in EASI from Baseline) at Week 16 received nemolizumab 30 mg, every 4 weeks (Q4W) at Weeks 16, 20, 24, 28, 32, 36, 40, and 44 by a single SC injection during Maintenance Period. |  |
| Reporting group title  | Maintenance Period: Nemolizumab 30 mg Q4W to Q8W           |
| Reporting group description:<br>Subjects who received nemolizumab, Q4W during Initial Treatment Period and were clinical responders (defined as subjects with an IGA of 0 (clear) or 1 (almost clear) or a $\geq 75\%$ improvement in EASI from Baseline) at Week 16 received nemolizumab 30 mg, Q8W at Weeks 16, 24, 32, and 40 by a single SC injection during Maintenance Period.                                 |  |
| Reporting group title  | Maintenance Period: Nemolizumab 30 mg Q4W to Placebo Q4W   |
| Reporting group description:<br>Subjects who received nemolizumab, Q4W during Initial Treatment Period and were clinical responders (defined as subjects with an IGA of 0 [clear] or 1 [almost clear] or a $\geq 75\%$ improvement in EASI from Baseline) at Week 16 received placebo, Q4W at Weeks 16, 20, 24, 28, 32, 36, 40, and 44 by a single SC injection during Maintenance Period.                           |  |
| Reporting group title  | Maintenance Period: Placebo Q4W Re-assigned to Placebo Q4W |
| Reporting group description:<br>Subjects who received placebo, Q4W during Initial Treatment Period and were clinical responders (defined as subjects with an IGA of 0 [clear] or 1 [almost clear] or a $\geq 75\%$ improvement in EASI from Baseline) at Week 16 received placebo, Q4W at Weeks 16, 20, 24, 28, 32, 36, 40, and 44 by a single SC injection during Maintenance Period.                               |  |
| Subject analysis set title   | Initial Treatment Period: Placebo                          |
| Subject analysis set type  | Sub-group analysis   |
| Subject analysis set description:<br>Subjects received placebo via 2 SC injections at Day 1, thereafter, Q4W at Weeks 4, 8, and 12 by a single SC injection during Initial Treatment Period.   |  |
| Subject analysis set title   | Initial Treatment Period: Nemolizumab 30 mg                |
| Subject analysis set type  | Sub-group analysis   |
| Subject analysis set description:<br>Subjects received nemolizumab 30 mg via 2 SC injections at Day 1, thereafter, Q4W at Weeks 4, 8, and 12 by a single SC injection during Initial Treatment Period.   |  |

### Primary: Percentage of Subjects With an Investigator's Global Assessment (IGA) Success (IGA of 0 or 1 and a More Than Equal to $\geq$ 2-point Reduction): Intent-To-Treat (ITT) Population

|   |   |
|---|---|
| End point title   | Percentage of Subjects With an Investigator's Global Assessment (IGA) Success (IGA of 0 or 1 and a More Than Equal to $\geq$ 2-point Reduction): Intent-To-Treat (ITT) Population |
| End point description:<br>IGA success was defined as an IGA score of 0 (clear) or 1 (almost clear) and at least a 2-grade |   |

improvement from baseline to Week 16. The IGA is a 5-point scale ranging from 0 (clear) to 4 (severe) used by the Investigator or trained designee to evaluate the global severity of atopic dermatitis (AD) and the clinical response to treatment. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered treatment failure. Subjects with missing data at Week 16 were considered non-responders. The ITT population consisted of all randomised subjects. Data was planned to be collected and analysed for Initial Treatment Period.

|                      |         |
|----------------------|---------|
| End point type       | Primary |
| End point timeframe: |         |
| Week 16              |         |

| End point values              | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 321                               | 620   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 24.6                              | 35.6  |  |  |

## Statistical analyses

|                            |            |
|----------------------------|------------|
| Statistical analysis title | Analysis 1 |
|----------------------------|------------|

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level.

|   |   |
|---|---|
| Comparison groups                       | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis | 941   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other   |
| P-value                                 | = 0.0003 <sup>[1]</sup>   |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Strata-adjusted percentage difference   |
| Point estimate                          | 11.5  |
| Confidence interval                     |   |
| level                                   | Other: 97.5 %   |
| sides                                   | 2-sided   |
| lower limit                             | 4.7   |
| upper limit                             | 18.3  |

Notes:

[1] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe] and PP NRS [ $\geq 7$ ,  $< 7$ ]).

## Primary: Percentage of Subjects With an Investigator's Global Assessment (IGA) Success (IGA of 0 or 1 and a More Than Equal to [ $\geq$ ] 2-point Reduction): Severe Pruritus Population

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With an Investigator's Global Assessment (IGA) Success (IGA of 0 or 1 and a More Than Equal to [ $\geq$ ] 2-point Reduction): Severe Pruritus Population |
|-----------------|---|

End point description:

IGA success was defined as an IGA score of 0 (clear) or 1 (almost clear) and at least a 2-grade improvement from baseline to Week 16. The IGA is a 5-point scale ranging from 0 (clear) to 4 (severe) used by the Investigator or trained designee to evaluate the global severity of AD and the clinical response to treatment. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered a treatment failure. Subjects with missing data at Week 16 are considered non-responders. Severe pruritus population consisted of all randomised subjects with a baseline PP NRS  $\geq 7$ . Data was planned to be collected and analysed for Initial Treatment Period.

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

End point timeframe:

Week 16

| End point values              | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 210                               | 406   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 21.4                              | 35.5  |  |  |

## Statistical analyses

|                            |            |
|----------------------------|------------|
| Statistical analysis title | Analysis 1 |
|----------------------------|------------|

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level.

|   |   |
|---|---|
| Comparison groups                       | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis | 616   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other   |
| P-value                                 | = 0.0002 <sup>[2]</sup>   |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Strata-adjusted percentage difference   |
| Point estimate                          | 14.3  |
| Confidence interval                     |   |
| level                                   | Other: 97.5 %   |
| sides                                   | 2-sided   |
| lower limit                             | 6.1   |
| upper limit                             | 22.5  |

Notes:

[2] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe]).

**Primary: Percentage of Subjects With  $\geq 75\%$  Improvement in Eczema Area and Severity Index (EASI-75) at Week 16: ITT Population**

|  |  |
|--|--|
| End point title  | Percentage of Subjects With $\geq 75\%$ Improvement in Eczema Area and Severity Index (EASI-75) at Week 16: ITT Population |
| End point description:   |  |
| EASI-75 was defined as $\geq 75$ percent (%) improvement in EASI from baseline to Week 16. EASI evaluates severity of subjects AD based on severity of AD clinical signs and % of body surface area (BSA) affected. Severity of clinical signs of AD (erythema, induration/papulation, excoriation and lichenification) scored separately for each of 4 body regions (head & neck, upper limbs, trunk & lower limbs) on 4-point scale: 0= absent; 1= mild; 2= moderate; 3= severe. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered a treatment failure. Subjects with missing data at Week 16 were considered non-responders. EASI total score is composite score ranging from 0 to 72. Higher scores represent greater severity of AD. The ITT population consisted of all randomised subjects. |  |
| End point type   | Primary  |
| End point timeframe:   |  |
| Week 16  |  |

| End point values              | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 321                               | 620   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 29.0                              | 43.5  |  |  |

## Statistical analyses

|   |   |
|---|---|
| Statistical analysis title  | Analysis 1  |
| Statistical analysis description:   |   |
| A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level. |   |
| Comparison groups   | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis   | 941   |
| Analysis specification  | Pre-specified   |
| Analysis type   | other   |
| P-value   | $< 0.0001$ <sup>[3]</sup>   |
| Method  | Cochran-Mantel-Haenszel   |
| Parameter estimate  | Strata-adjusted percentage difference   |
| Point estimate  | 14.9  |
| Confidence interval   |   |
| level   | Other: 97.5 %   |
| sides   | 2-sided   |
| lower limit   | 7.8   |
| upper limit   | 22  |

Notes:

[3] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe] and PP NRS [ $\geq 7$ ,  $< 7$ ]).

**Primary: Percentage of Subjects With  $\geq 75\%$  Improvement in Eczema Area and Severity Index (EASI-75) at Week 16: Severe Pruritus Population**

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With $\geq 75\%$ Improvement in Eczema Area and Severity Index (EASI-75) at Week 16: Severe Pruritus Population |
|-----------------|--|

## End point description:

EASI-75 was defined as  $\geq 75$  percent (%) improvement in EASI from baseline to Week 16. EASI evaluates severity of subjects AD based on severity of AD clinical signs and % of body surface area (BSA) affected. Severity of clinical signs of AD (erythema, induration/papulation, excoriation and lichenification) scored separately for each of 4 body regions (head & neck, upper limbs, trunk & lower limbs on 4-point scale: 0= absent; 1= mild; 2= moderate; 3= severe. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered a treatment failure. Subjects with missing data at Week 16 were considered non-responders. EASI total score is composite score ranging from 0 to 72. Higher scores represent greater severity of AD. The ITT population consisted of all randomised subjects.

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

## End point timeframe:

Week 16

| End point values              | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 210                               | 406   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 23.8                              | 41.6  |  |  |

**Statistical analyses**

|                            |            |
|----------------------------|------------|
| Statistical analysis title | Analysis 1 |
|----------------------------|------------|

## Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level.

|   |   |
|---|---|
| Comparison groups                       | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis | 616   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other   |
| P-value                                 | $< 0.0001$ <sup>[4]</sup>   |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Strata-adjusted percentage difference   |
| Point estimate                          | 18.1  |
| Confidence interval                     |   |
| level                                   | Other: 97.5 %   |
| sides                                   | 2-sided   |
| lower limit                             | 9.6   |
| upper limit                             | 26.6  |

Notes:

[4] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe]).

### Secondary: Percentage of Subjects With Improvement of $\geq 4$ Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 16: ITT Population

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With Improvement of $\geq 4$ Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 16: ITT Population |
|-----------------|---|

End point description:

The PP NRS is a scale that was used by the subjects to report the intensity of their pruritus (itch) during the last 24 hours on a scale of 0 to 10, with 0 being 'no itch' and 10 being the 'worst itch imaginable'. Weekly average PP NRS score was calculated using 7 consecutive days diary data and set to missing if less than 4 days data available. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered treatment failure. The ITT population consisted of all randomised subjects. Data was planned to be collected and analysed for Initial Treatment Period.

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

End point timeframe:

Week 16

| End point values              | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 321                               | 620   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 17.8                              | 42.7  |  |  |

### Statistical analyses

|                            |            |
|----------------------------|------------|
| Statistical analysis title | Analysis 1 |
|----------------------------|------------|

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level. Subjects with missing data are considered non-responders.

|   |   |
|---|---|
| Comparison groups                       | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis | 941   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other   |
| P-value                                 | $< 0.0001$ [5]  |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Strata-adjusted percentage difference   |
| Point estimate                          | 24.9  |

|                     |               |
|---------------------|---------------|
| Confidence interval |               |
| level               | Other: 97.5 % |
| sides               | 2-sided       |
| lower limit         | 18.4          |
| upper limit         | 31.5          |

Notes:

[5] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe] and PP NRS [ $\geq 7$ ,  $< 7$ ]).

|                                   |                            |
|-----------------------------------|----------------------------|
| <b>Statistical analysis title</b> | Analysis 2 - MI-MAR Method |
|-----------------------------------|----------------------------|

Statistical analysis description:

Nemolizumab 30 mg versus Placebo using multiple imputation (MI) with missing at random (MAR) assumption. The estimates are from 50 complete datasets by MI-MAR assumption.

|   |   |
|---|---|
| Comparison groups                       | Initial Treatment Period: Nemolizumab 30 mg v Initial Treatment Period: Placebo |
| Number of subjects included in analysis | 941   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other   |
| P-value                                 | $< 0.0001$ <sup>[6]</sup>   |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Strata-adjusted percentage difference   |
| Point estimate                          | 28.1  |
| Confidence interval                     |   |
| level                                   | Other: 97.5 %   |
| sides                                   | 2-sided   |
| lower limit                             | 22  |
| upper limit                             | 34.3  |

Notes:

[6] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe] and PP NRS [ $\geq 7$ ,  $< 7$ ]).

### **Secondary: Percentage of Subjects With Improvement of $\geq 4$ Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 16: Severe Pruritus Population**

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With Improvement of $\geq 4$ Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 16: Severe Pruritus Population |
|-----------------|---|

End point description:

The PP NRS is a scale that was used by the subjects to report the intensity of their pruritus (itch) during the last 24 hours on a scale of 0 to 10, with 0 being 'no itch' and 10 being the 'worst itch imaginable'. Weekly average PP NRS score was calculated using 7 consecutive days diary data and set to missing if less than 4 days data available. If a subject received any rescue therapy, the data after receipt of rescue therapy is considered treatment failure. Severe pruritus population consisted of all randomised subjects with a baseline PP NRS  $\geq 7$ . Data was planned to be collected and analysed for Initial Treatment Period.

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

End point timeframe:

Week 16

| End point values              | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 210                               | 406   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 18.6                              | 46.1  |  |  |

## Statistical analyses

| Statistical analysis title | Analysis 1 |
|----------------------------|------------|
|----------------------------|------------|

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level. Subjects with missing data are considered non-responders.

|   |   |
|---|---|
| Comparison groups                       | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis | 616   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other   |
| P-value                                 | < 0.0001 <sup>[7]</sup>   |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Strata-adjusted percentage difference   |
| Point estimate                          | 27.5  |
| Confidence interval                     |   |
| level                                   | Other: 97.5 %   |
| sides                                   | 2-sided   |
| lower limit                             | 19.4  |
| upper limit                             | 35.7  |

Notes:

[7] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe]).

| Statistical analysis title | Analysis 2: MI-MAR Method |
|----------------------------|---------------------------|
|----------------------------|---------------------------|

Statistical analysis description:

Nemolizumab 30 mg versus Placebo using MI-MAR assumption. The estimates are from 50 complete datasets by MI-MAR assumption.

|   |   |
|---|---|
| Comparison groups                       | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis | 616   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other   |
| P-value                                 | < 0.0001 <sup>[8]</sup>   |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Strata-adjusted percentage difference   |
| Point estimate                          | 32.1  |



|                     |               |
|---------------------|---------------|
| Confidence interval |               |
| level               | Other: 97.5 % |
| sides               | 2-sided       |
| lower limit         | 24.4          |
| upper limit         | 39.8          |

Notes:

[8] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe]).

## Secondary: Percentage of Subjects With <2 Points in Weekly Average PP NRS at Week 16: ITT Population

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With <2 Points in Weekly Average PP NRS at Week 16: ITT Population |
|-----------------|---|

End point description:

The PP NRS is a scale that was used by the subjects to report the intensity of their pruritus (itch) during the last 24 hours on a scale of 0 to 10, with 0 being 'no itch' and 10 being the 'worst itch imaginable'. Weekly average PP NRS score was calculated using 7 consecutive days diary data and set to missing if less than 4 days data available. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered treatment failure. Subject with missing data were considered non-responders. The ITT population consisted of all randomised subjects. Data was planned to be collected and analysed for Initial Treatment Period.

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

End point timeframe:

Week 16

| End point values              | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 321                               | 620   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 11.2                              | 30.6  |  |  |

## Statistical analyses

|                            |            |
|----------------------------|------------|
| Statistical analysis title | Analysis 1 |
|----------------------------|------------|

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level.

|                   |   |
|-------------------|---|
| Comparison groups | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
|-------------------|---|

|   |                                       |
|---|---------------------------------------|
| Number of subjects included in analysis | 941                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| P-value                                 | < 0.0001 [9]                          |
| Method                                  | Cochran-Mantel-Haenszel               |
| Parameter estimate                      | Strata-adjusted percentage difference |
| Point estimate                          | 19.5                                  |
| Confidence interval                     |                                       |
| level                                   | Other: 97.5 %                         |
| sides                                   | 2-sided                               |
| lower limit                             | 13.7                                  |
| upper limit                             | 25.2                                  |

Notes:

[9] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe] and PP NRS [ $\geq 7$ ,  $< 7$ ]).

## Secondary: Percentage of Subjects With <2 Points in Weekly Average PP NRS at Week 16: Severe Pruritus Population

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With <2 Points in Weekly Average PP NRS at Week 16: Severe Pruritus Population |
|-----------------|---|

End point description:

The PP NRS is a scale that was used by the subject to report the intensity of their pruritus (itch) during the last 24 hours on a scale of 0 to 10, with 0 being 'no itch' and 10 being the 'worst itch imaginable'. Weekly average PP NRS score was calculated using 7 consecutive days diary data and set to missing if less than 4 days data available. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered treatment failure. Subjects with missing data were considered non-responders. Severe pruritus population consisted of all randomised subjects with a baseline PP NRS  $\geq 7$ . Data was planned to be collected and analysed for Initial Treatment Period.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Week 16              |           |

| End point values              | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 210                               | 406   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 7.6                               | 27.8  |  |  |

## Statistical analyses

|                            |            |
|----------------------------|------------|
| Statistical analysis title | Analysis 1 |
|----------------------------|------------|

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level.

|   |   |
|---|---|
| Comparison groups                       | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis | 616   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other   |
| P-value                                 | < 0.0001 <sup>[10]</sup>  |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Strata-adjusted percentage difference   |
| Point estimate                          | 20.3  |
| Confidence interval                     |   |
| level                                   | Other: 97.5 %   |
| sides                                   | 2-sided   |
| lower limit                             | 13.8  |
| upper limit                             | 26.8  |

Notes:

[10] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe]).

### Secondary: Percentage of Subjects With an Improvement of Sleep Disturbance Numeric Rating Scale (SD NRS) >=4 at Week 16: ITT Population

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With an Improvement of Sleep Disturbance Numeric Rating Scale (SD NRS) >=4 at Week 16: ITT Population |
|-----------------|--|

End point description:

The sleep disturbance NRS is a scale used by the subjects to report the degree of their sleep loss related to AD. Subjects were asked the following question in their local language: how would you rate your sleep last night? On a scale of 0 to 10, with 0 being 'no sleep loss related to signs/symptoms of AD' and 10 being 'I cannot sleep at all due to the signs/symptoms of AD'. Weekly average SD NRS score was calculated using 7 consecutive days diary data and set to missing if less than 4 days data available. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered treatment failure. Subjects with missing data were considered non-responders. The ITT population consisted of all randomised subjects.

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

End point timeframe:

Week 16

| End point values              | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 321                               | 620   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 19.9                              | 37.9  |  |  |

### Statistical analyses

|                            |            |
|----------------------------|------------|
| Statistical analysis title | Analysis 1 |
|----------------------------|------------|

**Statistical analysis description:**

A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level.

|   |   |
|---|---|
| Comparison groups                       | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis | 941   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other   |
| P-value                                 | < 0.0001 <sup>[11]</sup>  |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Strata-adjusted percentage difference   |
| Point estimate                          | 17.9  |
| Confidence interval                     |   |
| level                                   | Other: 97.5 %   |
| sides                                   | 2-sided   |
| lower limit                             | 11.3  |
| upper limit                             | 24.5  |

**Notes:**

[11] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe] and PP NRS [ $\geq 7$ ,  $< 7$ ]).

**Secondary: Percentage of Subjects With an Improvement of Sleep Disturbance Numeric Rating Scale (SD NRS)  $\geq 4$  at Week 16: Severe Pruritus Population**

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With an Improvement of Sleep Disturbance Numeric Rating Scale (SD NRS) $\geq 4$ at Week 16: Severe Pruritus Population |
|-----------------|---|

**End point description:**

The sleep disturbance NRS is a scale used by the subjects to report the degree of their sleep loss related to AD. Subjects were asked the following question in their local language: how would you rate your sleep last night? On a scale of 0 to 10, with 0 being 'no sleep loss related to signs/symptoms of AD' and 10 being 'I cannot sleep at all due to the signs/symptoms of AD'. Weekly average SD NRS score was calculated using 7 consecutive days diary data and set to missing if less than 4 days data available. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered treatment failure. Subjects with missing data were considered non-responders. Severe pruritus population consisted of all randomised subjects with a baseline PP NRS  $\geq 7$ .

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

**End point timeframe:**

Week 16

| End point values              | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 210                               | 406   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 22.4                              | 42.1  |  |  |

## Statistical analyses

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Analysis 1  |
| Statistical analysis description:<br>A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level. |   |
| Comparison groups  | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis  | 616   |
| Analysis specification   | Pre-specified   |
| Analysis type  | other   |
| P-value  | < 0.0001 <sup>[12]</sup>  |
| Method   | Cochran-Mantel-Haenszel   |
| Parameter estimate   | Strata-adjusted percentage difference   |
| Confidence interval  |   |
| level  | Other: 97.5 %   |
| sides  | 2-sided   |
| lower limit  | 11.2  |
| upper limit  | 28.2  |

Notes:

[12] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe]).

### Secondary: Percentage of Subjects With Improvement of $\geq 4$ Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 4: ITT Population

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With Improvement of $\geq 4$ Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 4: ITT Population |
|-----------------|--|

End point description:

The PP NRS is a scale that was used by the subjects to report the intensity of their pruritus (itch) during the last 24 hours on a scale of 0 to 10, with 0 being 'no itch' and 10 being the 'worst itch imaginable'. Weekly average PP NRS score was calculated using 7 consecutive days diary data and set to missing if less than 4 days data available. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered treatment failure. Subjects with missing data were considered non-responders. The ITT population consisted of all randomised subjects. Data was planned to be collected and analysed for Initial Treatment Period.

|                                |           |
|--------------------------------|-----------|
| End point type                 | Secondary |
| End point timeframe:<br>Week 4 |           |

| End point values              | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 321                               | 620   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 6.5                               | 27.4  |  |  |

## Statistical analyses

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Analysis 1  |
| Statistical analysis description:<br>A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level. |   |
| Comparison groups  | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis  | 941   |
| Analysis specification   | Pre-specified   |
| Analysis type  | other   |
| P-value  | < 0.0001 <sup>[13]</sup>  |
| Method   | Cochran-Mantel-Haenszel   |
| Parameter estimate   | Strata-adjusted percentage difference   |
| Point estimate   | 20.9  |
| Confidence interval  |   |
| level  | Other: 97.5 %   |
| sides  | 2-sided   |
| lower limit  | 15.8  |
| upper limit  | 26  |

Notes:

[13] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe] and PP NRS [ $\geq 7$ ,  $< 7$ ]).

## Secondary: Percentage of Subjects With Improvement of $\geq 4$ Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 4: Severe Pruritus Population

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With Improvement of $\geq 4$ Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 4: Severe Pruritus Population |
|-----------------|--|

End point description:

The PP NRS is a scale that was used by the subjects to report the intensity of their pruritus (itch) during the last 24 hours on a scale of 0 to 10, with 0 being 'no itch' and 10 being the 'worst itch imaginable'. Weekly average PP NRS score was calculated using 7 consecutive days diary data and set to missing if less than 4 days data available. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered treatment failure. Subjects with missing data were considered non-responders. Severe pruritus population consisted of all randomised subjects with a baseline PP NRS  $\geq 7$ . Data was planned to be collected and analysed for Initial Treatment Period.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Week 4               |           |

|                               |                                   |   |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| <b>End point values</b>       | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 210                               | 406   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 7.1                               | 28.3  |  |  |

## Statistical analyses

|                                   |            |
|-----------------------------------|------------|
| <b>Statistical analysis title</b> | Analysis 1 |
|-----------------------------------|------------|

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level.

|   |   |
|---|---|
| Comparison groups                       | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis | 616   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other   |
| P-value                                 | < 0.0001 <sup>[14]</sup>  |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Strata-adjusted percentage difference   |
| Point estimate                          | 21.2  |
| Confidence interval                     |   |
| level                                   | Other: 97.5 %   |
| sides                                   | 2-sided   |
| lower limit                             | 14.8  |
| upper limit                             | 27.6  |

Notes:

[14] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe]).

## Secondary: Percentage of Subjects With Peak Pruritus Numeric Rating Scale (PP NRS) <2 at Week 4: ITT Population

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With Peak Pruritus Numeric Rating Scale (PP NRS) <2 at Week 4: ITT Population |
|-----------------|--|

End point description:

The PP NRS is a scale that was used by the subjects to report the intensity of their pruritus (itch) during the last 24 hours on a scale of 0 to 10, with 0 being 'no itch' and 10 being the 'worst itch imaginable'. Weekly average PP NRS score was calculated using 7 consecutive days diary data and set to missing if less than 4 days data available. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered treatment failure. Subjects with missing data were considered non-responders. The ITT population consisted of all randomised subjects. Data was planned to be collected and analysed for Initial Treatment Period.

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

End point timeframe:

Week 4

| <b>End point values</b>       | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 321                               | 620   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 3.7                               | 16  |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>   | Analysis 1  |
|---|---|
| Statistical analysis description:   |   |
| A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level. |   |
| Comparison groups   | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis   | 941   |
| Analysis specification  | Pre-specified   |
| Analysis type   | other   |
| P-value   | < 0.0001 <sup>[15]</sup>  |
| Method  | Cochran-Mantel-Haenszel   |
| Parameter estimate  | Strata-adjusted percentage difference   |
| Point estimate  | 12.2  |
| Confidence interval   |   |
| level   | Other: 97.5 %   |
| sides   | 2-sided   |
| lower limit   | 8.2   |
| upper limit   | 16.3  |

Notes:

[15] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe] and PP NRS [ $\geq 7$ ,  $< 7$ ]).

## Secondary: Percentage of Subjects With Peak Pruritus Numeric Rating Scale (PP NRS) <2 at Week 4: Severe Pruritus Population

|   |  |
|---|--|
| End point title   | Percentage of Subjects With Peak Pruritus Numeric Rating Scale (PP NRS) <2 at Week 4: Severe Pruritus Population |
| End point description:  |  |
| The PP NRS is a scale that was used by the subjects to report the intensity of their pruritus (itch) during the last 24 hours on a scale of 0 to 10, with 0 being 'no itch' and 10 being the 'worst itch imaginable'. Weekly average PP NRS score was calculated using 7 consecutive days diary data and set to missing if less than 4 days data available. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered treatment failure. Subjects with missing data were considered non-responders. Severe pruritus population consisted of all randomised subjects with a baseline PP NRS $\geq 7$ . Data was planned to be collected and analysed for Initial Treatment Period. |  |
| End point type  | Secondary  |



End point timeframe:

Week 4

| End point values              | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 210                               | 406   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 2.9                               | 12.6  |  |  |

## Statistical analyses

| Statistical analysis title | Analysis 1 |
|----------------------------|------------|
|----------------------------|------------|

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level.

|   |   |
|---|---|
| Comparison groups                       | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis | 616   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other   |
| P-value                                 | < 0.0001 <sup>[16]</sup>  |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Strata-adjusted percentage difference   |
| Point estimate                          | 9.7   |
| Confidence interval                     |   |
| level                                   | Other: 97.5 %   |
| sides                                   | 2-sided   |
| lower limit                             | 5.2   |
| upper limit                             | 14.2  |

Notes:

[16] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe]).

## Secondary: Percentage of Subjects With Improvement of $\geq 4$ Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 2: ITT Population

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With Improvement of $\geq 4$ Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 2: ITT Population |
|-----------------|--|

End point description:

The PP NRS is a scale that was used by the subjects to report the intensity of their pruritus (itch) during the last 24 hours on a scale of 0 to 10, with 0 being 'no itch' and 10 being the 'worst itch imaginable'. Weekly average PP NRS score was calculated using 7 consecutive days diary data and set to missing if less than 4 days data available. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered treatment failure. Subjects with missing data were considered non-responders. The ITT population consisted of all randomised subjects. Data was planned to be collected and analysed

for Initial Treatment Period.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Week 2               |           |

| End point values              | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 321                               | 620   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 3.1                               | 17.7  |  |  |

## Statistical analyses

|                            |            |
|----------------------------|------------|
| Statistical analysis title | Analysis 1 |
|----------------------------|------------|

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level.

|   |   |
|---|---|
| Comparison groups                       | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis | 941   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other   |
| P-value                                 | < 0.0001 <sup>[17]</sup>  |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Strata-adjusted percentage difference   |
| Point estimate                          | 14.6  |
| Confidence interval                     |   |
| level                                   | Other: 97.5 %   |
| sides                                   | 2-sided   |
| lower limit                             | 10.6  |
| upper limit                             | 18.7  |

Notes:

[17] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe] and PP NRS [ $\geq 7$ ,  $< 7$ ]).

## Secondary: Percentage of Subjects With Improvement of $\geq 4$ Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 2: Severe Pruritus Population

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With Improvement of $\geq 4$ Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 2: Severe Pruritus Population |
|-----------------|--|

End point description:

The PP NRS is a scale that was used by the subjects to report the intensity of their pruritus (itch) during

the last 24 hours on a scale of 0 to 10, with 0 being 'no itch' and 10 being the 'worst itch imaginable'. Weekly average PP NRS score was calculated using 7 consecutive days diary data and set to missing if less than 4 days data available. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered treatment failure. Subjects with missing data were considered non-responders. Severe pruritus population consisted of all randomised subjects with a baseline PP NRS  $\geq 7$ . Data was planned to be collected and analysed for Initial Treatment Period.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Week 2               |           |

| End point values              | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 210                               | 406   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 3.8                               | 20.7  |  |  |

## Statistical analyses

|                            |            |
|----------------------------|------------|
| Statistical analysis title | Analysis 1 |
|----------------------------|------------|

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level.

|   |   |
|---|---|
| Comparison groups                       | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis | 616   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other   |
| P-value                                 | $< 0.0001$ <sup>[18]</sup>  |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Strata-adjusted percentage difference   |
| Point estimate                          | 16.9  |
| Confidence interval                     |   |
| level                                   | Other: 97.5 %   |
| sides                                   | 2-sided   |
| lower limit                             | 11.5  |
| upper limit                             | 22.3  |

Notes:

[18] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe]).

## Secondary: Percentage of Subjects With Improvement of $\geq 4$ Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 1: ITT Population

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With Improvement of $\geq 4$ Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) |
|-----------------|--|

## End point description:

The PP NRS is a scale that was used by the subjects to report the intensity of their pruritus (itch) during the last 24 hours on a scale of 0 to 10, with 0 being 'no itch' and 10 being the 'worst itch imaginable'. Weekly average PP NRS score was calculated using 7 consecutive days diary data and set to missing if less than 4 days data available. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered treatment failure. Subjects with missing data were considered non-responders. The ITT population consisted of all randomised subjects. Data was planned to be collected and analysed for Initial Treatment Period.

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

End point timeframe:

|        |
|--------|
| Week 1 |
|--------|

| End point values              | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 321                               | 620   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 1.2                               | 4.5   |  |  |

## Statistical analyses

|                            |            |
|----------------------------|------------|
| Statistical analysis title | Analysis 1 |
|----------------------------|------------|

## Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level.

|   |   |
|---|---|
| Comparison groups                       | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis | 941   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other   |
| P-value                                 | = 0.0064 <sup>[19]</sup>  |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Strata-adjusted percentage difference   |
| Point estimate                          | 3.4   |
| Confidence interval                     |   |
| level                                   | Other: 97.5 %   |
| sides                                   | 2-sided   |
| lower limit                             | 1.1   |
| upper limit                             | 5.8   |

## Notes:

[19] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe] and PP NRS [ $\geq 7$ ,  $<7$ ]).

## Secondary: Percentage of Subjects With Improvement of $\geq 4$ Points in Weekly Average Peak Pruritus Numeric Rating Scale: Severe Pruritus Population

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With Improvement of $\geq 4$ Points in Weekly Average Peak Pruritus Numeric Rating Scale: Severe Pruritus Population |
|-----------------|---|

### End point description:

The PP NRS is a scale that was used by the subjects to report the intensity of their pruritus (itch) during the last 24 hours on a scale of 0 to 10, with 0 being 'no itch' and 10 being the 'worst itch imaginable'. Weekly average PP NRS score was calculated using 7 consecutive days diary data and set to missing if less than 4 days data available. If a subject received any rescue therapy, the data after receipt of rescue therapy was considered treatment failure. Subjects with missing data were considered non-responders. Severe pruritus population consisted of all randomised subjects with a baseline PP NRS  $\geq 7$ . Data was planned to be collected and analysed for Initial Treatment Period.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Week 1               |           |

| End point values              | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg |  |  |
|-------------------------------|-----------------------------------|---|--|--|
| Subject group type            | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed   | 210                               | 406   |  |  |
| Units: percentage of subjects |                                   |   |  |  |
| number (not applicable)       | 1.9                               | 6.2   |  |  |

## Statistical analyses

|                            |            |
|----------------------------|------------|
| Statistical analysis title | Analysis 1 |
|----------------------------|------------|

### Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was performed sequentially in order the endpoints were reported and continued when the test for preceding endpoint was statistically significant at two-sided 2.5% significance level.

|   |   |
|---|---|
| Comparison groups                       | Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg |
| Number of subjects included in analysis | 616   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other   |
| P-value                                 | = 0.0177 [20]   |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Strata-adjusted percentage difference   |
| Point estimate                          | 4.3   |
| Confidence interval                     |   |
| level                                   | Other: 97.5 %   |
| sides                                   | 2-sided   |
| lower limit                             | 0.9   |
| upper limit                             | 7.7   |

---

Notes:

[20] - Strata-adjusted p-values were calculated from Cochran-Mantel-Haenszel test adjusting randomised stratification variables (IGA severity [3=moderate, 4=severe]).

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Initial Treatment Period: From baseline to Week 16 pre-dose; Maintenance Period: From end of Initial Treatment Period to Week 48

Adverse event reporting additional description:

The safety population comprised all subjects who received at least 1 dose of study drug. One subject was re-randomized to Nemolizumab Q8W for Maintenance Period, but erroneously received Nemolizumab three times consecutively and thus counted in Nemolizumab 30 mg Q4W to Q4W for safety analysis.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 25.0 |
|--------------------|------|

### Reporting groups

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Initial Treatment Period: Placebo |
|-----------------------|-----------------------------------|

Reporting group description:

Subjects received placebo via 2 subcutaneous (SC) injections at Day 1, thereafter, every 4 weeks (Q4W), at Weeks 4, 8, and 12 by a single SC injection during Initial Treatment Period.

|                       |   |
|-----------------------|---|
| Reporting group title | Initial Treatment Period: Nemolizumab 30 mg |
|-----------------------|---|

Reporting group description:

Subjects received nemolizumab 30 mg via 2 SC injections at Day 1, thereafter, Q4W at Weeks 4, 8, and 12 by a single SC injection during Initial Treatment Period.

|                       |  |
|-----------------------|--|
| Reporting group title | Maintenance Period: Nemolizumab 30 mg Q4W to Q4W |
|-----------------------|--|

Reporting group description:

Subjects who received nemolizumab, Q4W during Initial Treatment Period and were clinical responders at Week 16 received nemolizumab 30 mg, Q4W at Weeks 16, 20, 24, 28, 32, 36, 40, and 44 by a single SC injection during Maintenance Period.

|                       |  |
|-----------------------|--|
| Reporting group title | Maintenance Period: Nemolizumab 30 mg Q4W to Q8W |
|-----------------------|--|

Reporting group description:

Subjects who received nemolizumab, Q4W during Initial Treatment Period and were clinical responders at Week 16 received nemolizumab 30 mg, Q8W at Weeks 16, 24, 32, and 40 by a single SC injection during Maintenance Period.

|                       |  |
|-----------------------|--|
| Reporting group title | Maintenance Period: Nemolizumab 30 mg Q4W to Placebo Q8W |
|-----------------------|--|

Reporting group description:

Subjects who received nemolizumab, Q4W during Initial Treatment Period and were clinical responders at Week 16 received placebo, Q4W at Weeks 16, 20, 24, 28, 32, 36, 40, and 44 by a single SC injection during Maintenance Period.

|                       |  |
|-----------------------|--|
| Reporting group title | Maintenance Period: Placebo Q4W Re-assigned to Placebo Q4W |
|-----------------------|--|

Reporting group description:

Subjects who received placebo, Q4W during Initial Treatment Period and were clinical responders at Week 16 received placebo, Q4W at Weeks 16, 20, 24, 28, 32, 36, 40, and 44 by a single SC injection during Maintenance Period.

| Serious adverse events                            | Initial Treatment Period: Placebo | Initial Treatment Period: Nemolizumab 30 mg | Maintenance Period: Nemolizumab 30 mg Q4W to Q4W |
|---|-----------------------------------|---|--|
| Total subjects affected by serious adverse events |                                   |   |  |
| subjects affected / exposed                       | 4 / 321 (1.25%)                   | 6 / 616 (0.97%)                             | 4 / 91 (4.40%)                                   |

|   |                 |                 |                |
|---|-----------------|-----------------|----------------|
| number of deaths (all causes)<br>number of deaths resulting from<br>adverse events  | 0               | 0               | 0              |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps)<br>Plasmablastic lymphoma<br>subjects affected / exposed | 0 / 321 (0.00%) | 0 / 616 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 0           | 0 / 0           | 0 / 0          |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0           | 0 / 0          |
| Salivary gland cancer<br>subjects affected / exposed  | 0 / 321 (0.00%) | 1 / 616 (0.16%) | 0 / 91 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 0           | 1 / 1           | 0 / 0          |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0           | 0 / 0          |
| Uterine leiomyoma<br>subjects affected / exposed  | 0 / 321 (0.00%) | 1 / 616 (0.16%) | 0 / 91 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 0           | 1 / 1           | 0 / 0          |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0           | 0 / 0          |
| Injury, poisoning and procedural<br>complications<br>Meniscus injury<br>subjects affected / exposed                             | 0 / 321 (0.00%) | 0 / 616 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 0           | 0 / 0           | 0 / 0          |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0           | 0 / 0          |
| Splenic injury<br>subjects affected / exposed   | 0 / 321 (0.00%) | 0 / 616 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 0           | 0 / 0           | 0 / 0          |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0           | 0 / 0          |
| Nervous system disorders<br>Lumbar radiculopathy<br>subjects affected / exposed   | 0 / 321 (0.00%) | 1 / 616 (0.16%) | 0 / 91 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 0           | 1 / 1           | 0 / 0          |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0           | 0 / 0          |
| Skin and subcutaneous tissue disorders<br>Dermatitis atopic<br>subjects affected / exposed                                      | 3 / 321 (0.93%) | 2 / 616 (0.32%) | 0 / 91 (0.00%) |
| occurrences causally related to<br>treatment / all  | 3 / 3           | 0 / 2           | 0 / 0          |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0           | 0 / 0          |



|   |                 |                 |                |
|---|-----------------|-----------------|----------------|
| Psychiatric disorders                           |                 |                 |                |
| Anxiety   |                 |                 |                |
| subjects affected / exposed                     | 0 / 321 (0.00%) | 0 / 616 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Renal and urinary disorders                     |                 |                 |                |
| Renal colic                                     |                 |                 |                |
| subjects affected / exposed                     | 0 / 321 (0.00%) | 1 / 616 (0.16%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Endocrine disorders                             |                 |                 |                |
| Goitre  |                 |                 |                |
| subjects affected / exposed                     | 0 / 321 (0.00%) | 0 / 616 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                 |                 |                |
| Dupuytren's contracture                         |                 |                 |                |
| subjects affected / exposed                     | 0 / 321 (0.00%) | 0 / 616 (0.00%) | 1 / 91 (1.10%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Periarthritis                                   |                 |                 |                |
| subjects affected / exposed                     | 0 / 321 (0.00%) | 0 / 616 (0.00%) | 1 / 91 (1.10%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Infections and infestations                     |                 |                 |                |
| Appendicitis                                    |                 |                 |                |
| subjects affected / exposed                     | 0 / 321 (0.00%) | 0 / 616 (0.00%) | 1 / 91 (1.10%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| COVID-19  |                 |                 |                |
| subjects affected / exposed                     | 0 / 321 (0.00%) | 0 / 616 (0.00%) | 1 / 91 (1.10%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| COVID-19 pneumonia                              |                 |                 |                |

|   |                 |                 |                |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed                     | 1 / 321 (0.31%) | 0 / 616 (0.00%) | 0 / 91 (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          |
| Cellulitis                                      |                 |                 |                |
| subjects affected / exposed                     | 0 / 321 (0.00%) | 0 / 616 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Erysipelas                                      |                 |                 |                |
| subjects affected / exposed                     | 0 / 321 (0.00%) | 0 / 616 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |

| <b>Serious adverse events</b>                                       | Maintenance Period:<br>Nemolizumab 30 mg<br>Q4W to Q8W | Maintenance Period:<br>Nemolizumab 30 mg<br>Q4W to Placebo<br>Q8W | Maintenance Period:<br>Placebo Q4W Re-<br>assigned to Placebo<br>Q4W |
|---|--|---|--|
| Total subjects affected by serious adverse events                   |  |   |  |
| subjects affected / exposed   | 3 / 90 (3.33%)   | 2 / 91 (2.20%)  | 1 / 100 (1.00%)  |
| number of deaths (all causes)                                       | 0  | 0   | 0  |
| number of deaths resulting from adverse events                      |  |   |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |   |  |
| Plasmablastic lymphoma  |  |   |  |
| subjects affected / exposed   | 0 / 90 (0.00%)   | 1 / 91 (1.10%)  | 0 / 100 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0  | 1 / 1   | 0 / 0  |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0   | 0 / 0  |
| Salivary gland cancer   |  |   |  |
| subjects affected / exposed   | 0 / 90 (0.00%)   | 0 / 91 (0.00%)  | 0 / 100 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0  | 0 / 0   | 0 / 0  |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0   | 0 / 0  |
| Uterine leiomyoma   |  |   |  |
| subjects affected / exposed   | 0 / 90 (0.00%)   | 0 / 91 (0.00%)  | 0 / 100 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0  | 0 / 0   | 0 / 0  |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0   | 0 / 0  |
| Injury, poisoning and procedural complications                      |  |   |  |
| Meniscus injury   |  |   |  |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 90 (0.00%) | 0 / 91 (0.00%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Splenic injury                                  |                |                |                 |
| subjects affected / exposed                     | 1 / 90 (1.11%) | 0 / 91 (0.00%) | 0 / 100 (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           |
| Nervous system disorders                        |                |                |                 |
| Lumbar radiculopathy                            |                |                |                 |
| subjects affected / exposed                     | 0 / 90 (0.00%) | 0 / 91 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Skin and subcutaneous tissue disorders          |                |                |                 |
| Dermatitis atopic                               |                |                |                 |
| subjects affected / exposed                     | 0 / 90 (0.00%) | 0 / 91 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Psychiatric disorders                           |                |                |                 |
| Anxiety   |                |                |                 |
| subjects affected / exposed                     | 1 / 90 (1.11%) | 0 / 91 (0.00%) | 0 / 100 (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           |
| Renal and urinary disorders                     |                |                |                 |
| Renal colic                                     |                |                |                 |
| subjects affected / exposed                     | 0 / 90 (0.00%) | 0 / 91 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Endocrine disorders                             |                |                |                 |
| Goitre  |                |                |                 |
| subjects affected / exposed                     | 0 / 90 (0.00%) | 1 / 91 (1.10%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Musculoskeletal and connective tissue disorders |                |                |                 |
| Dupuytren's contracture                         |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 90 (0.00%) | 0 / 91 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Periarthritis                                   |                |                |                 |
| subjects affected / exposed                     | 0 / 90 (0.00%) | 0 / 91 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Infections and infestations                     |                |                |                 |
| Appendicitis                                    |                |                |                 |
| subjects affected / exposed                     | 0 / 90 (0.00%) | 0 / 91 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| COVID-19  |                |                |                 |
| subjects affected / exposed                     | 0 / 90 (0.00%) | 0 / 91 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| COVID-19 pneumonia                              |                |                |                 |
| subjects affected / exposed                     | 0 / 90 (0.00%) | 0 / 91 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Cellulitis                                      |                |                |                 |
| subjects affected / exposed                     | 1 / 90 (1.11%) | 0 / 91 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 0           |
| Erysipelas                                      |                |                |                 |
| subjects affected / exposed                     | 0 / 90 (0.00%) | 1 / 91 (1.10%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |

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

| <b>Non-serious adverse events</b>   | Initial Treatment Period: Placebo  | Initial Treatment Period: Nemolizumab 30 mg                                    | Maintenance Period: Nemolizumab 30 mg Q4W to Q4W                           |
|---|--|--|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed  | 67 / 321 (20.87%)  | 144 / 616 (23.38%)   | 27 / 91 (29.67%)   |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)  | 11 / 321 (3.43%)<br>12   | 28 / 616 (4.55%)<br>37   | 5 / 91 (5.49%)<br>7  |
| Respiratory, thoracic and mediastinal disorders<br>Asthma<br>subjects affected / exposed<br>occurrences (all)   | 13 / 321 (4.05%)<br>14   | 33 / 616 (5.36%)<br>33   | 3 / 91 (3.30%)<br>3  |
| Skin and subcutaneous tissue disorders<br>Dermatitis atopic<br>subjects affected / exposed<br>occurrences (all)   | 33 / 321 (10.28%)<br>39  | 73 / 616 (11.85%)<br>92  | 7 / 91 (7.69%)<br>8  |
| Infections and infestations<br>COVID-19<br>subjects affected / exposed<br>occurrences (all)<br><br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 6 / 321 (1.87%)<br>6<br><br>8 / 321 (2.49%)<br>8<br><br>14 / 321 (4.36%)<br>14 | 10 / 616 (1.62%)<br>10<br><br>9 / 616 (1.46%)<br>9<br><br>9 / 616 (1.46%)<br>9 | 9 / 91 (9.89%)<br>9<br><br>7 / 91 (7.69%)<br>10<br><br>3 / 91 (3.30%)<br>3 |

| <b>Non-serious adverse events</b>  | Maintenance Period: Nemolizumab 30 mg Q4W to Q8W | Maintenance Period: Nemolizumab 30 mg Q4W to Placebo Q8W | Maintenance Period: Placebo Q4W Re-assigned to Placebo Q4W |
|--|--|--|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed     | 28 / 90 (31.11%)                                 | 33 / 91 (36.26%)   | 35 / 100 (35.00%)  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all) | 5 / 90 (5.56%)<br>10                             | 3 / 91 (3.30%)<br>4                                      | 1 / 100 (1.00%)<br>1                                       |
| Respiratory, thoracic and mediastinal disorders  |  |  |  |

|   |                      |                        |                         |
|---|----------------------|------------------------|-------------------------|
| Asthma<br>subjects affected / exposed<br>occurrences (all)  | 6 / 90 (6.67%)<br>6  | 5 / 91 (5.49%)<br>5    | 5 / 100 (5.00%)<br>8    |
| Skin and subcutaneous tissue disorders<br>Dermatitis atopic<br>subjects affected / exposed<br>occurrences (all) | 8 / 90 (8.89%)<br>8  | 12 / 91 (13.19%)<br>15 | 10 / 100 (10.00%)<br>11 |
| Infections and infestations<br>COVID-19<br>subjects affected / exposed<br>occurrences (all)                     | 9 / 90 (10.00%)<br>9 | 6 / 91 (6.59%)<br>7    | 10 / 100 (10.00%)<br>10 |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)   | 5 / 90 (5.56%)<br>6  | 7 / 91 (7.69%)<br>9    | 6 / 100 (6.00%)<br>6    |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                           | 3 / 90 (3.33%)<br>3  | 5 / 91 (5.49%)<br>5    | 9 / 100 (9.00%)<br>11   |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported