



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	2019-001888-75
Trial protocol	DE FR BE BG PL IT
Global end of trial date	26 September 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.118169
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03989349
WHO universal trial number (UTN)	-
Other trial identifiers	IND number: 17122

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., CTA.Coordinator@galderma.com
Scientific contact	Clinical Trial Information Desk, Galderma S.A., 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	26 September 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	26 September 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 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 regulations.

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	Poland: 265
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	Bulgaria: 79
Country: Number of subjects enrolled	Estonia: 14
Country: Number of subjects enrolled	France: 39
Country: Number of subjects enrolled	Germany: 107
Country: Number of subjects enrolled	Hungary: 36
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Georgia: 11
Country: Number of subjects enrolled	Singapore: 14
Country: Number of subjects enrolled	United States: 195
Worldwide total number of subjects	787
EEA total number of subjects	567

Notes:

Subjects enrolled per age group

In utero	0
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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)	132
Adults (18-64 years)	603
From 65 to 84 years	52
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 136 active sites in Belgium, Bulgaria, Estonia, France, Georgia, Germany, Hungary, Italy, Poland, Singapore, and the United States from 27 June 2019 to 26 September 2022.

Pre-assignment

Screening details:

A total of 787 randomized 2:1 to receive either nemolizumab or placebo. At Week 16, 235 nemolizumab treated responders re-randomized to receive nemolizumab Q4W, nemolizumab Q8W, or placebo during Maintenance Period. 85 subjects received placebo in Initial Treatment, responded to placebo at Week 16, re-assigned to placebo and continued with 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
Arm title	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:

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

Arm title	Initial Treatment Period: Nemolizumab 30 mg
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Arm description:

Subjects received nemolizumab 30 milligrams (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:

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.

Number of subjects in period 1	Initial Treatment Period: Placebo	Initial Treatment Period: Nemolizumab 30 mg
Started	265	522
Completed	241	470
Not completed	24	52
Consent withdrawn by subject	15	24
Physician decision	-	1
Adverse event, non-fatal	4	17
Randomised but not treated	2	3
Lost to follow-up	1	1
Protocol deviation	2	3
Lack of efficacy	-	3

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
Arm title	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, 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:

Subjects who received nemolizumab, Q4W during Initial Treatment Period and were clinical responders at Week 16 received placebo, Q8W at Weeks 20, 28, 36, and 44 by a single SC injection during Maintenance Period.

Arm title	Nemolizumab 30 mg Q4W to Q8W
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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
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Investigational medicinal product name	Nemolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

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.

Arm title	Maintenance Period: Nemolizumab 30 mg Q4W to Placebo Q4W
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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, Q8W 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	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects who received nemolizumab, Q4W during Initial Treatment Period and were clinical responders at Week 16 received placebo, Q8W at Weeks 20, 28, 36, and 44 by a single SC injection during Maintenance Period.

Arm title	Placebo Q4W Re-assigned to Placebo Q4W
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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	Placebo
Investigational medicinal product name	Nemolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

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.

Number of subjects in period 2 ^[1]	Maintenance Period: Nemolizumab 30 mg Q4W to Q4W	Nemolizumab 30 mg Q4W to Q8W	Maintenance Period: Nemolizumab 30 mg Q4W to Placebo Q4W
Started	79	78	78
Completed	65	68	65
Not completed	14	10	13
Consent withdrawn by subject	2	3	1
Physician decision	1	1	-

Re-randomized/Re-assigned but not Treated	1	-	1
Adverse event, non-fatal	3	2	3
other	4	2	2
Lost to follow-up	1	-	3
Lack of efficacy	2	2	3

Number of subjects in period 2^[1]	Placebo Q4W Re-assigned to Placebo Q4W
Started	85
Completed	74
Not completed	11
Consent withdrawn by subject	4
Physician decision	1
Re-randomized/Re-assigned but not Treated	1
Adverse event, non-fatal	2
other	-
Lost to follow-up	-
Lack of efficacy	3

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: Initial Treatment Period. At Week 16, 272 nemolizumab-treated participants who were clinical responders were re-randomized to receive nemolizumab Q4W, nemolizumab Q8W, or placebo during Maintenance Period. 85 participants who received placebo in Initial Treatment Period and responded to placebo at Week 16, were re-assigned to placebo and continued to receive placebo Q4W in 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 milligrams (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	265	522	787
Age categorical			
Units: Subjects			
Adolescents (12-17 years)	41	91	132
Adults (18-64 years)	209	394	603
From 65-84 years	15	37	52
Gender categorical			
Units: Subjects			
Female	136	270	406
Male	129	252	381
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	19	44	63
Not Hispanic or Latino	244	464	708
Unknown or Not Reported	2	14	16
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	18	35	53
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	20	25	45
White	227	458	685
Unknown or Not Reported	0	2	2

End points

End points 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 milligrams (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 (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, Q4W at Weeks 16, 20, 24, 28, 32, 36, 40, and 44 by a single SC injection during Maintenance Period.	
Reporting group title	Nemolizumab 30 mg Q4W to Q8W
Reporting group 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.	
Reporting group title	Maintenance Period: Nemolizumab 30 mg Q4W to Placebo Q4W
Reporting group 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, Q8W at Weeks 16, 20, 24, 28, 32, 36, 40, and 44 by a single SC injection during Maintenance Period.	
Reporting group title	Placebo Q4W Re-assigned to Placebo Q4W
Reporting group 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.	

Primary: Percentage of Subjects With Investigator's Global Assessment (IGA) Success at Week 16: Intent-To-Treat (ITT) Population

End point title	Percentage of Subjects With Investigator's Global Assessment (IGA) Success at Week 16: Intent-To-Treat (ITT) 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 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	265	522		
Units: Percentage of subjects				
number (not applicable)	26.0	37.7		

Statistical analyses

Statistical analysis title	Statistical 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	787
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0006 ^[1]
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	4.6
upper limit	19.8

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 [≥ 7 , < 7]).

Primary: Percentage of Subjects With Investigator's Global Assessment (IGA) Success at Week 16: Severe Pruritus Population

End point title	Percentage of Subjects With Investigator's Global Assessment (IGA) Success at Week 16: 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 ≥ 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	164	316		
Units: percentage of subjects				
number (not applicable)	22.0	36.7		

Statistical analyses

Statistical analysis title	Statistical 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	480
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0008 [2]
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	5.6
upper limit	24.3

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 ≥ 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	265	522		
Units: percentage of subjects				
number (not applicable)	30.2	42.1		

Statistical analyses

Statistical analysis title	Statistical 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	787
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0006 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	12.5
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	4.6
upper limit	20.3

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 [≥ 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
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End point description:

EASI-75 was defined as ≥ 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. Severe pruritus population consisted of all randomised subjects with a baseline PP NRS ≥ 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	164	316		
Units: percentage of subjects				
number (not applicable)	25.0	41.1		

Statistical analyses

Statistical analysis title	Statistical 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	480
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0004 ^[4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	16.3
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	6.6
upper limit	26

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 ≥ 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 ≥ 4 Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 16: ITT Population
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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	265	522		
Units: percentage of subjects				
number (not applicable)	18.1	41.0		

Statistical analyses

Statistical analysis title	Statistical 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	787
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	23.2
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	16.1
upper limit	30.3

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 [≥ 7 , <7]).

Statistical analysis title	Statistical 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: Placebo v Initial Treatment Period: Nemolizumab 30 mg

Number of subjects included in analysis	787
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	27.8
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	21.2
upper limit	34.5

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 [≥ 7 , < 7]).

Secondary: Percentage of Subjects With Improvement of ≥ 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 ≥ 4 Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 16: Severe Pruritus Population
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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 ≥ 7 . Data was planned to be collected and analysed for Initial Treatment Period.

End point type	Secondary
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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	164	316		
Units: percentage of subjects				
number (not applicable)	21.3	48.4		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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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	480
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	27.1
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	17.5
upper limit	36.6

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	Statistical Analysis 2: MI-MAR Method
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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	480
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	33.4
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	24.5
upper limit	42.3

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
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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
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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	265	522		
Units: percentage of subjects				
number (not applicable)	11.3	28.4		

Statistical analyses

Statistical analysis title	Statistical 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	787
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	17.1
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	10.9
upper limit	23.3

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 [≥ 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 ≥ 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	164	316		
Units: percentage of subjects				
number (not applicable)	8.5	26.9		

Statistical analyses

Statistical analysis title	Statistical 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	480
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	18.4
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	11
upper limit	25.8

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. 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	265	522		
Units: percentage of subjects				
number (not applicable)	16.2	33.5		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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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	787
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[11]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	17.5
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	10.8
upper limit	24.3

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 [≥ 7 , < 7]).

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

End point title	Percentage of Subjects With an Improvement of Sleep Disturbance Numeric Rating Scale (SD NRS) ≥ 4 at Week 16: Severe Pruritus Population
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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 ≥ 7 . Data was planned to be collected and

analyzed 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	164	316		
Units: percentage of subjects				
number (not applicable)	20.7	42.7		

Statistical analyses

Statistical analysis title	Statistical 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	480
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[12]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	21.9
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	12.5
upper limit	31.4

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 ≥ 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 ≥ 4 Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 4: ITT Population
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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	

End point values	Initial Treatment Period: Placebo	Initial Treatment Period: Nemolizumab 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	522		
Units: percentage of subjects				
number (not applicable)	5.3	26.1		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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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	787
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[13]
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	15.6
upper limit	26.1

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 [≥ 7 , < 7]).

Secondary: Percentage of Subjects With Improvement of ≥ 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 ≥ 4 Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 4: Severe Pruritus Population
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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 ≥ 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	164	316		
Units: percentage of subjects				
number (not applicable)	7.9	30.4		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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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	480
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[14]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	22.5
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	15
upper limit	29.9

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
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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	

End point values	Initial Treatment Period: Placebo	Initial Treatment Period: Nemolizumab 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	522		
Units: percentage of subjects				
number (not applicable)	2.6	15.9		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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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	787
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[15]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	13.2
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	9
upper limit	17.4

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 [≥ 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 ≥ 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	164	316		
Units: percentage of subjects				
number (not applicable)	1.2	11.1		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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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	480
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0001 ^[16]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	9.9
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	5.5
upper limit	14.3

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 ≥ 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 ≥ 4 Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 2: ITT Population
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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	265	522		
Units: percentage of subjects				
number (not applicable)	1.9	16.9		

Statistical analyses

Statistical analysis title	Statistical 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	787
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[17]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	15.1
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	11
upper limit	19.2

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 [≥ 7 , < 7]).

Secondary: Percentage of Subjects With Improvement of ≥ 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 ≥ 4 Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS) at Week 2: Severe Pruritus Population
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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 ≥ 7 . Data was planned to be collected and analysed for Initial Treatment Period.

End point type	Secondary
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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	164	316		
Units: percentage of subjects				
number (not applicable)	3.0	19.3		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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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	480
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[18]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	16.3
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	10.5
upper limit	22.1

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 ≥ 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 ≥ 4 Points in Weekly Average Peak Pruritus Numeric Rating Scale (PP NRS)
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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
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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	265	522		
Units: percentage of subjects				
number (not applicable)	0.4	6.7		

Statistical analyses

Statistical analysis title	Statistical 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	787
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[19]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	6.4
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	3.8
upper limit	9.1

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 [≥ 7 , < 7]).

Secondary: Percentage of Subjects With Improvement of ≥ 4 Points in Weekly Average Peak Pruritus Numeric Rating Scale: Severe Pruritus Population

End point title	Percentage of Subjects With Improvement of ≥ 4 Points in
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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 ≥ 7 . Data was planned to be collected and analysed for Initial Treatment Period.

End point type	Secondary
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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	164	316		
Units: percentage of subjects				
number (not applicable)	0.6	8.5		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Initial Treatment Period: Placebo v Initial Treatment Period: Nemolizumab 30 mg
Number of subjects included in analysis	480
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0004
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted percentage difference
Point estimate	8
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	4.2
upper limit	11.8

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 twice consecutively and thus counted in Nemolizumab 30 mg Q4W to Q4W for safety analysis.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.0
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Reporting groups

Reporting group title	Initial Treatment Period: Nemolizumab 30 mg
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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	Initial Treatment Period: Placebo
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Reporting group description:

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.

Reporting group title	Maintenance Period: Nemolizumab 30 mg Q4W to Q4W
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Reporting group 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, 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
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Reporting group 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.

Reporting group title	Maintenance Period: Nemolizumab 30 mg Q4W to Placebo Q8W
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Reporting group 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, Q8W at Weeks 20, 28, 36, and 44 by a single SC injection during Maintenance Period.

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

Serious adverse events	Initial Treatment Period: Nemolizumab 30 mg	Initial Treatment Period: Placebo	Maintenance Period: Nemolizumab 30 mg Q4W to Q4W
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 519 (2.50%)	3 / 263 (1.14%)	6 / 79 (7.59%)

number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 519 (0.19%)	0 / 263 (0.00%)	0 / 79 (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
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	0 / 519 (0.00%)	0 / 263 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometriosis			
subjects affected / exposed	0 / 519 (0.00%)	0 / 263 (0.00%)	0 / 79 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 519 (0.00%)	0 / 263 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 519 (0.00%)	0 / 263 (0.00%)	0 / 79 (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			
Psychogenic tremor			
subjects affected / exposed	1 / 519 (0.19%)	0 / 263 (0.00%)	0 / 79 (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
Injury, poisoning and procedural complications			
Comminuted fracture			

subjects affected / exposed	0 / 519 (0.00%)	0 / 263 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematoma			
subjects affected / exposed	0 / 519 (0.00%)	0 / 263 (0.00%)	0 / 79 (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
Congenital, familial and genetic disorders			
Congenital cyst			
subjects affected / exposed	1 / 519 (0.19%)	0 / 263 (0.00%)	0 / 79 (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
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	0 / 519 (0.00%)	1 / 263 (0.38%)	0 / 79 (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
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 519 (0.19%)	0 / 263 (0.00%)	0 / 79 (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
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	1 / 519 (0.19%)	0 / 263 (0.00%)	0 / 79 (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
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 519 (0.00%)	0 / 263 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eosinophilic colitis			

subjects affected / exposed	1 / 519 (0.19%)	0 / 263 (0.00%)	0 / 79 (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
Inguinal hernia			
subjects affected / exposed	0 / 519 (0.00%)	1 / 263 (0.38%)	0 / 79 (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
Small intestinal obstruction			
subjects affected / exposed	1 / 519 (0.19%)	0 / 263 (0.00%)	0 / 79 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 519 (0.19%)	0 / 263 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	3 / 519 (0.58%)	0 / 263 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	1 / 519 (0.19%)	0 / 263 (0.00%)	0 / 79 (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
Intervertebral disc protrusion			
subjects affected / exposed	2 / 519 (0.39%)	0 / 263 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			

subjects affected / exposed	0 / 519 (0.00%)	1 / 263 (0.38%)	0 / 79 (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
Chronic sinusitis			
subjects affected / exposed	0 / 519 (0.00%)	1 / 263 (0.38%)	0 / 79 (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
Gastroenteritis			
subjects affected / exposed	0 / 519 (0.00%)	0 / 263 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex			
subjects affected / exposed	1 / 519 (0.19%)	0 / 263 (0.00%)	0 / 79 (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
Herpes zoster			
subjects affected / exposed	1 / 519 (0.19%)	0 / 263 (0.00%)	0 / 79 (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
Infected cyst			
subjects affected / exposed	1 / 519 (0.19%)	0 / 263 (0.00%)	0 / 79 (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
Ophthalmic herpes zoster			
subjects affected / exposed	1 / 519 (0.19%)	0 / 263 (0.00%)	0 / 79 (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
Superinfection bacterial			
subjects affected / exposed	1 / 519 (0.19%)	0 / 263 (0.00%)	0 / 79 (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

Serious adverse events	Maintenance Period: Nemolizumab 30 mg Q4W to Q8W	Maintenance Period: Nemolizumab 30 mg Q4W to Placebo	Maintenance Period: Placebo Q4W Re- assigned to Placebo
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		Q8W	Q4W
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 77 (0.00%)	2 / 77 (2.60%)	1 / 84 (1.19%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Endometriosis			
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 84 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Pulmonary embolism			
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 84 (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
Psychiatric disorders			
Psychogenic tremor			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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			

Comminuted fracture			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Post procedural haematoma			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Congenital cyst			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Eosinophilic colitis			

subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Inguinal hernia			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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			
Groin pain			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Chronic sinusitis			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Gastroenteritis			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Herpes simplex			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Herpes zoster			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Infected cyst			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Ophthalmic herpes zoster			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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
Superinfection bacterial			
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 84 (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

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Initial Treatment Period: Nemolizumab 30 mg	Initial Treatment Period: Placebo	Maintenance Period: Nemolizumab 30 mg Q4W to Q4W
Total subjects affected by non-serious adverse events subjects affected / exposed	71 / 519 (13.68%)	40 / 263 (15.21%)	17 / 79 (21.52%)
Skin and subcutaneous tissue disorders Dermatitis atopic subjects affected / exposed occurrences (all)	34 / 519 (6.55%) 42	15 / 263 (5.70%) 15	6 / 79 (7.59%) 7
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	19 / 519 (3.66%) 24	12 / 263 (4.56%) 13	7 / 79 (8.86%) 12
Upper respiratory tract infection subjects affected / exposed occurrences (all)	6 / 519 (1.16%) 6	5 / 263 (1.90%) 5	1 / 79 (1.27%) 1
COVID-19 subjects affected / exposed occurrences (all)	14 / 519 (2.70%) 14	8 / 263 (3.04%) 8	3 / 79 (3.80%) 3

Non-serious adverse events	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 subjects affected / exposed	11 / 77 (14.29%)	26 / 77 (33.77%)	16 / 84 (19.05%)
Skin and subcutaneous tissue disorders Dermatitis atopic subjects affected / exposed occurrences (all)	3 / 77 (3.90%) 4	6 / 77 (7.79%) 7	5 / 84 (5.95%) 5
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 77 (3.90%) 6	5 / 77 (6.49%) 6	6 / 84 (7.14%) 8
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 77 (2.60%) 2	5 / 77 (6.49%) 5	2 / 84 (2.38%) 2
COVID-19			

subjects affected / exposed	4 / 77 (5.19%)	13 / 77 (16.88%)	6 / 84 (7.14%)
occurrences (all)	4	13	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 October 2019	This substantial protocol amendment was required as it updated and clarified study drug information, systemic rescue therapy use, added sleep metrics to clarify secondary endpoints to be assessed based on the subject sleep diary, Added timepoints for PEF collection in subjects without a medical history of asthma, added information to support dose selection rationale, Updated the schedule of assessments to align with the eCRF, corrected and clarified the schedule of assessments, added study design rationale for full population and subpopulation of PP NRS ≥ 7 analyses, approved contraceptive methods for females to maximize pregnancy prevention in female subjects.
27 February 2020	This substantial protocol amendment was required as it updated inclusion criteria to clarify 'true abstinence' and remove single-barrier methods as effective forms of contraception. Also, it clarified steps for emergency breaking of the blind by the Investigator
01 June 2020	This amendment included update in study drug description, methods of contraception, exclusion criterion including clarification regarding asthma that was not well controlled, subjects with specified infections at baseline and subjects with COVID-19 infection were to be excluded, failure of dupilumab, history of malignancy to allow a shortened timeframe between treatment and study entry for subjects with certain previously treated malignancies and AESIs to include COVID-19
04 November 2021	This amendment updated and clarified administrative items from memo dated 06 May 2021, Clarified points related to inclusion criteria/exclusion criteria

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported