



Clinical trial results:

A study to assess the safety and efficacy of nemolizumab (CD14152) in subjects with prurigo nodularis (PN)

Summary

EudraCT number	2017-001715-36
Trial protocol	DE AT FR PL
Global end of trial date	26 September 2018

Results information

Result version number	v1 (current)
This version publication date	12 October 2019
First version publication date	12 October 2019

Trial information

Trial identification

Sponsor protocol code	RD.03.SRE.115828
-----------------------	------------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03181503
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galderma R&D, SNC
Sponsor organisation address	Les Templiers, 2400 route des Colles, Biot, France, 06410
Public contact	RA CTA Coordinator, GALDERMA R&D, SNC, +33 (0)493 95 70 85, cta.coordinator@galderma.com
Scientific contact	Galderma Medical Expert, Zarif.Jabbar, GALDERMA R&D, SNC, Zarif.Jabbar-Lopez@galderma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 November 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	26 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of nemolizumab compared to placebo in the treatment of pruritus in subjects suffering from prurigo nodularis (PN).

Protection of trial subjects:

At each study site, the protocol and informed consent form (ICF) for this study were reviewed and approved by a duly constituted Institutional Review Board (IRB) or Independent Ethics Committee (IEC) and provided to PAREXEL before subjects were screened for entry. Amendments to the protocol and ICF were reviewed and approved in the same manner before being implemented. This study was conducted in accordance with Good Clinical Practice (GCP) as required by the International Council for Harmonisation (ICH) guidelines and in accordance with country-specific laws and regulations governing clinical studies of investigational products. Compliance with these requirements also constitutes conformity with the ethical principles of the Declaration of Helsinki (1964) and subsequent amendments. All subjects who participated in this clinical study were informed about the clinical study according to GCP guidelines, federal regulations, Health Insurance Portability and Accountability Act (HIPAA) for the United States (US), and in accordance with local requirements. Subjects were provided with both verbal and written information regarding the study, including its objectives, possible benefits and risks, and its consequences. Sufficient time was allowed for the subjects to read the study information and ask questions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 9
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	France: 28
Country: Number of subjects enrolled	Germany: 24
Worldwide total number of subjects	70
EEA total number of subjects	70

Notes:

Subjects enrolled per age group

In utero	0
----------	---

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	46
From 65 to 84 years	23
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The subjects were randomized at 16 investigational sites in Austria, France, Germany and Poland.

Pre-assignment

Screening details:

This study consisted of a screening period of up to 4 weeks. All assessments at screening were done as per the schedule of assessment.

Period 1

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

Blinding implementation details:

This was a double-blind clinical study, therefore neither the subject nor the Investigator/evaluator knew which treatment was assigned to each subject. Except for the pharmacist (or other qualified personnel) who handled study drug preparation, and the Clinical Research Associate (CRA) who monitored the drug records and study data, the study remained blinded to all study individuals until after final database lock and subsequent unblinding.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Each subject was randomized to receive three subcutaneous injections of matching placebo every 4 weeks (Q4W) (at Baseline, Week 4 & Week 8).

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

Dosage and administration details:

Three Subcutaneous injections (Baseline, Week 4, Week 8)

Arm title	Nemolizumab
------------------	-------------

Arm description:

Each subject was randomized to receive three subcutaneous injections of 0.5 mg/kg of nemolizumab Q4W (at Baseline, Week 4 & Week 8).

Arm type	Experimental
Investigational medicinal product name	Nemolizumab
Investigational medicinal product code	CD14152
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Three Subcutaneous injections (Baseline, Week 4, Week 8)

Number of subjects in period 1	Placebo	Nemolizumab
Started	36	34
Completed	29	31
Not completed	7	3
Protocol violation	1	-
Adverse event	2	2
Lost to follow-up	1	1
Withdrawal by subject	3	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: Each subject was randomized to receive three subcutaneous injections of matching placebo every 4 weeks (Q4W) (at Baseline, Week 4 & Week 8).	
Reporting group title	Nemolizumab
Reporting group description: Each subject was randomized to receive three subcutaneous injections of 0.5 mg/kg of nemolizumab Q4W (at Baseline, Week 4 & Week 8).	

Reporting group values	Placebo	Nemolizumab	Total
Number of subjects	36	34	70
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	52.4	59.7	
standard deviation	± 17.47	± 13.16	-
Gender categorical Units: Subjects			
Female	22	19	41
Male	14	15	29

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Each subject was randomized to receive three subcutaneous injections of matching placebo every 4 weeks (Q4W) (at Baseline, Week 4 & Week 8).	
Reporting group title	Nemolizumab
Reporting group description: Each subject was randomized to receive three subcutaneous injections of 0.5 mg/kg of nemolizumab Q4W (at Baseline, Week 4 & Week 8).	

Primary: Percent change from Baseline in pruritus numeric rating scale (NRS) to Week 4 (weekly average of the peak), using last observation carried forward (LOCF) approach

End point title	Percent change from Baseline in pruritus numeric rating scale (NRS) to Week 4 (weekly average of the peak), using last observation carried forward (LOCF) approach
End point description: To assess the efficacy of nemolizumab compared to placebo in the treatment of pruritus in subjects suffering from PN. The pruritus NRS was used by subjects to report the intensity of their pruritus (itch) during the last 24 hours. Subjects were asked the following questions in their local language: <ul style="list-style-type: none">For average itch intensity: On a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable', how would they rate their itch overall during the previous 24 hours;For maximum itch intensity: On a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable', how would they rate their itch at the worst moment during the previous 24 hours.	
End point type	Primary
End point timeframe: From Baseline to Week 4	

End point values	Placebo	Nemolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	33		
Units: Percentage				
arithmetic mean (standard deviation)	-13.8 (± 16.10)	-52.6 (± 33.96)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Nemolizumab

Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-51
upper limit	-25

Primary: Percent change from Baseline in pruritus NRS to Week 4 (weekly average of the peak), sensitivity analysis using multiple imputation method

End point title	Percent change from Baseline in pruritus NRS to Week 4 (weekly average of the peak), sensitivity analysis using multiple imputation method
-----------------	--

End point description:

To assess the efficacy of nemolizumab compared to placebo in the treatment of pruritus in subjects suffering from PN. The pruritus NRS was used by subjects to report the intensity of their pruritus (itch) during the last 24 hours. Subjects were asked the following questions in their local language:

- For average itch intensity: On a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable', how would they rate their itch overall during the previous 24 hours;
- For maximum itch intensity: On a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable', how would they rate their itch at the worst moment during the previous 24 hours.

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

End point timeframe:

From Baseline to Week 4

End point values	Placebo	Nemolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Percentage				
arithmetic mean (standard deviation)	-18.3 (± 22.39)	-52.0 (± 33.94)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Nemolizumab v Placebo

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-47
upper limit	-19.1

Primary: Percent change from Baseline in pruritus NRS to Week 4 (weekly average of the peak), sensitivity analysis using observed data

End point title	Percent change from Baseline in pruritus NRS to Week 4 (weekly average of the peak), sensitivity analysis using observed data
-----------------	---

End point description:

To assess the efficacy of nemolizumab compared to placebo in the treatment of pruritus in subjects suffering from PN. The pruritus NRS was used by subjects to report the intensity of their pruritus (itch) during the last 24 hours. Subjects were asked the following questions in their local language:

- For average itch intensity: On a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable', how would they rate their itch overall during the previous 24 hours;
- For maximum itch intensity: On a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable', how would they rate their itch at the worst moment during the previous 24 hours.

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

End point timeframe:

From Baseline to Week 4

End point values	Placebo	Nemolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: Percentage				
arithmetic mean (standard deviation)	-15.2 (± 17.42)	-54.9 (± 33.80)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Nemolizumab

Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-38.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-52.2
upper limit	-25.3

Secondary: Percent change from Baseline in weekly average of the peak pruritus NRS by timepoint, using LOCF approach

End point title	Percent change from Baseline in weekly average of the peak pruritus NRS by timepoint, using LOCF approach
-----------------	---

End point description:

To evaluate the efficacy of nemolizumab compared to placebo in the treatment of pruritus in subjects with PN. The pruritus NRS was used by subjects to report the intensity of their pruritus (itch) during the last 24 hours. Subjects were asked the following questions in their local language:

- For average itch intensity: On a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable', how would they rate their itch overall during the previous 24 hours;
- For maximum itch intensity: On a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable', how would they rate their itch at the worst moment during the previous 24 hours.

n=number of subjects in analysis

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

End point timeframe:

From baseline to Weeks 1, 2, 4, 8, 12, 16, 18

End point values	Placebo	Nemolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Percentage				
arithmetic mean (standard deviation)				
Week 1 (n = 33, 32)	-6.1 (± 11.45)	-26.0 (± 21.93)		
Week 2 (n = 34, 33)	-7.4 (± 14.85)	-41.7 (± 30.31)		
Week 4, (n = 34, 33)	-13.8 (± 16.10)	-52.6 (± 33.96)		
Week 8, (n = 34, 33)	-19.7 (± 20.03)	-56.5 (± 34.73)		
Week 12, (n = 34, 33)	-18.7 (± 22.80)	-61.8 (± 34.95)		
Week 16, (n = 34, 33)	-20.8 (± 22.29)	-61.1 (± 35.35)		
Week 18, (n = 34, 33)	-21.7 (± 22.95)	-59.6 (± 35.89)		

Statistical analyses

Statistical analysis title	Statistical analysis for Week 1
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-19.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.5
upper limit	-10.9

Statistical analysis title	Statistical analysis for Week 2
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-45.7
upper limit	-22.4

Statistical analysis title	Statistical analysis for Week 4
Comparison groups	Placebo v Nemolizumab

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-51
upper limit	-25

Statistical analysis title	Statistical analysis for Week 8
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-36.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50
upper limit	-22.1

Statistical analysis title	Statistical analysis for Week 12
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-42.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-57.7
upper limit	-28.2

Statistical analysis title	Statistical analysis for Week 16
-----------------------------------	----------------------------------

Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-39.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.4
upper limit	-25

Statistical analysis title	Statistical analysis for Week 18
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-37.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-52.4
upper limit	-22.3

Secondary: Absolute change from Baseline in weekly average of the peak pruritus NRS by timepoint, using LOCF approach

End point title	Absolute change from Baseline in weekly average of the peak pruritus NRS by timepoint, using LOCF approach
End point description:	<p>To evaluate the efficacy of nemolizumab compared to placebo in the treatment of pruritus in subjects with PN. The pruritus NRS was used by subjects to report the intensity of their pruritus (itch) during the last 24 hours. Subjects were asked the following questions in their local language:</p> <ul style="list-style-type: none"> For average itch intensity: On a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable', how would they rate their itch overall during the previous 24 hours; For maximum itch intensity: On a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable', how would they rate their itch at the worst moment during the previous 24 hours. <p>n=number of subjects in analysis</p>
End point type	Secondary
End point timeframe:	
From baseline to Weeks 1, 2, 4, 8, 12, 16, 18	

End point values	Placebo	Nemolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Percentage				
arithmetic mean (standard deviation)				
Week 1, (n = 33, 32)	-0.5 (± 0.87)	-2.1 (± 1.66)		
Week 2, (n = 34, 33)	-0.6 (± 1.21)	-3.4 (± 2.38)		
Week 4, (n = 34, 33)	-1.2 (± 1.33)	-4.3 (± 2.77)		
Week 8, (n = 34, 33)	-1.6 (± 1.62)	-4.7 (± 2.90)		
Week 12, (n = 34, 33)	-1.5 (± 1.84)	-5.1 (± 2.95)		
Week 16, (34, 33)	-1.7 (± 1.81)	-5.1 (± 3.00)		
Week 18, (n = 34, 33)	-1.8 (± 1.87)	-4.9 (± 3.07)		

Statistical analyses

Statistical analysis title	Statistical analysis for Week 1
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-0.9

Statistical analysis title	Statistical analysis for Week 2
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	-1.8

Statistical analysis title	Statistical analysis for Week 4
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	-2

Statistical analysis title	Statistical analysis for Week 8
Comparison groups	Nemolizumab v Placebo
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	-1.8

Statistical analysis title	Statistical analysis for Week 12
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	-2.3

Statistical analysis title	Statistical analysis for Week 16
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.5
upper limit	-2

Statistical analysis title	Statistical analysis for Week 18
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	-1.8

Secondary: Percent change from Baseline in weekly average of the peak pruritus verbal rating scale (VRS) by timepoint using LOCF approach

End point title	Percent change from Baseline in weekly average of the peak pruritus verbal rating scale (VRS) by timepoint using LOCF approach
-----------------	--

End point description:

The VRS, consisting of a list of adjectives describing different levels of symptom intensity, was used by subjects to report the intensity of their pruritus (itch) during last 24 hours. Subjects were asked the following questions in their local language:

- For average itch intensity: On a scale of 0 to 4, with 0 being 'no itch' and 4 being 'very severe itch', how would they rate their itch overall during the previous 24 hours;
 - For maximum itch intensity: On a scale of 0 to 4, with 0 being 'no itch' and 4 being 'very severe itch', how would they rate their worst itch during the previous 24 hours.
- n=number of subjects in analysis

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

End point timeframe:

From baseline to Weeks 1, 2, 4, 8, 12, 16, 18

End point values	Placebo	Nemolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Percentage				
arithmetic mean (standard deviation)				
Week 1, (n = 33, 31)	-9.8 (± 14.24)	-27.6 (± 17.21)		
Week 2, (n = 34, 32)	-12.3 (± 17.64)	-39.1 (± 25.38)		
Week 4, (n = 34, 32)	-15.6 (± 20.95)	-50.7 (± 29.37)		
Week 8, (n = 34, 32)	-20.7 (± 21.22)	-54.3 (± 30.61)		
Week 12, (n = 34, 32)	-19.4 (± 23.60)	-56.9 (± 32.64)		
Week 16, (n = 34, 32)	-21.2 (± 22.24)	-55.6 (± 34.48)		
Week 18, (n = 34, 32)	-23.0 (± 21.97)	-53.4 (± 36.56)		

Statistical analyses

Statistical analysis title	Statistical analysis for Week 1
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-17.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.8
upper limit	-9.6

Statistical analysis title	Statistical analysis for Week 2
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-26.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.8
upper limit	-15.6

Statistical analysis title	Statistical analysis for Week 4
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-34.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-47
upper limit	-21.9

Statistical analysis title	Statistical analysis for Week 8
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46
upper limit	-20.1

Statistical analysis title	Statistical analysis for Week 12
Comparison groups	Nemolizumab v Placebo
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-37.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-51.4
upper limit	-22.9

Statistical analysis title	Statistical analysis for Week 16
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-33.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-48
upper limit	-19.2

Statistical analysis title	Statistical analysis for Week 18
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-30

Confidence interval	
level	95 %
sides	2-sided
lower limit	-45
upper limit	-14.9

Secondary: Absolute change from Baseline in weekly average of the peak pruritus VRS by timepoint using LOCF approach

End point title	Absolute change from Baseline in weekly average of the peak pruritus VRS by timepoint using LOCF approach
-----------------	---

End point description:

The VRS, consisting of a list of adjectives describing different levels of symptom intensity, was used by subjects to report the intensity of their pruritus (itch) during last 24 hours.

Subjects were asked the following questions in their local language:

- For average itch intensity: On a scale of 0 to 4, with 0 being 'no itch' and 4 being 'very severe itch', how would they rate their itch overall during the previous 24 hours;
- For maximum itch intensity: On a scale of 0 to 4, with 0 being 'no itch' and 4 being 'very severe itch', how would they rate their worst itch during the previous 24 hours.

n=number of subjects in analysis

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

End point timeframe:

From baseline to Weeks 1, 2, 4, 8, 12, 16, 18

End point values	Placebo	Nemolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Percentage				
arithmetic mean (standard deviation)				
Week 1, (n = 33, 31)	-0.3 (± 0.47)	-0.9 (± 0.57)		
Week 2, (n = 34, 32)	-0.4 (± 0.61)	-1.3 (± 0.83)		
Week 4, (n = 34, 32)	-0.6 (± 0.74)	-1.6 (± 1.00)		
Week 8, (n = 34, 32)	-0.7 (± 0.74)	-1.8 (± 1.06)		
Week 12, (n = 34, 32)	-0.7 (± 0.83)	-1.8 (± 1.09)		
Week 16, (n = 34, 32)	-0.7 (± 0.78)	-1.8 (± 1.16)		
Week 18, (n = 34, 32)	-0.8 (± 0.77)	-1.7 (± 1.26)		

Statistical analyses

Statistical analysis title	Statistical analysis for Week 1
Comparison groups	Placebo v Nemolizumab

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	-0.3

Statistical analysis title	Statistical analysis for Week 2
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.5

Statistical analysis title	Statistical analysis for Week 4
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-0.7

Statistical analysis title	Statistical analysis for Week 8
-----------------------------------	---------------------------------

Comparison groups	Nemolizumab v Placebo
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-0.6

Statistical analysis title	Statistical analysis for Week 12
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	-0.7

Statistical analysis title	Statistical analysis for Week 16
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-0.6

Statistical analysis title	Statistical analysis for Week 18
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-0.5

Secondary: Dynamic pruritus score (DPS) at 24, 48, and 72 hours after first injection and before second injection (Week 4)

End point title	Dynamic pruritus score (DPS) at 24, 48, and 72 hours after first injection and before second injection (Week 4)
End point description: The 9-point DPS scale was used by-subjects to evaluate the change of their pruritus compared with an earlier timepoint. The scale ranges from 0 (strongly worsened pruritus) to 8 ([almost] no pruritus anymore), including intermediate marks for slightly improved/worsened, moderately improved/worsened, and rather improved/worsened. n=number of subjects in analysis	
End point type	Secondary
End point timeframe: At 24, 48, and 72 hours (Baseline) and Week 4	

End point values	Placebo	Nemolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
First injection, after 24 hours (n=23,22)	4.3 (± 0.96)	5.0 (± 1.20)		
First injection, after 48 hours (n=22, 23)	4.0 (± 1.69)	5.3 (± 1.40)		
First injection, after 72 hours (n=25,24)	4.0 (± 1.37)	5.7 (± 1.34)		
Before Second Injection (Week 4) (n=30,32)	4.4 (± 1.07)	6.3 (± 1.89)		

Statistical analyses

Statistical analysis title	First injection, after 24 hours
Comparison groups	Placebo v Nemolizumab

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Cochran-Mantel-Haenszel

Statistical analysis title	First injection, after 48 hours
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	First injection, after 72 hours
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Before Second Injection (Week 4)
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel

Secondary: Percent Change From Baseline in Prurigo Activity Score (PAS) Item 5 (Number of Lesions) at Week 12

End point title	Percent Change From Baseline in Prurigo Activity Score (PAS) Item 5 (Number of Lesions) at Week 12
End point description:	The PAS was used by the Investigator (or trained designee) to evaluate the disease.
End point type	Secondary
End point timeframe:	From Baseline to Week 12

End point values	Placebo	Nemolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Percentage				
number (not applicable)	14.8	35.4		

Statistical analyses

Statistical analysis title	Statistical analysis for Week 12
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	Cochran-Mantel-Haenszel

Secondary: PAS Item 6 (excoriation/crusts and healed lesions stages) at each visit

End point title	PAS Item 6 (excoriation/crusts and healed lesions stages) at each visit
End point description: The PAS was used by the Investigator (or trained designee) to evaluate the disease.	
End point type	Secondary
End point timeframe: At Day 1 (Baseline), Weeks 4, 8, 12, 18	

End point values	Placebo	Nemolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Unit on a scale				
number (not applicable)				
Excoriations/crusts, Day 1 (Baseline), 0=0%	0	0		
Excoriations/crusts, Day 1 (Baseline), 1=1-25%	2	4		
Excoriations/crusts, Day 1 (Baseline), 2=26-50%	7	5		
Excoriations/crusts, Day 1 (Baseline), 3=51-75%	14	12		
Excoriations/crusts, Day 1 (Baseline), 4=76-100%	13	13		
Excoriations/crusts, Week 4, 0=0%	2	2		

Excoriations/crusts, Week 4, 1=1-25%	6	10		
Excoriations/crusts, Week 4, 2=26-50%	7	9		
Excoriations/crusts, Week 4, 3=51-75%	10	9		
Excoriations/crusts, Week 4, 4=76-100%	9	3		
Excoriations/crusts, Week 8, 0=0%	2	4		
Excoriations/crusts, Week 8, 1=1-25%	5	13		
Excoriations/crusts, Week 8, 2=26-50%	7	6		
Excoriations/crusts, Week 8, 3=51-75%	11	9		
Excoriations/crusts, Week 8, 4=76-100%	7	0		
Excoriations/crusts, Week 12, 0=0%	1	3		
Excoriations/crusts, Week 12, 1=1-25%	7	17		
Excoriations/crusts, Week 12, 2=26-50%	5	9		
Excoriations/crusts, Week 12, 3=51-75%	12	3		
Excoriations/crusts, Week 12, 4=76-100%	5	0		
Excoriations/crusts, Week 18, 0=0%	1	6		
Excoriations/crusts, Week 18, 1=1-25%	4	12		
Excoriations/crusts, Week 18, 2=26-50%	8	4		
Excoriations/crusts, Week 18, 3=51-75%	11	5		
Excoriations/crusts, Week 18, 4=76-100%	6	4		
Healed lesions, Day 1 (Baseline), 0=100%	1	0		
Healed lesions, Day 1 (Baseline), 1=75-99%	0	1		
Healed lesions, Day 1 (Baseline), 2=50-74%	3	5		
Healed lesions, Day 1 (Baseline), 3=25-49%	13	9		
Healed lesions, Day 1 (Baseline), 4=0-24%	19	19		
Healed lesions, Week 4, 0=100%	2	3		
Healed lesions, Week 4, 1=75-99%	2	5		
Healed lesions, Week 4, 2=50-74%	6	5		
Healed lesions, Week 4, 3=25-49%	11	14		
Healed lesions, Week 4, 4=0-24%	13	6		
Healed lesions, Week 8, 0=100%	2	3		
Healed lesions, Week 8, 1=75-99%	3	8		
Healed lesions, Week 8, 2=50-74%	7	8		
Healed lesions, Week 8, 3=25-49%	9	12		
Healed lesions, Week 8, 4=0-24%	11	1		
Healed lesions, Week 12, 0=100%	1	2		
Healed lesions, Week 12, 1=75-99%	2	9		
Healed lesions, Week 12, 2=50-74%	7	16		
Healed lesions, Week 12, 3=25-49%	8	5		
Healed lesions, Week 12, 4=0-24%	12	0		
Healed lesions, Week 18, 0=100%	1	3		
Healed lesions, Week 18, 1=75-99%	2	12		
Healed lesions, Week 18, 2=50-74%	7	7		
Healed lesions, Week 18, 3=25-49%	8	5		

Healed lesions, Week 18, 4=0-24%	12	4		
----------------------------------	----	---	--	--

Statistical analyses

Statistical analysis title	Statistical analysis for Week 4 Excoriation/crust
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis for Week 8 Excoriation/crust
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis for Week 12 Excoriation/crust
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis for Week 18 Excoriation/crust
Comparison groups	Nemolizumab v Placebo
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis for Day 1 Excoriation/crust
-----------------------------------	--

Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.934
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis for Day 1 Healed lesions
Comparison groups	Nemolizumab v Placebo
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.98
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis for Week 4 Healed lesions
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.025
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis for Week 8 Healed lesions
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis for Week 12 Healed lesions
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis for Week 18 Healed lesions
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel

Secondary: Investigator global assessment (IGA) of prurigo at each visit

End point title	Investigator global assessment (IGA) of prurigo at each visit
End point description: IGA was used to evaluate the severity of the disease. The 5-point scale ranging from 0 (clear) to 4 (severe), rates the overall assessment of the severity of prurigo including presence of crust and nodules or skin bleeding. n=number of subjects in analysis	
End point type	Secondary
End point timeframe: At Baseline and at Weeks 4, 8, 12, 18	

End point values	Placebo	Nemolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Week 4, (n=35,33))	3.3 (± 0.61)	2.8 (± 0.81)		
Week 8, (n = 32, 32)	3.1 (± 0.67)	2.4 (± 0.80)		
Week 12, (n = 30, 32)	2.8 (± 0.82)	2.0 (± 0.80)		
Week 18, (n = 30, 31)	3.0 (± 0.93)	2.0 (± 1.11)		
Baseline (n = 36, 34)	3.4 (± 0.49)	3.5 (± 0.51)		

Statistical analyses

Statistical analysis title	Statistical analysis for Week 4
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis for Week 8
-----------------------------------	---------------------------------

Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis for Week 12
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis for Week 18
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis for Baseline
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.156
Method	Cochran-Mantel-Haenszel

Secondary: Proportion of subjects achieving IGA success (defined as IGA=0 [clear] or IGA=1 [Almost clear] with two-point improvement from Baseline) at Week 12

End point title	Proportion of subjects achieving IGA success (defined as IGA=0 [clear] or IGA=1 [Almost clear] with two-point improvement from Baseline) at Week 12
-----------------	---

End point description:

IGA was to evaluate the severity of the disease. The 5-point scale ranging from 0 (clear) to 4 (severe), rates the overall assessment of the severity of prurigo including presence of crust and nodules or skin bleeding.

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

End point timeframe:

At Week 12

End point values	Placebo	Nemolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Subjects				
number (not applicable)	1	7		

Statistical analyses

Statistical analysis title	Statistical analysis for Week 12
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	17.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.2
upper limit	30.3

Secondary: Percent change from Baseline in weekly average of the average pruritus NRS by timepoint, using LOCF approach

End point title	Percent change from Baseline in weekly average of the average pruritus NRS by timepoint, using LOCF approach
-----------------	--

End point description:

To evaluate the efficacy of nemolizumab compared to placebo in the treatment of pruritus in subjects with PN. The pruritus NRS was used by subjects to report the intensity of their pruritus (itch) during the last 24 hours. Subjects were asked the following questions in their local language:

- For average itch intensity: On a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable', how would they rate their itch overall during the previous 24 hours;
- For maximum itch intensity: On a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable', how would they rate their itch at the worst moment during the previous 24 hours.

n=number of subjects in analysis

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

End point timeframe:

Change from baseline to Weeks 1, 2, 4, 8, 12, 16, 18

End point values	Placebo	Nemolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Percentage				
arithmetic mean (standard deviation)				
Week 1, (n = 33, 31)	-7.5 (± 12.82)	-26.6 (± 21.25)		
Week 2, (n = 34, 32)	-9.6 (± 15.28)	-44.0 (± 29.54)		
Week 4, (n = 34, 32)	-16.5 (± 18.25)	-53.4 (± 33.23)		
Week 8, (n = 34, 32)	-24.6 (± 23.38)	-57.3 (± 34.78)		
Week 12, (n = 34, 32)	-23.0 (± 26.31)	-62.6 (± 34.98)		
Week 16, (n = 34, 32)	-25.9 (± 24.89)	-62.4 (± 35.93)		
Week 18, (n = 34, 32)	-26.2 (± 25.39)	-60.4 (± 36.15)		

Statistical analyses

Statistical analysis title	Statistical analysis for Week 1
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-18.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.2
upper limit	-9.8

Statistical analysis title	Statistical analysis for Week 2
Comparison groups	Placebo v Nemolizumab

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-34.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-45.7
upper limit	-22.6

Statistical analysis title	Statistical analysis for Week 4
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-36.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.2
upper limit	-23.1

Statistical analysis title	Statistical analysis for Week 8
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.6
upper limit	-17.3

Statistical analysis title	Statistical analysis for Week 12
-----------------------------------	----------------------------------

Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-39.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.8
upper limit	-24.1

Statistical analysis title	Statistical analysis for Week 16
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-35.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-51.3
upper limit	-20.6

Statistical analysis title	Statistical analysis for Week 18
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-33.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.6
upper limit	-18.2

Secondary: Absolute change from Baseline in weekly average of the average pruritus NRS by timepoint, using LOCF approach

End point title	Absolute change from Baseline in weekly average of the average pruritus NRS by timepoint, using LOCF approach
End point description: To evaluate the efficacy of nemolizumab compared to placebo in the treatment of pruritus in subjects with PN. The pruritus NRS was used by subjects to report the intensity of their pruritus (itch) during the last 24 hours. Subjects were asked the following questions in their local language: <ul style="list-style-type: none">• For average itch intensity: On a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable', how would they rate their itch overall during the previous 24 hours;• For maximum itch intensity: On a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable', how would they rate their itch at the worst moment during the previous 24 hours. n=number of subjects in analysis	
End point type	Secondary
End point timeframe: Change from baseline to Weeks 1, 2, 4, 8, 12, 16, 18	

End point values	Placebo	Nemolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Percentage				
arithmetic mean (standard deviation)				
Week 1, (n = 33, 31)	-0.5 (± 0.82)	-1.9 (± 1.47)		
Week 2, (n = 34, 32)	-0.8 (± 1.14)	-3.2 (± 2.03)		
Week 4, (n = 34, 32)	-1.3 (± 1.41)	-3.9 (± 2.44)		
Week 8, (n = 34, 32)	-1.9 (± 1.80)	-4.2 (± 2.60)		
Week 12, (n = 34, 32)	-1.8 (± 2.05)	-4.6 (± 2.71)		
Week 16, (n = 34, 32)	-2.0 (± 1.97)	-4.6 (± 2.86)		
Week 18, (n = 34, 32)	-2.1 (± 2.02)	-4.5 (± 2.94)		

Statistical analyses

Statistical analysis title	Statistical analysis for Week 1
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	-0.7

Statistical analysis title	Statistical analysis for Week 2
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	-1.6

Statistical analysis title	Statistical analysis for Week 4
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	-1.6

Statistical analysis title	Statistical analysis for Week 8
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	-1.1

Statistical analysis title	Statistical analysis for Week 12
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	-1.7

Statistical analysis title	Statistical analysis for Week 16
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.9
upper limit	-1.4

Statistical analysis title	Statistical analysis for Week 18
Comparison groups	Placebo v Nemolizumab

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	-1.2

Secondary: Percent change from Baseline in weekly average of the average pruritus VRS by timepoint using LOCF approach

End point title	Percent change from Baseline in weekly average of the average pruritus VRS by timepoint using LOCF approach
-----------------	---

End point description:

The VRS, consisting of a list of adjectives describing different levels of symptom intensity, was used by subjects to report the intensity of their pruritus (itch) during last 24 hours.

Subjects were asked the following questions in their local language:

- For average itch intensity: On a scale of 0 to 4, with 0 being 'no itch' and 4 being 'very severe itch', how would they rate their itch overall during the previous 24 hours;
- For maximum itch intensity: On a scale of 0 to 4, with 0 being 'no itch' and 4 being 'very severe itch', how would they rate their worst itch during the previous 24 hours.

n=number of subjects in analysis

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

End point timeframe:

From baseline to Weeks 1, 2, 4, 8, 12, 16, 18

End point values	Placebo	Nemolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Percentage				
arithmetic mean (standard deviation)				
Week 1, (n = 33, 31)	-10.5 (± 19.72)	-29.6 (± 16.90)		
Week 2, (n = 34, 32)	-13.0 (± 19.20)	-42.9 (± 24.22)		
Week 4, (n = 34, 32)	-16.4 (± 24.10)	-52.1 (± 27.63)		
Week 8, (n = 34, 32)	-23.5 (± 22.89)	-55.4 (± 30.63)		
Week 12, (n = 34, 32)	-21.9 (± 25.90)	-62.1 (± 29.98)		
Week 16, (n = 34, 32)	-25.1 (± 24.15)	-62.0 (± 32.48)		
Week 18, (n = 34, 32)	-26.2 (± 24.40)	-58.7 (± 34.81)		

Statistical analyses

Statistical analysis title	Statistical analysis for Week 1
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-18.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.7
upper limit	-9.5

Statistical analysis title	Statistical analysis for Week 2
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-29.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.2
upper limit	-18.8

Statistical analysis title	Statistical analysis for Week 4
Comparison groups	Placebo v Nemolizumab

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-35.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-48.1
upper limit	-22.4

Statistical analysis title	Statistical analysis for Week 8
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-31.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-45
upper limit	-18.1

Statistical analysis title	Statistical analysis for Week 12
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-40
Confidence interval	
level	95 %
sides	2-sided
lower limit	-53.6
upper limit	-26.3

Statistical analysis title	Statistical analysis for Week 16
-----------------------------------	----------------------------------

Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-36.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50.1
upper limit	-22.1

Statistical analysis title	Statistical analysis for Week 18
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-47.1
upper limit	-17

Secondary: Absolute change from Baseline in weekly average of the average pruritus VRS by timepoint using LOCF approach

End point title	Absolute change from Baseline in weekly average of the average pruritus VRS by timepoint using LOCF approach
-----------------	--

End point description:

The VRS, consisting of a list of adjectives describing different levels of symptom intensity, was used by subjects to report the intensity of their pruritus (itch) during last 24 hours.

Subjects were asked the following questions in their local language:

- For average itch intensity: On a scale of 0 to 4, with 0 being 'no itch' and 4 being 'very severe itch', how would they rate their itch overall during the previous 24 hours;
- For maximum itch intensity: On a scale of 0 to 4, with 0 being 'no itch' and 4 being 'very severe itch', how would they rate their worst itch during the previous 24 hours.

n=number of subjects in analysis

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

End point timeframe:

From baseline to Weeks 1, 2, 4, 8, 12, 16, 18

End point values	Placebo	Nemolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Percentage				
arithmetic mean (standard deviation)				
Week 1, (n = 33, 31)	-0.4 (± 0.50)	-0.9 (± 0.49)		
Week 2, (n = 34, 32)	-0.4 (± 0.61)	-1.3 (± 0.68)		
Week 4, (n = 34, 32)	-0.6 (± 0.73)	-1.6 (± 0.84)		
Week 8, (n = 34, 32)	-0.7 (± 0.72)	-1.7 (± 0.96)		
Week 12, (n = 34, 32)	-0.7 (± 0.82)	-1.9 (± 0.94)		
Week 16, (n = 34, 32)	-0.8 (± 0.78)	-1.9 (± 1.06)		
Week 18, (n = 34, 32)	-0.8 (± 0.79)	-1.8 (± 1.16)		

Statistical analyses

Statistical analysis title	Statistical analysis for Week 1
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	-0.3

Statistical analysis title	Statistical analysis for Week 2
Comparison groups	Nemolizumab v Placebo
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.5

Statistical analysis title	Statistical analysis for Week 4
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.6

Statistical analysis title	Statistical analysis for Week 8
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.5

Statistical analysis title	Statistical analysis for Week 12
Comparison groups	Placebo v Nemolizumab

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-0.7

Statistical analysis title	Statistical analysis for Week 16
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-0.6

Statistical analysis title	Statistical analysis for Week 18
Comparison groups	Placebo v Nemolizumab
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.4

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From screening until follow-up visit (up to Week 18)/early termination

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

Dictionary used

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

Dictionary version	19.0
--------------------	------

Reporting groups

Reporting group title	Placebo
-----------------------	---------

Reporting group description:

Each subject was randomized to receive three subcutaneous injections of matching placebo every 4 weeks (Q4W) (at Baseline, Week 4 & Week 8).

Reporting group title	Nemolizumab
-----------------------	-------------

Reporting group description:

Each subject was randomized to receive three subcutaneous injections of 0.5 mg/kg of nemolizumab Q4W (at Baseline, Week 4 & Week 8).

Serious adverse events	Placebo	Nemolizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 36 (8.33%)	4 / 34 (11.76%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis psoriasiform			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema nummular			

subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurodermatitis			
subjects affected / exposed	3 / 36 (8.33%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus bladder			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Fibromyalgia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Placebo	Nemolizumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 36 (66.67%)	23 / 34 (67.65%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
General disorders and administration			

site conditions			
Chest discomfort			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Chest pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Oedema peripheral			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	2	
Pyrexia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Thirst			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Rubber sensitivity			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	0 / 34 (0.00%) 0	
Dysphonia subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Dyspnoea subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Psychomotor retardation subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Investigations Weight increased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Injury, poisoning and procedural complications Eye injury subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Laceration subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Post procedural inflammation subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Road traffic accident subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Wound			

subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Muscle strain subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Cardiac disorders Diastolic dysfunction subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Mitral valve incompetence subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Tricuspid valve incompetence subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Tremor subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Headache subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Lymphadenopathy subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	0 / 34 (0.00%) 0	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Vertigo			

subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 36 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Diarrhoea			
subjects affected / exposed	0 / 36 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Abdominal pain upper			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Aerophagia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Dental caries			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Colitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorder			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			

subjects affected / exposed	0 / 36 (0.00%)	3 / 34 (8.82%)
occurrences (all)	0	4
Dermatitis contact		
subjects affected / exposed	0 / 36 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	2
Neurodermatitis		
subjects affected / exposed	2 / 36 (5.56%)	2 / 34 (5.88%)
occurrences (all)	2	2
Eczema		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Intertrigo		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Panniculitis		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Photosensitivity reaction		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Rash		
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)
occurrences (all)	1	1
Rash maculo-papular		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	2
Rash papular		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Seborrhoeic dermatitis		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Skin fissures		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Skin ulcer		

subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Alopecia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Dermatitis allergic			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Dry skin			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	2 / 36 (5.56%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Rosacea			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Skin burning sensation			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Skin irritation			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Polyuria			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Proteinuria			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 34 (2.94%)	
occurrences (all)	2	1	
Back pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Myalgia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Pain in jaw			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	2	
Spinal pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Groin pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Neck pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 36 (11.11%)	5 / 34 (14.71%)	
occurrences (all)	5	5	
Conjunctivitis			
subjects affected / exposed	2 / 36 (5.56%)	3 / 34 (8.82%)	
occurrences (all)	2	3	
Bronchitis			

subjects affected / exposed	0 / 36 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Herpes zoster			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Wound infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	2 / 36 (5.56%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Erysipelas			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Oral herpes			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Periodontitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Postoperative wound infection			
subjects affected / exposed	2 / 36 (5.56%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Rhinitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Increased appetite			
subjects affected / exposed	0 / 36 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 April 2018	Global amendment: • Clarification regarding dosing was added throughout; • The collection of NRS data between Screening Visit 2 and the Baseline Visit was clarified; • For exclusion criterion 13, the text “immunosuppressive or immunomodulatory drugs (e.g., azathioprine, methotrexate, thalidomide, cyclosporine)” was expanded to include the drugs apremilast, hydroxychloroquine; • Pharmacokinetics (PK) sampling time and PK sampling identification were further clarified for visits at Weeks 1, 2, 12, 16 and 18 because no injections were done at these visits; • Fibrinogen was removed from blood sampling assessments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported