Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Nemolizumab (CD14152) in Subjects with Prurigo Nodularis

Summary

EudraCT number	2019-004293-25
Trial protocol	GB SE DE HU AT DK IT PL
Global end of trial date	21 February 2023

Results information

Result version number	v1 (current)
This version publication date	18 July 2024
First version publication date	18 July 2024

Trial information

Trial identification

Sponsor protocol code	RD.06.SPR.202685

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Galderma S.A.
Sponsor organisation address	Avenue Gratta-Paille 2, Lausanne, Switzerland, 1018
Public contact	Clinical Trial Information Desk, CTD Coordinator Galderma R&D S.A., CTA.coordinator@galderma.com
Scientific contact	Clinical Trial Information Desk, CTD Coordinator Galderma R&D S.A., CTA.coordinator@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	11 April 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the efficacy and safety of nemolizumab (CD14152) compared to placebo in subjects greater than or equal to (>=) 18 years of age with prurigo nodularis (PN) after a 16 week treatment period.

Protection of trial subjects:

This clinical study was conducted in accordance with the protocol, the Declaration of Helsinki, and the International Conference on Harmonization Good Clinical Practices (ICH GCP), and in compliance with other applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 August 2020
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: 21
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	United Kingdom: 17
Country: Number of subjects enrolled	Austria: 24
Country: Number of subjects enrolled	Denmark: 14
Country: Number of subjects enrolled	Germany: 99
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Italy: 31
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	United States: 67
Worldwide total number of subjects	286
EEA total number of subjects	195

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)	204
From 65 to 84 years	82
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 77 active sites in 10 countries.

Pre-assignment

Screening details:

A total of 286 subjects were randomised to receive either nemolizumab (CD14152) or placebo.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Nemolizumab

Arm description:

Subjects weighing less than (<) 90 kilogram (kg) received two subcutaneous (SC) injections of 30 milligrams (mg) nemolizumab (60 mg loading dose) at baseline then one SC injection once for every 4 weeks (Q4W). Subjects weighing greater than or equal to (>=) 90 kg received two SC injections of 30 mg nemolizumab (60 mg total) at baseline (no loading dose) and two SC injections Q4W throughout the treatment period of 16 weeks.

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

Dosage and administration details:

Subjects weighing less than < 90 kg received two SC injections of 30 mg nemolizumab (60 mg loading dose) at baseline then one SC injection Q4W. Subjects weighing >= 90 kg received two SC injections of 30 mg nemolizumab (60 mg total) at baseline (no loading dose) and two SC injections Q4W throughout the treatment period of 16 weeks.

Arm title	Placebo

Arm description:

Subjects weighing <90 kg received two SC injections of matching placebo at baseline, then one SC injection Q4W. Subjects weighing >=90 kg received two SC injections of matching placebo at baseline, then two SC injections Q4W throughout the treatment period of 16 weeks.

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:

Subjects weighing < 90 kg received two SC injections of matching placebo at baseline, then one SC injection Q4W. Subjects weighing >= 90 kg received two SC injections of matching placebo at baseline, then two SC injections Q4W throughout the treatment period of 16 weeks.

Number of subjects in period 1	Nemolizumab	Placebo
Started	190	96
Treated	187	95
Completed	168	85
Not completed	22	11
Physician decision	-	1
Other- site permanently closing	-	1
Adverse event	11	4
Randomised but not treated	3	1
Subject's request	8	4

Baseline characteristics

Reporting groups	
Reporting group title	Nemolizumab
Reporting group description:	
Subjects weighing less than (<) 90 kilogram (kg) received two subcutaneous (SC) injections of 30 milligrams (mg) nemolizumab (60 mg loading dose) at baseline then one SC injection once for every 4 weeks (Q4W). Subjects weighing greater than or equal to (>=) 90 kg received two SC injections of 30 mg nemolizumab (60 mg total) at baseline (no loading dose) and two SC injections Q4W throughout the treatment period of 16 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects weighing <90 kg received two SC injections of matching placebo at baseline, then one SC injection Q4W. Subjects weighing >=90 kg received two SC injections of matching placebo at baseline, then two SC injections Q4W throughout the treatment period of 16 weeks.	

Reporting group values	Nemolizumab	Placebo	Total
Number of subjects	190	96	286
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	57.5	57.6	
standard deviation	± 12.77	± 13.36	-
Gender categorical Units: Subjects			
Female	110	56	166
Male	80	40	120
Ethinicity Units: Subjects			
Hispanic or Latino	4	5	9
Not Hispanic or Latino	184	88	272
Unknown	1	0	1
Not Reported	1	3	4
Race Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	10	2	12
Black or African American	18	10	28
Native Hawaiian or Other Pacific Islander	0	0	0
White	160	81	241
More than one race	0	0	0
Other	1	2	3
Not Reported	0	1	1
Region of Enrollment Units: Subjects			
Europe	141	71	212
North America	49	25	74

End points

End points reporting groups

Reporting group title	Nemolizumab

Reporting group description:

Subjects weighing less than (<) 90 kilogram (kg) received two subcutaneous (SC) injections of 30 milligrams (mg) nemolizumab (60 mg loading dose) at baseline then one SC injection once for every 4 weeks (Q4W). Subjects weighing greater than or equal to (>=) 90 kg received two SC injections of 30 mg nemolizumab (60 mg total) at baseline (no loading dose) and two SC injections Q4W throughout the treatment period of 16 weeks.

Reporting group title	Placebo

Reporting group description:

Subjects weighing <90 kg received two SC injections of matching placebo at baseline, then one SC injection Q4W. Subjects weighing >=90 kg received two SC injections of matching placebo at baseline, then two SC injections Q4W throughout the treatment period of 16 weeks.

Primary: Number of Subjects With Improvement of Greater Than or Equal to (>=) 4 From Baseline in Weekly Average PP NRS at Week 16

End point title	Number of Subjects With Improvement of Greater Than or Equal to (>=) 4 From Baseline in Weekly Average PP NRS at Week 16

End point description:

The Peak Pruritus NRS is a scale that was used by the subjects to report the intensity of their pruritus (itch) during the last 24 hours. For maximum itch intensity: the scores were provided on a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable'. Higher scores indicate worse outcome. Weekly values are calculated as the average of 7 consecutive days of data up to the target study day (excluding) and set to missing if less than 4 days of data are available. Analysis window extension was applied to both timepoints, as described in the SAP. If a subject received any rescue therapy, composite variable strategy is applied, the underlying data at/after receipt of rescue therapy is set as worst possible value, and the response is derived from underlying data value. Subjects with missing results are
considered as non-responders. ITT population included all randomised subjects.

End point type	Primary

End point timeframe:

Baseline, Week 16

End point values	Nemolizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	96		
Units: subjects	111	16		

Statistical analyses

Statistical analysis title	Nemolizumab versus Placebo

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was then performed sequentially in order the endpoints were reported and continued when previous endpoint was statistically significant at two-sided 0.05.

Comparison groups	Nemolizumab v Placebo
Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata adjusted percentage difference
Point estimate	40.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	29.4
upper limit	50.8

Notes:

[1] - A 2-sided p-value was derived from Cochran-Mantel-Haenszel (CMH) test using the randomised stratification variables (analysis center and body weight at randomisation [< 90 kg, >= 90 kg]). Threshold of significance at 0.05.

Primary: Number of Subjects With an Investigator Global Assessment (IGA) Success at Week 16

End point title	Number of Subjects With an Investigator Global Assessment (IGA) Success at Week 16

End point description:

IGA success is defined as clear (0) or almost clear (1), and a reduction from baseline of greater than or equal to 2 points at week 16. Full scale is scored from 0-4, higher score indicates more severe symptoms. If a subject received any rescue therapy, composite variable strategy is applied, the underlying data at/after receipt of rescue therapy is set as worst possible value, and the response is derived from underlying data value. Subjects with missing results are considered as non-responders. ITT population included all randomised subjects.

End point type	Primary

End point timeframe:

Baseline, Week 16

End point values	Nemolizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	96		
Units: subjects	50	7		

Statistical analyses

Statistical analysis title	Nemolizumab versus Placebo

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was then performed sequentially in order the endpoints were reported and continued when previous endpoint was statistically significant at two-sided 0.05.

Comparison groups	Nemolizumab v Placebo

Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0025 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata adjusted percentage difference
Point estimate	14.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.7
upper limit	22.6

Notes:

[2] - A 2-sided p-value was derived from CMH test using the randomised stratification variables (analysis center and body weight at randomisation [< 90 kg, >= 90 kg]). Threshold of significance at 0.05.

Secondary: Number of Subjects With Adverse Events, Treatment-Emergent Adverse Events (TEAEs), Adverse Events of Special Interest (AESIs), and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Adverse Events, Treatment-Emergent Adverse Events (TEAEs), Adverse Events of Special Interest (AESIs), and Serious Adverse Events (SAEs)

End point description:

An AE was any untoward medical occurrence, new or worsening of any pre-existing condition, in a clinical study subject administered a medicinal product and which did not necessarily had to have a causal relationship with the treatment. TEAEs: AES with an onset date on or after the start date of the IMP administration. AESIs: skin-related events (SRE) (except exacerbation and infective exacerbation of PN) or injection site reactions (ISRs) as per common terminology criteria for AEs (Grade 3: ulceration or necrosis; severe tissue damage; operative intervention indicated, Grade 4: life-threatening consequences; urgent intervention indicated, Grade 5: death). An SAE: AE that resulted in any of the following outcomes: death; life threatening; results in persistent disability; requires in-patient hospitalisation congenital anomaly; is medically significant. Safety population included all randomised subjects who received at least 1 administration of study drug.

End point type	Secondary

End point timeframe:

From Baseline up to Week 32

End point values	Nemolizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	187	95		
Units: subjects				
TEAEs	134	62		
SAEs	32	19		
AESIs	21	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With an Improvement of >= 4 From Baseline in Weekly Average PP NRS at Week 4

End point title	Number of Subjects With an Improvement of >= 4 From Baseline in Weekly Average PP NRS at Week 4

End point description:

The Peak Pruritus NRS is a scale that was used by the subjects to report the intensity of their pruritus (itch) during the last 24 hours. For maximum itch intensity: the scores were provided on a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable'. Higher scores indicate worse outcome. Weekly values are calculated as average of 7 consecutive days data up to the target study day (excluding) and set to missing, if less than 4 days data are available. Analysis window extension was applied to baseline, as described in the SAP. If a subject received any rescue therapy, composite variable strategy is applied, the underlying data at/after receipt of rescue therapy is set as worst possible value, and the response is derived from underlying data value. Subjects with missing results are considered as non-responders. ITT population included all randomised subjects.

End point type	Secondary

End point timeframe:

Baseline, Week 4

End point values	Nemolizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	96		
Units: subjects	78	6		

Statistical analyses

Statistical analysis title	Nemolizumab versus Placebo

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was then performed sequentially in order the endpoints were reported and continued when previous endpoint was statistically significant at two-sided 0.05.

Comparison groups	Nemolizumab v Placebo
Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata adjusted percentage difference
Point estimate	31.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	23
upper limit	40.4

Notes:

[3] - A 2-sided p-value was derived from CMH test using the randomized stratification variables (analysis center and body weight at randomization [< 90 kg, >= 90 kg]). Threshold of significance at 0.05.

Secondary: Number of Subjects With PP NRS < 2 at Week 16

End point title	Number of Subjects With PP NRS < 2 at Week 16

End point description:

The Peak Pruritus NRS is a scale that was used by the subjects to report the intensity of their pruritus (itch) during the last 24 hours. For maximum itch intensity: the scores were provided on a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable'. Higher scores indicate worse outcome. Weekly values are calculated as average of 7 consecutive days data up to the target study day (excluding) and set to missing, if less than 4 days data are available. Analysis window extension was applied to Week 16, as described in the SAP. If a subject received any rescue therapy, composite variable strategy is applied, the underlying data at/after receipt of rescue therapy is set as worst possible value, and the response is derived from underlying data value. Subjects with missing results are considered as non-responders. ITT population included all randomised subjects.

End point type	Secondary

End point timeframe:

Week 16

End point values	Nemolizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	96		
Units: subjects	65	4		

Statistical analyses

Statistical analysis title	Nemolizumab versus Placebo

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was then performed sequentially in order the endpoints were reported and continued when previous endpoint was statistically significant at two-sided 0.05.

Comparison groups	Nemolizumab v Placebo
Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata adjusted percentage difference
Point estimate	30.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.3
upper limit	38.7

Notes:

[4] - A 2-sided p-value was derived from CMH test using the randomized stratification variables (analysis center and body weight at randomization [< 90 kg, >= 90 kg]). Threshold of significance at 0.05.

Secondary: Number of Subjects With an Improvement of >=4 From Baseline in Sleep Disturbance Numeric Rating Scale (SD NRS) at Week 16

End point title	Number of Subjects With an Improvement of >=4 From Baseline in Sleep Disturbance Numeric Rating Scale (SD NRS) at Week 16

End point description:

The SD NRS is a scale to report the degree of subject sleep loss related to PN. The baseline SD NRS was determined based on the average of daily SD NRS (score ranging from 0 to 10) during the 7 days up to the treatment start (including until treatment start time). A minimum of 4 daily scores out of the 7 days up to baseline study day is required for this calculation. On a scale of 0 to 10, with 0 being 'no sleep loss related to the symptoms of my skin disease (prurigo nodularis)' and 10 being 'I did not sleep at all due to the symptoms of prurigo nodularis'. Higher scores indicate worse outcome. Analysis window extension was applied to both timepoints, as described in the SAP. If a subject received any rescue therapy, composite variable strategy is applied, the underlying data at/after receipt of rescue therapy is set as worst possible value, and the response is derived from underlying data value. Subjects with missing results are considered as non-responders. ITT population.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Nemolizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	96		
Units: subjects	95	11		

Statistical analyses

Statistical analysis title	Nemolizumab versus Placebo

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was then performed sequentially in order the endpoints were reported and continued when previous endpoint was statistically significant at two-sided 0.05.

Comparison groups	Nemolizumab v Placebo
Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata adjusted percentage difference
Point estimate	38
Confidence interval	
level	95 %
sides	2-sided
lower limit	27.8
upper limit	48.2

Notes:

[5] - A 2-sided p-value was derived from CMH test using the randomized stratification variables (analysis center and body weight at randomization [< 90 kg, >= 90 kg]). Threshold of significance at 0.05.

Secondary: Number of Subjects With an Improvement of >=4 From Baseline in SD

NRS at Week 4

End point title	Number of Subjects With an Improvement of >=4 From Baseline in SD NRS at Week 4

End point description:

The SD NRS is a scale to be used by the subject to report the degree of their sleep loss related to PN. The baseline SD NRS was determined based on the average of daily SD NRS (score ranging from 0 to10) during the 7 days up to the treatment start (including until treatment start time). A minimum of 4 daily scores out of the 7 days up to baseline study day is required for this calculation. On a scale of 0 to 10, with 0 being 'no sleep loss related to the symptoms of my skin disease (prurigo nodularis)' and 10 being 'I did not sleep at all due to the symptoms of prurigo nodularis'. Higher scores indicate worse outcome. Analysis window extension was applied to baseline, as described in the SAP. If a subject received any rescue therapy, composite variable strategy is applied, the underlying data at/ after receipt of rescue therapy is set as worst possible value, and the response is derived from underlying data value. Subjects with missing results are considered as non-responders. ITT.

End point type	Secondary

End point timeframe:

Baseline, Week 4

End point values	Nemolizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	96		
Units: subjects	59	5		

Statistical analyses

Statistical analysis title	Nemolizumab versus Placebo

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was then performed sequentially in order the endpoints were reported and continued when previous endpoint was statistically significant at two-sided 0.05.

Comparison groups	Nemolizumab v Placebo
Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata adjusted percentage difference
Point estimate	22.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.7
upper limit	30.7

Notes:

[6] - A 2-sided p-value was derived from CMH test using the randomized stratification variables (analysis center and body weight at randomization [< 90 kg, >= 90 kg]). Threshold of significance at 0.05.

Secondary: Number of Subjects With PP NRS < 2 at Week 4

End point title	Number of Subjects With PP NRS < 2 at Week 4

End point description:

The Peak Pruritus NRS is a scale that was used by the subjects to report the intensity of their pruritus (itch) during the last 24 hours. For maximum itch intensity: the scores were provided on a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable'. Higher scores indicate worse outcome. Weekly values are calculated as average of 7 consecutive days data up to the target study day (excluding) and set to missing, if less than 4 days data are available. Analysis window extension was applied to baseline, as described in the SAP. If a subject received any rescue therapy, composite variable strategy is applied, the underlying data at/after receipt of rescue therapy is set as worst possible value, and the response is derived from underlying data value. Subjects with missing results are considered as non-responders. ITT population included all randomised subjects.

End point type	Secondary

End point timeframe:

Week 4

End point values	Nemolizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	96		
Units: subjects	41	1		

Statistical analyses

Statistical analysis title	Nemolizumab versus Placebo

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was then performed sequentially in order the endpoints were reported and continued when previous endpoint was statistically significant at two-sided 0.05.

Comparison groups	Nemolizumab v Placebo
Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata adjusted percentage difference
Point estimate	18.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.3
upper limit	25

Notes:

[7] - A 2-sided p-value was derived from CMH test using the randomized stratification variables (analysis center and body weight at randomization [< 90 kg, >= 90 kg]). Threshold of significance at 0.05.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline up to Week 32

Adverse event reporting additional description:

Safety population included all randomised subjects who received at least 1 administration of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Nemolizumab

Reporting group description:

Subjects weighing < 90 kg received two SC injections of 30 mg nemolizumab (60 mg loading dose) at baseline then one SC injection Q4W. Subjects weighing >= 90 kg received two SC injections of 30 mg nemolizumab (60 mg total) at baseline (no loading dose) and two SC injections Q4W throughout the treatment period of 16 weeks.
Nemolizumab: Subjects received either 30 mg or 60 mg dose of nemolizumab as SC injection.

Reporting group title	Placebo

Reporting group description:

Subjects weighing < 90 kg received two SC injections of matching placebo at baseline, then one SC injection Q4W. Subjects weighing >= 90 kg received two SC injections of matching placebo at baseline, then two SC injections Q4W throughout the treatment period of 16 weeks.
Placebo: Subjects received matching placebo as SC injection.

Serious adverse events	Nemolizumab	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 187 (11.23%)	10 / 95 (10.53%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 187 (0.53%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 187 (0.53%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neoplasm			

subjects affected / exposed	1 / 187 (0.53%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 187 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Vocal cord polyp			
subjects affected / exposed	0 / 187 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	1 / 187 (0.53%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic disorder			
subjects affected / exposed	0 / 187 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Subdural haemorrhage			
subjects affected / exposed	1 / 187 (0.53%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 187 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	1 / 187 (0.53%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 187 (0.53%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac sarcoidosis			
subjects affected / exposed	0 / 187 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	0 / 187 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Arachnoid cyst			
subjects affected / exposed	1 / 187 (0.53%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tension headache			
subjects affected / exposed	1 / 187 (0.53%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	1 / 187 (0.53%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 187 (0.53%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Cholecystitis acute			
subjects affected / exposed	1 / 187 (0.53%)	0 / 95 (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			
Neurodermatitis			
subjects affected / exposed	4 / 187 (2.14%)	2 / 95 (2.11%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pemphigoid			
subjects affected / exposed	2 / 187 (1.07%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	2 / 187 (1.07%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 187 (0.53%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	2 / 187 (1.07%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter colitis			
subjects affected / exposed	1 / 187 (0.53%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			

subjects affected / exposed	1 / 187 (0.53%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 187 (0.53%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 187 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 187 (0.53%)	0 / 95 (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: 5 %

Non-serious adverse events	Nemolizumab	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	61 / 187 (32.62%)	38 / 95 (40.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 187 (6.95%)	2 / 95 (2.11%)	
occurrences (all)	16	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 187 (4.81%)	5 / 95 (5.26%)	
occurrences (all)	11	6	
Dyspnoea			
subjects affected / exposed	6 / 187 (3.21%)	5 / 95 (5.26%)	
occurrences (all)	12	5	
Skin and subcutaneous tissue disorders			

Neurodermatitis			
subjects affected / exposed	15 / 187 (8.02%)	18 / 95 (18.95%)	
occurrences (all)	17	21	
Eczema			
subjects affected / exposed	10 / 187 (5.35%)	1 / 95 (1.05%)	
occurrences (all)	10	1	
Infections and infestations			
COVID-19			
subjects affected / exposed	14 / 187 (7.49%)	14 / 95 (14.74%)	
occurrences (all)	14	14	
Nasopharyngitis			
subjects affected / exposed	11 / 187 (5.88%)	8 / 95 (8.42%)	
occurrences (all)	12	8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 June 2020	Following changes were made: Included Galderma R&D, LLC as sponsor; Updated sponsor signatory; Updated number of sites; Included secondary objectives; Reordered primary endpoints; Updated key secondary endpoints; Updated secondary endpoints; Updated number of subjects and randomization ratio; Updated weight cutoff for dosing; Updated duration of study; Updated IC2 PN definition; Updated IC4 (prev IC5) methods of contraception; Updated IC5 (prev IC6) women of non-childbearing potential; Updated EC2 active pruritic conditions; Updated EC7 infections; Included EC 24-27 optional biopsy sampling; Updated PD sample collection, including biopsies; Updated statistical methods; Updated AESIs to include COVID-19; Updated reasons for study drug discontinuation; Included details of study drug discontinuation due to COVID-19; Clarified self-injection; Updated hypersensitivity reaction monitoring; Included details of CYP450 substrates; Updated collection timepoints in Schedule of Assessments; Updated pregnancy test footnote in Schedule of Assessments; Included subject sleep diary endpoint details; Updated medical history of asthma screening assessment; Included guidance appendix for study conduct and subject safety during COVID-19 pandemic; Updated PAS appendix.
22 December 2020	Following changes were made: Updated the number of study sites from 60 to 70; Clarified the methods of contraception; Clarified that females of non-childbearing potential with the absence of menstrual bleeding for 1 year before screening without any other medical reason must have had a confirmed follicle-stimulating hormone level in the postmenopausal range; Added, if PEF was < 80% of the predicted value at screening in subjects without any history of asthma or in subjects with history of asthma but with the ACT score >19, PEF testing could have been repeated once within 48 hours; Added that subjects with positive HCV antibody from previous exposure/infection did not need to be excluded if a negative PCR confirmed there was no active infection. Additionally, in the event of rescreening, serology test results performed within 6 weeks before the baseline visit, could be used to assess eligibility; Clarified excluded prior treatments; Clarified current and history of untreated or inadequately treated active or latent TB infection, and rescreening procedures; Clarified that the investigational drug exclusion period was 8 weeks or 5 half-lives of the investigational drug, whichever was longer; Clarified that rescue with oral psoralen required discontinuation of study drug; Added rationale for placebo-controlled design; Updated prohibited therapy and information on permitted non-live vaccinations (seasonal, emergency, COVID-19); Clarified management of subjects with either symptomatic or asymptomatic COVID-19; Clarified permitted rescue therapies to include systemic corticosteroids and gabapentinoids; Deleted residual error in self-injection description from the schedule of assessments footnote; Clarified PK parameters and analyses; Updated the form for PD sample recording; Corrected the error in the sample size calculation (to power at 5%); Updated guidance for management of subjects during the COVID-19 pandemic.
19 November 2021	Following changes were made: Added the secondary efficacy endpoint of the proportion of subjects with PP NRS improvement >= 4 from baseline and IGA success at Week 16, Week 20, and Week 24; Updated restricted prior treatments, prohibited therapy, and ADA assay information to be harmonised with other protocols in the nemolizumab program; Specified that ADA was to be determined using validated ECLIA (not ELISA).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported