



Clinical trial results:

A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Nemolizumab in Subjects with Moderate-to-Severe Atopic Dermatitis with Inadequate Response to or for Whom Cyclosporine A is not Medically Advisable

Summary

EudraCT number	2021-002166-40
Trial protocol	CZ PL LV ES IT DE
Global end of trial date	14 April 2023

Results information

Result version number	v1 (current)
This version publication date	04 May 2024
First version publication date	04 May 2024

Trial information

Trial identification

Sponsor protocol code	RD.06.SPR.201591
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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	Zählerweg 10, Zug, Switzerland, 6300
Public contact	Clinical Trial Information Desk, Galderma S.A., CTA.Coordinator@galderma.com
Scientific contact	Clinical Trial Information Desk, Galderma S.A., CTA.Coordinator@galderma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	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	08 January 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 April 2023
Global end of trial reached?	Yes
Global end of trial date	14 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to investigate the efficacy of nemolizumab administered in combination with topical background therapy (topical corticosteroids [TCS] with or without topical calcineurin inhibitors [TCI]) in adult subjects with moderate-to-severe atopic dermatitis (AD) who are not adequately controlled with or are not advised to use oral cyclosporine A (CsA) for medical reasons.

Protection of trial subjects:

The study was conducted in accordance with the accepted version of the Declaration of Helsinki and/or all relevant regulations, in compliance with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) and Good Clinical Practice (GCP) guidelines and according to the appropriate regulatory requirements in the countries where the study was conducted. Before initiation of the study at each study site, the protocol, the informed consent form (ICF), other written material given to the subjects, and any other relevant study documentation were to be reviewed and approved by a duly constituted Independent Ethics Committee (IEC).

All subjects were to be informed about the clinical study according to GCP guidelines, and in accordance with the EU legislation and the applicable local requirements. Informed consent was to be obtained from each subject before the subject was admitted to the study. The Investigator did not undertake any study-related examination or activity before the subject had given written informed consent to participate.

Background therapy:

Subjects applied a moisturizer at least once daily and a prescribed authorized background topical therapy for atopic dermatitis (AD), including a medium-potency topical corticosteroids (TCS) for the body and a low-potency TCS or topical calcineurin inhibitors (TCI) for sensitive areas such as the face, neck, and intertriginous areas.

Evidence for comparator:

Placebo

Actual start date of recruitment	18 February 2022
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: 132
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	Czechia: 55
Country: Number of subjects enrolled	Germany: 47
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Latvia: 22
Worldwide total number of subjects	276
EEA total number of subjects	276

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)	267
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were screened at 50 study sites in 6 European countries: Italy (5 sites), Spain (7 sites), Czech Republic (4 sites), Poland (17 sites), Latvia (4 sites), and Germany (13 sites). Overall 46 sites randomized the subjects from 18 February 2022 to 16 November 2022.

Pre-assignment

Screening details:

A total of 326 subjects were screened at 50 study sites and 276 subjects were randomized 1:1 to receive either Nemolizumab or placebo.

Period 1

Period 1 title	Treatment period up to week 16 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

To avoid bias and to ensure the integrity of the blind, personnel directly involved with the conduct of the study from the Sponsor, contract research organization (CRO), or study sites did not have access to any information that may have led to unblinding. Randomization through the interactive response technology (IRT) guarded against selection bias.

Arms

Are arms mutually exclusive?	Yes
Arm title	Nemolizumab arm

Arm description:

Subjects randomized to receive Nemolizumab. Subjects continued using background topical therapy, which was to be adjusted according to disease activity and tolerability, including tapering when signs and symptoms improved, discontinuing when lesions cleared, and restarting if signs and symptoms recurred, based on Investigator's clinical judgement.

Arm type	Experimental
Investigational medicinal product name	Nemolizumab 30 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

At the baseline visit, subjects received a loading dose of nemolizumab by 2 SC injections. During the Treatment Period, nemolizumab was administered via a single SC injection every 4 weeks (Q4W) at Weeks 4, 8, and 12.

Arm title	Placebo arm
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Arm description:

Subjects randomized to receive Placebo. Subjects continued using background topical therapy, which was to be adjusted according to disease activity and tolerability, including tapering when signs and symptoms improved, discontinuing when lesions cleared, and restarting if signs and symptoms recurred, based on Investigator's clinical judgement.

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

Dosage and administration details:

At the baseline visit, subjects received 2 SC injections with placebo. During the Treatment Period, placebo was administered via a single SC injection every 4 weeks (Q4W) at Weeks 4, 8, and 12.

Number of subjects in period 1	Nemolizumab arm	Placebo arm
Started	138	138
Completed	132	131
Not completed	6	7
Consent withdrawn by subject	2	5
Adverse event, non-fatal	1	2
Lost to follow-up	2	-
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	Nemolizumab arm
Reporting group description:	
Subjects randomized to receive Nemolizumab. Subjects continued using background topical therapy, which was to be adjusted according to disease activity and tolerability, including tapering when signs and symptoms improved, discontinuing when lesions cleared, and restarting if signs and symptoms recurred, based on Investigator's clinical judgement.	
Reporting group title	Placebo arm
Reporting group description:	
Subjects randomized to receive Placebo. Subjects continued using background topical therapy, which was to be adjusted according to disease activity and tolerability, including tapering when signs and symptoms improved, discontinuing when lesions cleared, and restarting if signs and symptoms recurred, based on Investigator's clinical judgement.	

Reporting group values	Nemolizumab arm	Placebo arm	Total
Number of subjects	138	138	276
Age categorical Units: Subjects			
Adults (18-64 years)	132	135	267
From 65 to 84 years	6	3	9
Age continuous Units: years			
arithmetic mean	38.3	36.1	-
standard deviation	± 13.15	± 12.21	-
Gender categorical Units: Subjects			
Female	66	66	132
Male	72	72	144
Ethnicity Units: Subjects			
Hispanic or Latino	5	6	11
Not Hispanic or Latino	132	132	264
Unknown	1	0	1
EASI score Units: units on a scale			
arithmetic mean	29.535	31.328	-
standard deviation	± 8.5041	± 9.6653	-
Body surface area Units: percent			
arithmetic mean	44.61	46.09	-
standard deviation	± 17.532	± 17.966	-
PP NRS Units: units on a scale			
arithmetic mean	7.405	7.475	-
standard deviation	± 1.3811	± 1.4634	-

End points

End points reporting groups

Reporting group title	Nemolizumab arm
Reporting group description: Subjects randomized to receive Nemolizumab. Subjects continued using background topical therapy, which was to be adjusted according to disease activity and tolerability, including tapering when signs and symptoms improved, discontinuing when lesions cleared, and restarting if signs and symptoms recurred, based on Investigator's clinical judgement.	
Reporting group title	Placebo arm
Reporting group description: Subjects randomized to receive Placebo. Subjects continued using background topical therapy, which was to be adjusted according to disease activity and tolerability, including tapering when signs and symptoms improved, discontinuing when lesions cleared, and restarting if signs and symptoms recurred, based on Investigator's clinical judgement.	

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

End point title	Percentage of Subjects with $\geq 75\%$ Improvement in Eczema Area and Severity Index (EASI-75) at Week 16
End point description: The EASI score is used to measure the severity and extent of atopic dermatitis (AD) and measured erythema, infiltration, excoriation and lichenification on 4 anatomic regions of the body: head, trunk, upper and lower extremities. The EASI score is a composite score ranging from 0 to 72. EASI-75 responders were the subjects who achieved $\geq 75\%$ overall improvement in EASI score from baseline to Week 16.	
End point type	Primary
End point timeframe: At Week 16 compared with the baseline	

End point values	Nemolizumab arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	138	138		
Units: percent				
number (not applicable)				
EASI-75 improvement	47.1	34.8		

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description: Treatment difference of nemolizumab and placebo (in combination with TCS with or without TCI) in response rate. The Intent-to Treat (ITT) population consisted of all randomized subjects	
Comparison groups	Nemolizumab arm v Placebo arm

Number of subjects included in analysis	276
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted difference in proportion
Point estimate	12.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	23.6

Primary: Percentage of subjects with Peak Pruritus Numerical Rating Scale (PP NRS) Improvement of ≥ 4 from baseline at week 16

End point title	Percentage of subjects with Peak Pruritus Numerical Rating Scale (PP NRS) Improvement of ≥ 4 from baseline at week 16
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End point description:

The PP-NRS is an assessment tool used by the subjects to report the intensity of their pruritus (itch) during the last 24 hours on a scale of 0 to 10, with 0 being "no itch" and 10 being "worst itch imaginable". We report here the percentage of subjects with a weekly average improvement of Peak Pruritus Numerical Rating Scale (PP NRS) ≥ 4 from baseline at Week 16. Subjects who completed the Treatment Period up to Week 16 with an improvement of PP NRS ≥ 4 from baseline at Week 16 were classified as a success. Subjects who did not satisfy this criterion, who discontinued from the study prior to Week 16, or who required rescue therapy were classified as failures.

End point type	Primary
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End point timeframe:

At Week 16 compared with the baseline

End point values	Nemolizumab arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	138	138		
Units: percent				
number (not applicable)				
PP NRS improvement ≥ 4 from baseline	39.1	17.4		

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
Treatment difference of nemolizumab and placebo (in combination with TCS with or without TCI) in response rate. The Intent-to Treat (ITT) population consisted of all randomized subjects	
Comparison groups	Nemolizumab arm v Placebo arm

Number of subjects included in analysis	276
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted difference in proportion
Point estimate	21.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.4
upper limit	32

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the baseline through week 16.

Adverse event reporting additional description:

For non-serious adverse events (NSAE): only subjects and events from selected preferred terms are included in the counts. Selected preferred terms are preferred terms from which at least 2% of the subjects experienced a NSAE in either group. Subjects who experienced NSAE only in non-selected preferred terms are excluded from the counts.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.0
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Reporting groups

Reporting group title	Safety Analysis Set - Nemolizumab arm
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Reporting group description:

All subjects randomized to Nemolizumab and received at least 1 dose of study drug.

Reporting group title	Safety Analysis Set - Placebo arm
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Reporting group description:

All subjects randomized to placebo and received at least 1 dose of placebo.

Serious adverse events	Safety Analysis Set - Nemolizumab arm	Safety Analysis Set - Placebo arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 137 (2.19%)	2 / 137 (1.46%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Jaw fracture			
subjects affected / exposed	0 / 137 (0.00%)	1 / 137 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin wound			
subjects affected / exposed	0 / 137 (0.00%)	1 / 137 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			

subjects affected / exposed	1 / 137 (0.73%)	0 / 137 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 137 (0.00%)	1 / 137 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Aggression			
subjects affected / exposed	1 / 137 (0.73%)	0 / 137 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dependence			
subjects affected / exposed	1 / 137 (0.73%)	0 / 137 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Personality disorder			
subjects affected / exposed	1 / 137 (0.73%)	0 / 137 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide threat			
subjects affected / exposed	1 / 137 (0.73%)	0 / 137 (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			
Localised infection			
subjects affected / exposed	1 / 137 (0.73%)	0 / 137 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 137 (0.73%)	0 / 137 (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	Safety Analysis Set - Nemolizumab arm	Safety Analysis Set - Placebo arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 137 (31.39%)	37 / 137 (27.01%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	5 / 137 (3.65%)	1 / 137 (0.73%)	
occurrences (all)	5	1	
Peak expiratory flow rate decreased			
subjects affected / exposed	3 / 137 (2.19%)	1 / 137 (0.73%)	
occurrences (all)	3	2	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	5 / 137 (3.65%)	2 / 137 (1.46%)	
occurrences (all)	6	2	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	10 / 137 (7.30%)	6 / 137 (4.38%)	
occurrences (all)	10	7	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	4 / 137 (2.92%)	1 / 137 (0.73%)	
occurrences (all)	4	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 137 (0.00%)	3 / 137 (2.19%)	
occurrences (all)	0	3	
COVID-19			
subjects affected / exposed	7 / 137 (5.11%)	4 / 137 (2.92%)	
occurrences (all)	7	4	
Nasopharyngitis			
subjects affected / exposed	13 / 137 (9.49%)	14 / 137 (10.22%)	
occurrences (all)	14	17	
Rhinitis			

subjects affected / exposed	4 / 137 (2.92%)	1 / 137 (0.73%)	
occurrences (all)	4	1	
Tonsillitis			
subjects affected / exposed	0 / 137 (0.00%)	3 / 137 (2.19%)	
occurrences (all)	0	3	
Upper respiratory tract infection			
subjects affected / exposed	5 / 137 (3.65%)	1 / 137 (0.73%)	
occurrences (all)	6	1	
Urinary tract infection			
subjects affected / exposed	3 / 137 (2.19%)	3 / 137 (2.19%)	
occurrences (all)	3	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported