Clinical trial results:
A Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group Study of Nipocalimab in Adult Participants with Active Systemic Lupus Erythematosus

Summary

EudraCT number	2020-005569-14
Trial protocol	HU PL ES BG
Global end of trial date	25 December 2024

Results information

Result version number	v1 (current)
This version publication date	23 January 2026
First version publication date	23 January 2026

Trial information

Trial identification

Sponsor protocol code	80202135SLE2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04882878
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International N.V.
Sponsor organisation address	Turnhoutseweg 30, Beerse, Belgium, B-2340
Public contact	Clinical Registry Group, Janssen-Cilag International N.V., ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag International N.V., ClinicalTrialsEU@its.jnj.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	25 December 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate the efficacy and safety of nipocalimab vs placebo in participants with active systemic lupus erythematosus (SLE).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy:

Protocol permitted standard of care therapies.

Evidence for comparator: -

Actual start date of recruitment	20 August 2021
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	Argentina: 52
Country: Number of subjects enrolled	Bulgaria: 13
Country: Number of subjects enrolled	Colombia: 33
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Hungary: 10
Country: Number of subjects enrolled	Japan: 8
Country: Number of subjects enrolled	Poland: 29
Country: Number of subjects enrolled	Taiwan: 9
Country: Number of subjects enrolled	Ukraine: 6
Country: Number of subjects enrolled	United States: 39
Country: Number of subjects enrolled	South Africa: 21
Worldwide total number of subjects	228
EEA total number of subjects	60

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)	225
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 228 participants were randomized and treated in the study. Out of 228, 192 participants completed the study.

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	Placebo

Arm description:

Participants with active, autoantibody-positive systemic lupus erythematosus (SLE) who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive placebo matching to nipocalimab as an intravenous (IV) infusion every 2 weeks (q2w) from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received placebo matching to nipocalimab as an IV infusion q2w through Week 50.

Arm title	Nipocalimab 5 mg/kg IV

Arm description:

Participants with active, autoantibody-positive SLE who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive nipocalimab 5 milligrams per kilogram (mg/kg) as an IV infusion q2w from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.

Arm type	Experimental
Investigational medicinal product name	Nipocalimab
Investigational medicinal product code	JNJ-80202135
Other name	M281
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received nipocalimab 5 mg/kg as an IV infusion q2w through Week 50.

Arm title	Nipocalimab 15 mg/kg IV

Arm description:

Participants with active, autoantibody-positive SLE who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive nipocalimab 15 mg/kg as an IV infusion q2w from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.

Arm type	Experimental
Investigational medicinal product name	Nipocalimab
Investigational medicinal product code	JNJ-80202135
Other name	M281
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received nipocalimab 15 mg/kg as an IV infusion q2w through Week 50.

Number of subjects in period 1	Placebo	Nipocalimab 5 mg/kg IV	Nipocalimab 15 mg/kg IV
Started	75	77	76
Completed	60	65	67
Not completed	15	12	9
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	9	4	4
Unspecified	5	6	3
Lost to follow-up	1	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo

Reporting group description:

Participants with active, autoantibody-positive systemic lupus erythematosus (SLE) who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive placebo matching to nipocalimab as an intravenous (IV) infusion every 2 weeks (q2w) from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.

Reporting group title	Nipocalimab 5 mg/kg IV

Reporting group description:

Participants with active, autoantibody-positive SLE who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive nipocalimab 5 milligrams per kilogram (mg/kg) as an IV infusion q2w from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.

Reporting group title	Nipocalimab 15 mg/kg IV

Reporting group description:

Participants with active, autoantibody-positive SLE who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive nipocalimab 15 mg/kg as an IV infusion q2w from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.

Reporting group values	Placebo	Nipocalimab 5 mg/kg IV	Nipocalimab 15 mg/kg IV
Number of subjects	75	77	76
Age categorical Units: Subjects			
In Utero	0	0	0
Preterm newborn infants (gestional age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days - 23 months)	0	0	0
Children (2 - 11 years)	0	0	0
12 - 17 years	0	0	0
Adults (18 - 64 years)	75	76	74
From 65 - 84 years	0	1	2
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	45.3	41.1	43.9
standard deviation	± 11.35	± 11.82	± 11.85
Gender categorical Units: Subjects			
Male	4	4	4
Female	71	73	72

Reporting group values	Total		
Number of subjects	228		

Age categorical Units: Subjects			
In Utero	0		
Preterm newborn infants (gestional age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days - 23 months)	0		
Children (2 - 11 years)	0		
12 - 17 years	0		
Adults (18 - 64 years)	225		
From 65 - 84 years	3		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Male	12		
Female	216		

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants with active, autoantibody-positive systemic lupus erythematosus (SLE) who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive placebo matching to nipocalimab as an intravenous (IV) infusion every 2 weeks (q2w) from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.

Reporting group title	Nipocalimab 5 mg/kg IV

Reporting group description:

Participants with active, autoantibody-positive SLE who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive nipocalimab 5 milligrams per kilogram (mg/kg) as an IV infusion q2w from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.

Reporting group title	Nipocalimab 15 mg/kg IV

Reporting group description:

Participants with active, autoantibody-positive SLE who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive nipocalimab 15 mg/kg as an IV infusion q2w from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.

Primary: Percentage of Participants who Achieved a Systemic Lupus Erythematosus (SLE) Responder Index (SRI)-4 Composite Response at Week 24

End point title	Percentage of Participants who Achieved a Systemic Lupus Erythematosus (SLE) Responder Index (SRI)-4 Composite Response at Week 24

End point description:

SRI-4 measures reduction in SLE disease activity and was composite measure that included SLE Disease Activity Index (SLEDAI-2K), British Isles Lupus Activity Group (BILAG) and Physician Global Assessment (PGA). SRI-4 response: >=4-point reduction from baseline (BL) in SLEDAI-2K score, no new BILAG A or >1 new BILAG B (score A: severe disease; B: moderate disease), and no worsening in PGA (PGA <10% increase from BL). Composite response: SRI-4 response in participants who did not meet treatment failure criteria. SLEDAI-2K: assesses improvement in disease activity (ranged:0-105; higher score=higher severity). BILAG: assesses disease extent, severity (A[severe]-E[no disease]). PGA: assesses worsening in participant's health, recorded on visual analogue scale (VAS) with responses for disease activity ranged 0(none)-3(severe); higher score=higher disease activity. Full analysis set (FAS): all randomized participants who received at least 1 dose (partial/complete) of any study intervention.

End point type	Primary

End point timeframe:

At Week 24

End point values	Placebo	Nipocalimab 5 mg/kg IV	Nipocalimab 15 mg/kg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	75	77	76	
Units: Percentage of participants				
number (confidence interval 90%)	46.7 (37.2 to 56.1)	49.4 (39.9 to 58.9)	53.5 (44.1 to 63.0)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Nipocalimab 5 mg/kg IV v Placebo
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.331
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.7
upper limit	2.1

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Nipocalimab 15 mg/kg IV
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.081
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.9
upper limit	2.9

Secondary: Percentage of Participants With Baseline Active Mucocutaneous Lupus Manifestations (Cutaneous Lupus Erythematosus Disease Area and Severity Index [CLASI] Activity Score >=6) Achieving >=50% Reduction in CLASI Activity Score at Week 24

End point title	Percentage of Participants With Baseline Active Mucocutaneous Lupus Manifestations (Cutaneous Lupus Erythematosus Disease Area and Severity Index [CLASI] Activity Score >=6) Achieving >=50% Reduction in CLASI Activity Score at Week 24

End point description:

Percentage of participants with baseline active mucocutaneous lupus manifestations (CLASI activity score >=6) achieving >=50% reduction in CLASI activity score at Week 24 was reported. CLASI assess disease activity and damage caused to skin for cutaneous lupus erythematosus patients with/without systemic involvement across 13 body areas. CLASI consisted of 2 scores; (1) Activity Score (ranged: 0-70) (2) Damage Score (ranged: 0-56). Activity was scored by the investigator based on erythema (0-3 per area), scale/hyperkeratosis (0-2 per area), mucous membrane involvement (0-1), acute hair loss (0-1) and non-scarring alopecia (0-3). Damage was scored in terms of dyspigmentation (0-2 per area), scarring (0-2 per area), scarring alopecia (3 points if present), deep scarring (1 point). Scores were calculated by addition based on the extent of symptoms. Higher scores=worse disease activity. FAS used. N (overall number of participants analyzed)=participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At Week 24

End point values	Placebo	Nipocalimab 5 mg/kg IV	Nipocalimab 15 mg/kg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	43	40	
Units: Percentage of participants				
number (confidence interval 90%)	46.3 (33.5 to 59.2)	53.2 (40.4 to 66.1)	53.8 (40.7 to 66.9)	

Statistical analyses

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Nipocalimab 5 mg/kg IV
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.247
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.6
upper limit	3.1

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Nipocalimab 15 mg/kg IV

Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.09
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.9
upper limit	4.5

Secondary: Percentage of Participants With Baseline Arthritis (with at Least 4 Active Joints at Baseline) Achieving Greater Than or Equal to (>=) 50% Reduction in Active Joints at Week 24

End point title	Percentage of Participants With Baseline Arthritis (with at Least 4 Active Joints at Baseline) Achieving Greater Than or Equal to (>=) 50% Reduction in Active Joints at Week 24

End point description:

The active joint was defined as a joint that was painful as reported by the participant and demonstrated tenderness and at least one additional sign of inflammation (for example [e.g.]: observed swelling such as edema or effusion) on physical examination as determined by the joint assessor. Each of 64 joints would be evaluated for symptoms of pain, tenderness and 62 joints for swelling or effusion (hips are excluded). 50% reduction in active joints: Participants with baseline arthritis who had >=50% reduction in active joints from baseline. FAS: all randomized participants who received at least 1 dose (partial or complete) of any study intervention. Here 'N' (overall number of participants analyzed) refers to the number of participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At Week 24

End point values	Placebo	Nipocalimab 5 mg/kg IV	Nipocalimab 15 mg/kg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	68	72	69	
Units: Percentage of participants				
number (confidence interval 90%)	75.0 (66.4 to 83.6)	82.0 (74.4 to 89.6)	75.4 (66.8 to 83.9)	

Statistical analyses

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v Nipocalimab 5 mg/kg IV

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.122
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.8
upper limit	3.7

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo v Nipocalimab 15 mg/kg IV
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.296
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.6
upper limit	2.6

Secondary: Percentage of Participants With >=4 Point Improvement From Baseline in SLE Disease Activity Index 2000 (SLEDAI-2K) at Week 24

End point title	Percentage of Participants With >=4 Point Improvement From Baseline in SLE Disease Activity Index 2000 (SLEDAI-2K) at Week 24

End point description:

SLEDAI-2K was a validated SLE activity index, based on the presence of 24 features in 9 organ systems and measures disease activity in SLE patients at the time of visit or in previous 30 days; the index was weighted according to the feature. Features were scored by assessing physician if present at the time of visit or within last 30 days, with more severe features having higher scores, and added to determine total SLEDAI-2K score, ranged: 0-105; higher scores=increased disease activity. Baseline measurement for SLEDAI-2K was defined as the closest measurement taken prior to initiation of the Week 0 study intervention administration. SLEDAI improvement was defined as a reduction from baseline in total SLEDAI-2K score. No worsening of total SLEDAI-2K from baseline was defined as a change <=0 in SLEDAI-2K score and meaningful improvement was defined as a reduction in SLEDAI-2K of 4 or more. FAS used. 'N' (overall number of participants analyzed)=participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At Week 24

End point values	Placebo	Nipocalimab 5 mg/kg IV	Nipocalimab 15 mg/kg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	75	77	75	
Units: Percentage of participants				
number (confidence interval 90%)	46.7 (37.2 to 56.1)	49.3 (39.8 to 58.8)	54.3 (44.7 to 63.8)	

Statistical analyses

Statistical analysis title	Statistical Analysis 8
Comparison groups	Placebo v Nipocalimab 15 mg/kg IV
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.069
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.9
upper limit	3

Statistical analysis title	Statistical Analysis 7
Comparison groups	Placebo v Nipocalimab 5 mg/kg IV
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.338
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.7
upper limit	2.1

Secondary: Percentage of Participants Achieving the British Isles Lupus Assessment

Group (BILAG) Composite Lupus Assessment (BICLA) Response at Week 24

End point title	Percentage of Participants Achieving the British Isles Lupus Assessment Group (BILAG) Composite Lupus Assessment (BICLA) Response at Week 24

End point description:

The BILAG-based Composite Lupus Assessment (BICLA) was a composite index to assess disease activity in SLE. BICLA response defined as: (1) Reduction of all baseline (BL) BILAG-2004 A to B/C/D and BL BILAG-2004 B to C/D and no BILAG-2004 worsening in other organ systems, defined by >=1 new BILAG-2004 A or >=2 new BILAG-2004 B (Score A: Severely active disease; B: Moderately active disease; C: Mild stable disease; D: Inactive now but previously active; E: Never affected). (2) No worsening from BL in SLEDAI-2K: increase from BL of >0 points in SLEDAI-2K. Increase from BL corresponds to change from BL. (3) No worsening from BL in participants' lupus disease activity defined by increase >=0.30 points on 3-point PGA VAS. (4) No discontinuation of study intervention or use of rescue medication beyond protocol-allowed threshold before assessment. If any of the conditions cannot be evaluated at Week 24 (due to missing values) the participant was defined as BICLA non-responder. FAS was used.

End point type	Secondary

End point timeframe:

At Week 24

End point values	Placebo	Nipocalimab 5 mg/kg IV	Nipocalimab 15 mg/kg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	75	77	76	
Units: Percentage of participants				
number (confidence interval 90%)	32.0 (23.1 to 40.9)	39.3 (30.0 to 48.6)	36.1 (27.0 to 45.2)	

Statistical analyses

Statistical analysis title	Statistical Analysis 9
Comparison groups	Placebo v Nipocalimab 5 mg/kg IV
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.211
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.7
upper limit	2.4

Statistical analysis title	Statistical Analysis 10
Comparison groups	Placebo v Nipocalimab 15 mg/kg IV

Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.242
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.7
upper limit	2.3

Secondary: Time to First Flare Through Week 24

End point title	Time to First Flare Through Week 24

End point description:

Time to first flare: Time to first occurrence of a flare. Flare was defined as at least 1 new BILAG A item score or at least 2 new BILAG B item scores meeting at least 1 of following criteria: 1) Not present at baseline, 2) The occurrence of a new/worse manifestation in a different component of an organ system that is already present, 3) at least 1 A or 2 B scores in an organ system which improves to B/C/D for at least 2 sequential study visits followed by new/worse disease activity. Here, score A: Severely active disease; B: Moderately active disease; C: Mild stable disease; D: Inactive now but previously active; E: Never affected. BILAG flare was based on adjudicated flare. FAS: all randomized participants who received at least 1 dose (partial or complete) of any study intervention. 99999 signifies that median, lower and upper limit of confidence interval could not be calculated due to low number of participants with event.

End point type	Secondary

End point timeframe:

From Week 0 up to Week 24

End point values	Placebo	Nipocalimab 5 mg/kg IV	Nipocalimab 15 mg/kg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	75	77	76	
Units: Days				
median (confidence interval 90%)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

Statistical analysis title	Statistical Analysis 11
Comparison groups	Placebo v Nipocalimab 5 mg/kg IV

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.459
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.69
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.33
upper limit	1.44

Statistical analysis title	Statistical Analysis 12
Statistical analysis description:	
NA	
Comparison groups	Placebo v Nipocalimab 15 mg/kg IV
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.769
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.52
upper limit	1.92

Secondary: Percentage of Participants who Achieved SRI-4 Composite Response at Week 52

End point title	Percentage of Participants who Achieved SRI-4 Composite Response at Week 52

End point description:

SRI-4 measures reduction in SLE disease activity and was a composite measure that included the SLEDAI-2K, BILAG and PGA. SRI-4 response was defined as >=4-point reduction from baseline in SLEDAI-2K score, no new BILAG A or >1 new BILAG B, and no worsening in the PGA (PGA less than [<] 10% increase from baseline). Composite response was defined as SRI-4 response in participants who did not meet treatment failure criteria. SLEDAI-2K: assesses improvement in disease activity (ranged: 0 to 105; higher score = higher severity). BILAG: assesses disease extent, severity (range: A[severe] to E[no disease]). PGA: assesses worsening in participant's general health , recorded on a VAS with responses for disease activity ranging from 0 (none) to 3 (severe); higher score = higher disease activity. Modified full analysis set (mFAS) included all randomized participants, excluding those from Argentinian site W02-AR10008, who received at least 1 dose (partial or complete) of any study intervention.

End point type	Secondary

End point timeframe:

At Week 52

End point values	Placebo	Nipocalimab 5 mg/kg IV	Nipocalimab 15 mg/kg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	74	74	
Units: Percentage of participants				
number (confidence interval 90%)	39.7 (30.3 to 49.1)	51.7 (42.1 to 61.4)	53.6 (44.0 to 63.2)	

Statistical analyses

Statistical analysis title	Statistical Analysis 14
Comparison groups	Placebo v Nipocalimab 15 mg/kg IV
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.2
upper limit	3.9

Statistical analysis title	Statistical Analysis 13
Comparison groups	Placebo v Nipocalimab 5 mg/kg IV
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.054
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	1
upper limit	3.3

Secondary: Percentage of Participants Receiving >=10 milligram/day (mg/day)

Prednisone or Equivalent at Baseline who Achieved Week 6-16 Glucocorticoid (GC) Taper Goal (at Week 16 to <=7.5 mg/day Prednisone or Equivalent) and Maintained that Reduction Until Week 24

End point title	Percentage of Participants Receiving >=10 milligram/day (mg/day) Prednisone or Equivalent at Baseline who Achieved Week 6-16 Glucocorticoid (GC) Taper Goal (at Week 16 to <=7.5 mg/day Prednisone or Equivalent) and Maintained that Reduction Until Week 24

End point description:

Sustained (maintained) reduction was defined as achieving Week 6–16 GC taper goal (at Week 16 to less than or equal to [<=] 7.5 mg/day prednisone or equivalent) and maintaining that reduction until Week 24. FAS included all randomized participants who received at least 1 dose (partial or complete) of any study intervention. Here 'N' (overall number of participants analyzed) refers to the number of participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

End point values	Placebo	Nipocalimab 5 mg/kg IV	Nipocalimab 15 mg/kg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	36	32	
Units: Percentage of participants				
number (confidence interval 90%)	69.7 (56.5 to 82.9)	67.4 (54.2 to 80.6)	80.8 (69.2 to 92.4)	

Statistical analyses

Statistical analysis title	Statistical Analysis 16
Comparison groups	Placebo v Nipocalimab 15 mg/kg IV
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.135
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.7
upper limit	6.5

Statistical analysis title	Statistical Analysis 15
Comparison groups	Placebo v Nipocalimab 5 mg/kg IV

Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.718
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.3
upper limit	1.9

Secondary: Percentage of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs) Through Week 58

End point title	Percentage of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs) Through Week 58

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical study participant administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. Serious AE was the AE resulting in any of following outcomes/deemed significant for any other reason: death; initial/prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. TEAEs were defined as any AE occurring at or after the initial administration of study intervention. TEAEs included both serious and non-serious AEs. Safety analysis set included all randomized participants who received at least 1 dose (partial or complete) of any study intervention.

End point type	Secondary

End point timeframe:

From start of treatment (Week 0) up to Week 58

End point values	Placebo	Nipocalimab 5 mg/kg IV	Nipocalimab 15 mg/kg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	75	77	76	
Units: Percentage of participants				
number (not applicable)				
TEAEs	76.0	89.6	82.9	
TESAEs	8.0	7.8	13.2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of treatment (Week 0) up to Week 58	
Adverse event reporting additional description:	
Safety analysis set included all randomized participants who received at least 1 dose (partial or complete) of any study intervention.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants with active, autoantibody-positive systemic lupus erythematosus (SLE) who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive placebo matching to nipocalimab as an intravenous (IV) infusion every 2 weeks (q2w) from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.	
Reporting group title	Nipocalimab 15 mg/kg IV
Reporting group description:	
Participants with active, autoantibody-positive SLE who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive nipocalimab 15 mg/kg as an IV infusion q2w from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.	
Reporting group title	Nipocalimab 5 mg/kg IV
Reporting group description:	
Participants with active, autoantibody-positive SLE who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive nipocalimab 5 milligrams per kilogram (mg/kg) as an IV infusion q2w from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.	

Serious adverse events	Placebo	Nipocalimab 15 mg/kg IV	Nipocalimab 5 mg/kg IV
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 75 (8.00%)	10 / 76 (13.16%)	6 / 77 (7.79%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Deep Vein Thrombosis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 76 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute Myocardial Infarction			

subjects affected / exposed	1 / 75 (1.33%)	0 / 76 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular Accident			
subjects affected / exposed	0 / 75 (0.00%)	1 / 76 (1.32%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid Haemorrhage			
subjects affected / exposed	0 / 75 (0.00%)	0 / 76 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Ectopic Pregnancy			
subjects affected / exposed	0 / 75 (0.00%)	1 / 76 (1.32%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 75 (1.33%)	0 / 76 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 76 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Intestinal Obstruction			
subjects affected / exposed	0 / 75 (0.00%)	1 / 76 (1.32%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis Alcoholic			

subjects affected / exposed	0 / 75 (0.00%)	1 / 76 (1.32%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine Enlargement			
subjects affected / exposed	0 / 75 (0.00%)	1 / 76 (1.32%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Shrinking Lung Syndrome			
subjects affected / exposed	0 / 75 (0.00%)	0 / 76 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Foot Deformity			
subjects affected / exposed	0 / 75 (0.00%)	1 / 76 (1.32%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 75 (0.00%)	1 / 76 (1.32%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic Lupus Erythematosus			
subjects affected / exposed	0 / 75 (0.00%)	1 / 76 (1.32%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pyelonephritis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 76 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	1 / 75 (1.33%)	0 / 76 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 75 (1.33%)	0 / 76 (0.00%)	2 / 77 (2.60%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parametritis			
subjects affected / exposed	0 / 75 (0.00%)	1 / 76 (1.32%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 75 (0.00%)	1 / 76 (1.32%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic Shock			
subjects affected / exposed	0 / 75 (0.00%)	1 / 76 (1.32%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Wound Infection			
subjects affected / exposed	0 / 75 (0.00%)	0 / 76 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	Nipocalimab 15 mg/kg IV	Nipocalimab 5 mg/kg IV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 75 (54.67%)	51 / 76 (67.11%)	53 / 77 (68.83%)
Injury, poisoning and procedural complications			
Limb Injury			
subjects affected / exposed	3 / 75 (4.00%)	0 / 76 (0.00%)	5 / 77 (6.49%)
occurrences (all)	3	0	5
Vascular disorders			

Hypertension			
subjects affected / exposed	4 / 75 (5.33%)	4 / 76 (5.26%)	5 / 77 (6.49%)
occurrences (all)	5	4	5
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 75 (6.67%)	6 / 76 (7.89%)	11 / 77 (14.29%)
occurrences (all)	5	7	11
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 75 (1.33%)	2 / 76 (2.63%)	4 / 77 (5.19%)
occurrences (all)	10	2	5
Oedema Peripheral			
subjects affected / exposed	0 / 75 (0.00%)	5 / 76 (6.58%)	1 / 77 (1.30%)
occurrences (all)	0	5	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 75 (8.00%)	4 / 76 (5.26%)	3 / 77 (3.90%)
occurrences (all)	9	4	5
Abdominal Pain			
subjects affected / exposed	2 / 75 (2.67%)	4 / 76 (5.26%)	1 / 77 (1.30%)
occurrences (all)	2	5	1
Nausea			
subjects affected / exposed	4 / 75 (5.33%)	4 / 76 (5.26%)	8 / 77 (10.39%)
occurrences (all)	4	11	11
Vomiting			
subjects affected / exposed	2 / 75 (2.67%)	3 / 76 (3.95%)	4 / 77 (5.19%)
occurrences (all)	3	3	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 75 (2.67%)	4 / 76 (5.26%)	0 / 77 (0.00%)
occurrences (all)	2	4	0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	2 / 75 (2.67%)	7 / 76 (9.21%)	5 / 77 (6.49%)
occurrences (all)	7	9	8
Infections and infestations			

Asymptomatic Bacteriuria			
subjects affected / exposed	1 / 75 (1.33%)	4 / 76 (5.26%)	5 / 77 (6.49%)
occurrences (all)	1	5	9
Covid-19			
subjects affected / exposed	4 / 75 (5.33%)	5 / 76 (6.58%)	5 / 77 (6.49%)
occurrences (all)	4	6	5
Cystitis			
subjects affected / exposed	0 / 75 (0.00%)	4 / 76 (5.26%)	1 / 77 (1.30%)
occurrences (all)	0	8	1
Gastroenteritis			
subjects affected / exposed	4 / 75 (5.33%)	1 / 76 (1.32%)	4 / 77 (5.19%)
occurrences (all)	5	1	4
Gastroenteritis Viral			
subjects affected / exposed	4 / 75 (5.33%)	2 / 76 (2.63%)	2 / 77 (2.60%)
occurrences (all)	4	2	3
Urinary Tract Infection			
subjects affected / exposed	6 / 75 (8.00%)	10 / 76 (13.16%)	6 / 77 (7.79%)
occurrences (all)	9	14	7
Upper Respiratory Tract Infection			
subjects affected / exposed	5 / 75 (6.67%)	6 / 76 (7.89%)	5 / 77 (6.49%)
occurrences (all)	7	7	5
Pharyngitis			
subjects affected / exposed	6 / 75 (8.00%)	3 / 76 (3.95%)	2 / 77 (2.60%)
occurrences (all)	8	3	3
Nasopharyngitis			
subjects affected / exposed	9 / 75 (12.00%)	10 / 76 (13.16%)	10 / 77 (12.99%)
occurrences (all)	10	11	12
Influenza			
subjects affected / exposed	2 / 75 (2.67%)	3 / 76 (3.95%)	6 / 77 (7.79%)
occurrences (all)	3	3	7

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 May 2021	The overall rationale for the amendment was to include additional safety criteria related to hyperlipidemia, hypogammaglobulinemia, anaphylaxis, and oral contraceptive use.
08 July 2022	The overall rationale for the amendment was to include details on serious adverse events (SAE) classification procedures regarding major cardiovascular events (MACE) adjudication.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported