Clinical trial results:
A Phase 2 Randomized, Double-Blind, Placebo-Controlled Efficacy and Safety Study of VIB7734 for the Treatment of Moderate to Severely Active Systemic Lupus Erythematosus (RECAST SLE)

Summary

EudraCT number	2020-005528-12
Trial protocol	ES
Global end of trial date	09 June 2023

Results information

Result version number	v1 (current)
This version publication date	05 June 2024
First version publication date	05 June 2024

Trial information

Trial identification

Sponsor protocol code	VIB7734.P2.S1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04925934
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, United States,
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.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	09 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to evaluate the effect of daxdilimab compared to placebo in reducing SLE disease activity at week 48 in participants treated with standard-of-care therapy.

Protection of trial subjects:

The final trial protocol and informed consent form (ICF) received written approval from an Institutional Review Board (IRB) or Independent Ethics Committee (IEC) before participant enrollment. The Investigator informed the IRB/IEC of any protocol amendments and obtained their approval, except in urgent safety cases. All advertising for participant recruitment was approved by the IRB/IEC.

The protocol underwent IRB/IEC re-approval upon each amendment and annually as per local regulations. The Investigator ensured compliance with IRB/IEC requirements and provided reports, including serious adverse drug reactions, to the IRB/IEC. The Sponsor facilitated this process.

The trial adhered to International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)/Good Clinical Practice (GCP) standards, regulatory requirements, and the Sponsor's ethical policies.

The Investigator obtained written informed consent from participants before trial commencement. Consent documentation complied with regulations and ICH E6(R2). Participants were informed of record review by relevant parties and given the opportunity to ask questions. Consent allowed for record access for at least 25 years.

The Investigator retained the original signed and dated ICF, with a copy given to the participant. The Sponsor reserved the right to delay trial initiation at sites not meeting consent document standards.

An external Safety Data Monitoring Committee (SDMC) oversaw participant safety and trial integrity by reviewing accumulating safety data. It provided recommendations to the Sponsor regarding trial conduct and participant management. The SDMC members were independent of the Sponsor and any collaborating organizations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 May 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: 34
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Greece: 4
Country: Number of subjects enrolled	India: 20

Country: Number of subjects enrolled	Mexico: 39
Country: Number of subjects enrolled	Poland: 32
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	Serbia: 19
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	Ukraine: 7
Country: Number of subjects enrolled	United States: 46
Worldwide total number of subjects	214
EEA total number of subjects	38

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)	205
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants with systemic lupus erythematosus (SLE) were enrolled at 68 sites in the United States, Argentina, Greece, India, Mexico, Poland, Serbia, Spain, Taiwan, Ukraine and Russia between May 2021 and June 2023.

Pre-assignment

Screening details:

Participants were randomized to take daxdilimab 200 mg Q4W subcutaneously (SC), daxdilimab 200 mg Q12W SC (plus 200 mg at Week 4) or placebo. Randomization was stratified by SLE Disease Activity Index 2000 (SLEDAI-2K) score at screening (≥ 10 or < 10) and prednisone or equivalent oral glucocorticoid dose at baseline (≥ 10 mg/day or < 10 mg/day).

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 were randomized to receive matching placebo Q4W SC for a treatment period up to 48 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:

SC Q4W

Arm title	Daxdilimab 200 mg Q4W

Arm description:

Participants were randomized to receive daxdilimab 200 mg Q4W for a treatment period up to 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Daxdilimab
Investigational medicinal product code	
Other name	VIB7734
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

200 mg SC Q4W

Arm title	Daxdilimab 200 mg Q12W

Arm description:

Participants were randomized to receive daxdilimab 200 mg Q12W (with an additional 200 mg SC dose at Week 4) for a treatment period up to 48 weeks.

Arm type	Experimental

Investigational medicinal product name	Daxdilimab
Investigational medicinal product code	
Other name	VIB7734
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

200 mg SC Q12W, with an additional 200 mg SC dose at Week 4

Number of subjects in period 1	Placebo	Daxdilimab 200 mg Q4W	Daxdilimab 200 mg Q12W
Started	71	72	71
Completed	51	61	57
Not completed	20	11	14
Consent withdrawn by subject	8	5	9
Adverse Event	1	-	-
Other	2	2	2
Death	-	1	-
Eastern European Conflict	7	3	2
Lost to follow-up	2	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants were randomized to receive matching placebo Q4W SC for a treatment period up to 48 weeks.	
Reporting group title	Daxdilimab 200 mg Q4W
Reporting group description:	
Participants were randomized to receive daxdilimab 200 mg Q4W for a treatment period up to 48 weeks.	
Reporting group title	Daxdilimab 200 mg Q12W
Reporting group description:	
Participants were randomized to receive daxdilimab 200 mg Q12W (with an additional 200 mg SC dose at Week 4) for a treatment period up to 48 weeks.	

Reporting group values	Placebo	Daxdilimab 200 mg Q4W	Daxdilimab 200 mg Q12W
Number of subjects	71	72	71
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	41.0	44.5	45.3
standard deviation	± 11.0	± 13.1	± 11.6
Gender Categorical Units: Subjects			
Female	67	67	66
Male	4	5	5
Race (NIH/OMB) Units: Subjects			
American Indian or Alaskan Native	2	2	0
Asian	9	7	10
Black or African American	4	8	6
White	54	49	51
Other	1	6	4
Multiple categories checked	1	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	25	27	27
Not Hispanic or Latino	46	45	44
Number of Participants Within Each OGC Stratification Dose Level			
OGC dose represents the baseline dose of prednisone or any equivalent corticosteroids.			
Units: Subjects			
< 10 mg/day	36	35	36
≥ 10 mg/day	35	37	35
SLEDAI-2K Score			
The SLEDAI-2K assessment consists of 24 lupus-related items. It is a weighted instrument, in which descriptors are multiplied by an organ's "weight". For example, renal descriptors are multiplied by 4 and CNS descriptors by 8; these weighted organ manifestations are totalled into the final score. The scores			

range from 0 to 105, with higher scores indicating more severe disease activity.			
Units: Score			
arithmetic mean	9.9	10.6	10.1
standard deviation	± 2.8	± 4.0	± 2.9
Physician Global Assessment (PGA) Score			
The PGA takes into account various clinical factors, including the participant’s symptoms, physical examination findings, laboratory results, and the physician's judgment. The PGA is scored with a range 0 to 3 where higher scores indicate greater disease activity and severity.			
Units: Score			
arithmetic mean	1.89	1.96	1.90
standard deviation	± 0.37	± 0.32	± 0.41
British Isles Lupus Assessment Group (BILAG)-2004 Score			
The BILAG-2004 Index assesses lupus disease activity across various organ systems. Each organ system is graded from A (severe disease activity requiring urgent treatment) to E (system never involved).			
Units: Score			
arithmetic mean	19.2	19.5	19.8
standard deviation	± 4.7	± 4.6	± 5.5

Reporting group values	Total		
Number of subjects	214		
Age Categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical			
Units: Subjects			
Female	200		
Male	14		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaskan Native	4		
Asian	26		
Black or African American	18		
White	154		
Other	11		
Multiple categories checked	1		
Ethnicity			
Units: Subjects			
Hispanic or Latino	79		
Not Hispanic or Latino	135		
Number of Participants Within Each OGC Stratification Dose Level			
OGC dose represents the baseline dose of prednisone or any equivalent corticosteroids.			
Units: Subjects			
< 10 mg/day	107		
≥ 10 mg/day	107		

SLEDAI-2K Score			
The SLEDAI-2K assessment consists of 24 lupus-related items. It is a weighted instrument, in which descriptors are multiplied by an organ's "weight". For example, renal descriptors are multiplied by 4 and CNS descriptors by 8; these weighted organ manifestations are totalled into the final score. The scores range from 0 to 105, with higher scores indicating more severe disease activity.			
Units: Score arithmetic mean standard deviation	- 		
Physician Global Assessment (PGA) Score			
The PGA takes into account various clinical factors, including the participant's symptoms, physical examination findings, laboratory results, and the physician's judgment. The PGA is scored with a range 0 to 3 where higher scores indicate greater disease activity and severity.			
Units: Score arithmetic mean standard deviation	- 		
British Isles Lupus Assessment Group (BILAG)-2004 Score			
The BILAG-2004 Index assesses lupus disease activity across various organ systems. Each organ system is graded from A (severe disease activity requiring urgent treatment) to E (system never involved).			
Units: Score arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants were randomized to receive matching placebo Q4W SC for a treatment period up to 48 weeks.	
Reporting group title	Daxdilimab 200 mg Q4W
Reporting group description:	
Participants were randomized to receive daxdilimab 200 mg Q4W for a treatment period up to 48 weeks.	
Reporting group title	Daxdilimab 200 mg Q12W
Reporting group description:	
Participants were randomized to receive daxdilimab 200 mg Q12W (with an additional 200 mg SC dose at Week 4) for a treatment period up to 48 weeks.	

Primary: Number of Participants Achieving a BILAG-2004 Index-based Combined Lupus Assessment (BICLA) Response and an OGC Dose ≤ 7.5 mg/day and ≤ Baseline Dose of Prednisone or Equivalent at Week 48

End point title	Number of Participants Achieving a BILAG-2004 Index-based Combined Lupus Assessment (BICLA) Response and an OGC Dose ≤ 7.5 mg/day and ≤ Baseline Dose of Prednisone or Equivalent at Week 48
End point description:	
A BICLA response required improvement in all domains affected at baseline, assessed by the BILAG 2004, no worsening of other BILAG 2004 domains, no worsening of SLEDAI2K or PGA scores compared with baseline, no use of restricted medications beyond the protocol-allowed threshold, and no discontinuation of IP.	
End point type	Primary
End point timeframe:	
Week 48	

End point values	Placebo	Daxdilimab 200 mg Q4W	Daxdilimab 200 mg Q12W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	64	69	69	
Units: Participants				
Week 48	25	29	27	

Statistical analyses

Statistical analysis title	BICLA response at Week 48
Statistical analysis description:	
Adjusted response rate, rate difference and p-value are from logistic regression analysis with treatment and randomization stratification factors in the model.	
Comparison groups	Placebo v Daxdilimab 200 mg Q12W

Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9942
Method	Regression, Logistic
Parameter estimate	Rate Difference
Point estimate	-0.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-14.2
upper limit	14.1

Statistical analysis title	BICLA response at Week 48

Statistical analysis description:

Adjusted response rate, rate difference and p-value are from logistic regression analysis with treatment and randomization stratification factors in the model.

Comparison groups	Placebo v Daxdilimab 200 mg Q4W
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.7474
Method	Regression, Logistic
Parameter estimate	Rate Difference
Point estimate	2.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-11.4
upper limit	17

Notes:

[1] - daxdilimab 200 mg Q4W versus placebo

Secondary: Number of Participants With a Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity (CLASI-A) Score ≥ 10 at Baseline Achieving ≥ 50% Reduction From Baseline in CLASI-A Score at Week 12

End point title	Number of Participants With a Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity (CLASI-A) Score ≥ 10 at Baseline Achieving ≥ 50% Reduction From Baseline in CLASI-A Score at Week 12

End point description:

CLASI-A evaluates erythema (0-3 [higher scores indicate more severe redness]), scale/hypertrophy (0-2 [higher scores indicate more extensive scaling/thickening]), mucous membrane lesions (0 [absent] or 1 [present]), recent hair loss (0 [absent] or 1 [present]), and non-scarring alopecia (0-3 [(higher scores indicate more extensive hair loss without scarring]) at 13 anatomical sites on the skin. Total score is calculated by summing scores across all anatomical locations for each parameter. Higher total scores indicate greater disease activity and severity in SLE. Reduction of 50% in CLASI-A score was defined by meeting all following conditions: 1) A ≥ 50% reduction of CLASI-A score at Week 12 as compared to baseline. 2) No use of restricted medications beyond protocol-allowed threshold before assessment. 3) No discontinuation IP. FAS: included all randomized participants who received any dose of IP. Only participants with a CLASI-A score ≥ 10 at baseline were included in the analysis.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	Daxdilimab 200 mg Q4W	Daxdilimab 200 mg Q12W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	10	14	
Units: Participants				
Week 12	1	4	5	

Statistical analyses

Statistical analysis title	CLASI-A score reduction at Week 12

Statistical analysis description:

Adjusted response rate, rate difference and p-value are from logistic regression analysis with treatment, randomization stratification factors and Baseline CLASI-A score in the model.

Comparison groups	Placebo v Daxdilimab 200 mg Q12W
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2873
Method	Regression, Logistic
Parameter estimate	Rate Difference
Point estimate	24.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.5
upper limit	55.8

Statistical analysis title	CLASI-A score reduction at Week 12

Statistical analysis description:

Adjusted response rate, rate difference and p-value are from logistic regression analysis with treatment, randomization stratification factors and Baseline CLASI-A score in the model.

Comparison groups	Placebo v Daxdilimab 200 mg Q4W
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1626
Method	Regression, Logistic
Parameter estimate	Rate Difference
Point estimate	37.2

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.3
upper limit	74.7

Secondary: Number of Participants Achieving an SLE Responder Index (SRI)-4 Response and an OGC Dose ≤ 7.5 mg/day and ≤ Baseline Dose of Prednisone or Equivalent at Week 48

End point title	Number of Participants Achieving an SLE Responder Index (SRI)-4 Response and an OGC Dose ≤ 7.5 mg/day and ≤ Baseline Dose of Prednisone or Equivalent at Week 48

End point description:

The SRI-4 measures reduction in SLE disease activity and it is a composite measure that includes the SLEDAI-2K, BILAG-2004, and PGA. SRI responder was defined as meeting all of the following criteria: 1) Reduction of ≥4 points from baseline in SLEDAI-2K score; 2) no new BILAG A or no more than 1 new BILAG B disease activity scores and 3) no worsening (defined as an increase of ≥0.3 points [0-3 scale] from baseline) in the PGA.

End point type	Secondary

End point timeframe:

Week 48

End point values	Placebo	Daxdilimab 200 mg Q4W	Daxdilimab 200 mg Q12W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	64	69	69	
Units: Participants				
Week 48	26	34	30	

Statistical analyses

Statistical analysis title	SRI-4 response at Week 48

Statistical analysis description:

Adjusted response rate, rate difference and p-value are from logistic regression analysis with treatment and randomization stratification factors in the model.

Comparison groups	Placebo v Daxdilimab 200 mg Q12W
Number of subjects included in analysis	133
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.7364
Method	Regression, Logistic
Parameter estimate	Rate Difference
Point estimate	2.9

Confidence interval	
level	90 %
sides	2-sided
lower limit	-11.2
upper limit	17

Statistical analysis title	SRI-4 response at Week 48

Statistical analysis description:

Adjusted response rate, rate difference and p-value are from logistic regression analysis with treatment and randomization stratification factors in the model.

Comparison groups	Placebo v Daxdilimab 200 mg Q4W
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.322
Method	Regression, Logistic
Parameter estimate	Rate Difference
Point estimate	8.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.6
upper limit	22.7

Secondary: Number of Participants with an OGC Dose ≥ 10 mg/day of Prednisone or Equivalent at Baseline Who Maintained an OGC Dose ≤ 7.5 mg/day From Week 36 Through Week 48

End point title	Number of Participants with an OGC Dose ≥ 10 mg/day of Prednisone or Equivalent at Baseline Who Maintained an OGC Dose ≤ 7.5 mg/day From Week 36 Through Week 48

End point description:

Maintenance of OGC reduction from Week 36 to Week 48 was defined as meeting all the following criteria:
1) Achieved an OGC dose of ≤ 7.5 mg/day prednisone or equivalent at Week 36.
2) Maintained an OGC dose of ≤ 7.5 mg/day from Week 36 through Week 48.
3) No use of restricted medications beyond the protocol-allowed threshold before assessment.
4) No discontinuation of IP before assessment.
FAS: included all randomized participants who received any dose of IP. Participants were analyzed according to the treatment randomized. Data excludes participants from Russia and Ukraine sites. Only participants with an OGC dose ≥ 10 mg/day of prednisone or equivalent at baseline were included in the analysis.

End point type	Secondary

End point timeframe:

Week 36 to Week 48

End point values	Placebo	Daxdilimab 200 mg Q4W	Daxdilimab 200 mg Q12W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	34	34	
Units: Participants	20	27	26	

Statistical analyses

Statistical analysis title	Maintenance of OGC reduction Weeks 36 - 48

Statistical analysis description:

Adjusted response rate, rate difference and p-value are from logistic regression analysis with treatment, stratification factors (SLEDAI-2K only) and Baseline OGC dose included in the model.

Comparison groups	Placebo v Daxdilimab 200 mg Q4W
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2805
Method	Regression, Logistic
Parameter estimate	Rate Difference
Point estimate	11.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.1
upper limit	29.4

Statistical analysis title	Maintenance of OGC reduction Weeks 36 - 48

Statistical analysis description:

Adjusted response rate, rate difference and p-value are from logistic regression analysis with treatment, stratification factors (SLEDAI-2K only) and Baseline OGC dose included in the model.

Comparison groups	Placebo v Daxdilimab 200 mg Q12W
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3926
Method	Regression, Logistic
Parameter estimate	Rate Difference
Point estimate	9.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.6
upper limit	27.3

Secondary: Number of Participants Achieving Lupus Low Disease Activity State

(LLDAS) at Week 48	
End point title	Number of Participants Achieving Lupus Low Disease Activity State (LLDAS) at Week 48

End point description:

LLDAS was defined as meeting all the following:
1) SLEDAI-2K ≤ 4, with no activity in major organ systems (renal, central nervous system, cardiopulmonary, vasculitis, fever) and no hemolytic anemia or gastrointestinal activity measured as maintaining a D (no disease activity but suggests the system had previously been affected) or E (no current or previous disease activity) score in BILAG Gastrointestinal Body System
2) No new lupus disease activity compared with the previous
3) Physician's Global Assessment of Disease Activity ≤ 1 on a 3-point visual analog scale from no disease activity to severe disease activity
4) A current prednisolone (or equivalent) dose ≤ 7.5 mg daily
5) Well-tolerated standard maintenance doses of immunosuppressive drugs and approved biological agents
FAS: included all randomized participants who received any dose of IP. Participants were analyzed according to the treatment randomized.

End point type	Secondary

End point timeframe:

Week 48

End point values	Placebo	Daxdilimab 200 mg Q4W	Daxdilimab 200 mg Q12W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	64	69	69	
Units: Participants				
Week 48	11	23	15	

Statistical analyses

Statistical analysis title	Achieving LLDAS at Week 48

Statistical analysis description:

Adjusted response rate, rate difference and p-value are from logistic regression analysis with treatment and randomization stratification factors in the model.

Comparison groups	Placebo v Daxdilimab 200 mg Q12W
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4939
Method	Regression, Logistic
Parameter estimate	Rate Difference
Point estimate	4.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.7
upper limit	16.4

Statistical analysis title	Achieving LLDAS at Week 48

Statistical analysis description:

Adjusted response rate, rate difference and p-value are from logistic regression analysis with treatment and randomization stratification factors in the model.

Comparison groups	Placebo v Daxdilimab 200 mg Q4W
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.037
Method	Regression, Logistic
Parameter estimate	Rate Difference
Point estimate	16.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	4
upper limit	29

Secondary: Serum Concentration of Daxdilimab

End point title	Serum Concentration of Daxdilimab[2]

End point description:

End point type	Secondary

End point timeframe:

Baseline, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No additional statistical analysis was pre-specified for this endpoint.

End point values	Daxdilimab 200 mg Q4W	Daxdilimab 200 mg Q12W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	71		
Units: ug/mL				
arithmetic mean (standard deviation)				
Baseline (N = 72, 71)	0.011 (± 0.026)	0.008 (± 0.004)		
Week 4 (N = 71, 71)	3.319 (± 1.972)	3.301 (± 1.718)		
Week 8 (N = 72, 71)	4.714 (± 3.079)	4.643 (± 2.708)		
Week 12 (N = 70, 70)	5.344 (± 3.624)	1.372 (± 1.189)		
Week 16 (N = 68, 65)	5.035 (± 3.377)	4.268 (± 2.720)		
Week 20 (N = 66, 64)	5.884 (± 4.451)	1.239 (± 1.097)		
Week 24 (N = 63, 62)	5.539 (± 4.224)	0.530 (± 0.922)		

Week 28 (N = 65, 61)	4.855 (± 3.743)	3.590 (± 2.522)		
Week 32 (N = 65, 61)	4.951 (± 4.047)	1.096 (± 1.151)		
Week 36 (N = 63, 59)	5.321 (± 4.309)	0.366 (± 0.471)		
Week 40 (N = 65, 59)	4.652 (± 3.426)	3.439 (± 2.534)		
Week 44 (N = 64, 59)	4.908 (± 3.780)	1.115 (± 1.378)		
Week 48 (N = 60, 58)	5.543 (± 4.637)	0.406 (± 0.585)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-drug Antibodies (ADA) to Daxdilimab

End point title	Number of Participants with Anti-drug Antibodies (ADA) to Daxdilimab

End point description:

A baseline ADA-positive participant was defined as a participant who had an ADA positive sample at baseline. ADA incidence is the number of the participants ADA positive post-Baseline only or who boosted their preexisting ADA (≥ 4 × Baseline level) during the trial. Persistent positive was defined as ADA positive at ≥ 2 post-Baseline assessments (with ≥ 16 weeks between first and last positive) or positive at last post-Baseline assessment. Transient positive was defined as ADA post-Baseline positive but did not fulfill the criteria of persistent positive. Safety analysis set (SAS): included all participants who received any dose of IP. Participants were analyzed according to the treatment that they received.

End point type	Secondary

End point timeframe:

Baseline to Week 56

End point values	Placebo	Daxdilimab 200 mg Q4W	Daxdilimab 200 mg Q12W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	72	71	
Units: Participants				
ADA not detected (negative) on trial	47	59	56	
ADA incidence	14	6	6	
Boosted ADA (≥ 4 × Baseline level)	1	2	2	
ADA detected (positive) on trial: ADA prevalence	24	13	15	
Only Baseline positive	1	5	5	
Only post-Baseline positive	13	4	4	
Both Baseline and post-Baseline positive	10	4	6	
Persistent positive	19	8	8	
Transient positive	4	0	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Plasmacytoid Dendritic Cell (pDCs) Expression in Blood

End point title	Change From Baseline in Plasmacytoid Dendritic Cell (pDCs) Expression in Blood

End point description:

End point type	Secondary

End point timeframe:

Baseline, Week 4, Week 8, Week 12, Week 20, Week 24, Week 32, Week 36, Week 44, Week 48, Week 52, Week 56

End point values	Placebo	Daxdilimab 200 mg Q4W	Daxdilimab 200 mg Q12W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	43	48	46	
Units: cells/uL				
arithmetic mean (standard deviation)				
Baseline (N = 43, 48, 46)	2.5068 (± 1.8486)	2.2960 (± 1.7457)	1.9195 (± 1.1990)	
Week 4 (N = 33, 42, 41)	-0.2324 (± 1.8194)	-1.4240 (± 1.9493)	-1.2903 (± 1.2201)	
Week 8 (N = 32, 43, 38)	-0.4608 (± 1.4125)	-1.5194 (± 1.7555)	-1.1486 (± 1.2090)	
Week 12 (N = 33, 42, 39)	0.0275 (± 1.7580)	-1.5164 (± 1.8180)	-1.1134 (± 1.5290)	
Week 20 (N =32, 43, 35)	285.1519 (± 1613.566)	-1.5131 (± 1.6837)	-1.0320 (± 1.1063)	
Week 24 (N = 30, 40, 40)	-0.3911 (± 1.7344)	-1.5974 (± 1.7705)	-0.5507 (± 1.3090)	
Week 32 (N = 26, 40, 38)	0.3513 (± 1.7855)	-1.3367 (± 1.5678)	-0.8496 (± 1.2403)	
Week 36 (N = 26, 37, 33)	-0.1274 (± 1.6962)	-1.4614 (± 1.7634)	-0.9131 (± 0.9845)	
Week 44 (N = 28, 39, 33)	-0.3194 (± 1.6347)	-1.6540 (± 1.6184)	-1.1322 (± 1.3782)	
Week 48 (N = 28, 36, 36)	0.1973 (± 2.4112)	-1.4608 (± 1.5647)	-0.7964 (± 1.0055)	
Week 52 (N = 3, 3, 7)	0.1483 (± 3.7955)	-0.4353 (± 0.5127)	0.0149 (± 0.7999)	
Week 56 (N = 3, 3, 5)	-2.0823 (± 3.9807)	-2.3137 (± 3.2514)	-0.7056 (± 0.6729)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Participants who Experienced Treatment-emergent Adverse Events (TEAEs)

End point description:

An adverse event (AE) is any untoward medical occurrence associated with the use of an intervention in humans whether or not it is considered intervention-related. TEAEs are AEs that started on or after the first dose of IP. An AE was considered serious (SAE) if it resulted in any of the following outcomes: death, a life-threatening AE, inpatient hospitalization or prolonged existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, a congenital abnormality/birth defect, or an important medical event. AE severity was rated according to the Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0: grade 1 (mild), grade 2 (moderate), grade 3 (severe), grade 4 (life-threatening), grade 5 (death). SAS: included all participants who received any dose of IP. Participants were analyzed according to the treatment that they received.

End point type	Secondary

End point timeframe:

Up to Week 56

End point values	Placebo	Daxdilimab 200 mg Q4W	Daxdilimab 200 mg Q12W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	72	71	
Units: Participants				
TEAEs	49	49	58	
Treatment-related TEAEs	10	17	17	
AEs Grade 3 or higher	5	8	9	
SAEs	8	9	9	
Treatment-related SAEs	0	1	0	
AEs Resulting in Death	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced AEs of special interest (AESI)

End point title	Number of Participants who Experienced AEs of special interest (AESI)

End point description:

An AESI is an AE of scientific and medical interest specific to understanding of the IP and may require close monitoring and collection of additional information by the Investigator. AESIs for this study included:
a. Hypersensitivity reaction, including anaphylaxis.
b. Severe (Grade 3 or higher) viral infections/reactivations.
c. Opportunistic infection.
d. Malignancy (except non-melanoma skin cancer).
SAS: included all participants who received any dose of IP. Participants were analyzed according to the treatment that they received.

End point type	Secondary

End point timeframe:

Up to Week 56

End point values	Placebo	Daxdilimab 200 mg Q4W	Daxdilimab 200 mg Q12W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	72	71	
Units: Participants				
Hypersensitivity Reaction Including Anaphylaxis	1	0	1	
Opportunistic infection	1	1	1	
Viral infection/Reactivation	10	6	7	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 56 weeks

Adverse event reporting additional description:

SAS: included all participants who received any dose of IP. Participants were analyzed according to the treatment that they received. All-cause mortality is reported for all participants enrolled/randomized in the study. Serious adverse events and other adverse events are reported for all participants who received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants were randomized to receive matching placebo Q4W SC for a treatment period up to 48 weeks.

Reporting group title	Daxdilimab 200mg Q12W

Reporting group description:

Participants were randomized to receive daxdilimab 200 mg Q12W (with an additional 200 mg SC dose at Week 4) for a treatment period up to 48 weeks.

Reporting group title	Daxdilimab 200mg Q4W

Reporting group description:

Participants were randomized to receive daxdilimab 200 mg Q4W for a treatment period up to 48 weeks.

Serious adverse events	Placebo	Daxdilimab 200mg Q12W	Daxdilimab 200mg Q4W
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 71 (11.27%)	9 / 71 (12.68%)	9 / 72 (12.50%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Vascular disorders			
Peripheral artery occlusion			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Hydrosalpinx			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 72 (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

Uterine polyp			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Abortion induced incomplete			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 72 (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
Congenital, familial and genetic disorders			
Huntington's disease			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 72 (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
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Angina pectoris			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			

subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 72 (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
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 72 (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			
Iron deficiency anaemia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 72 (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
Gastrointestinal disorders			
Hiatus hernia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 72 (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
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 72 (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
Abdominal hernia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 72 (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

Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 72 (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
Musculoskeletal and connective tissue disorders			
Fibromyalgia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 72 (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
Intervertebral disc protrusion			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 72 (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
Osteoarthritis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 72 (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	1 / 71 (1.41%)	0 / 71 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	2 / 71 (2.82%)	0 / 71 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			

subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 72 (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

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

Non-serious adverse events	Placebo	Daxdilimab 200mg Q12W	Daxdilimab 200mg Q4W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 71 (23.94%)	29 / 71 (40.85%)	30 / 72 (41.67%)
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	4 / 72 (5.56%)
occurrences (all)	0	0	4
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 71 (7.04%)	1 / 71 (1.41%)	3 / 72 (4.17%)
occurrences (all)	5	1	3
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 71 (1.41%)	2 / 71 (2.82%)	4 / 72 (5.56%)
occurrences (all)	1	2	4
Dyspepsia			
subjects affected / exposed	1 / 71 (1.41%)	4 / 71 (5.63%)	0 / 72 (0.00%)
occurrences (all)	1	4	0
Infections and infestations			
COVID-19			

subjects affected / exposed	9 / 71 (12.68%)	9 / 71 (12.68%)	10 / 72 (13.89%)
occurrences (all)	10	10	10
Influenza			
subjects affected / exposed	0 / 71 (0.00%)	2 / 71 (2.82%)	4 / 72 (5.56%)
occurrences (all)	0	2	4
Sinusitis			
subjects affected / exposed	1 / 71 (1.41%)	2 / 71 (2.82%)	4 / 72 (5.56%)
occurrences (all)	1	2	4
Nasopharyngitis			
subjects affected / exposed	4 / 71 (5.63%)	2 / 71 (2.82%)	3 / 72 (4.17%)
occurrences (all)	5	3	3
Urinary tract infection			
subjects affected / exposed	4 / 71 (5.63%)	8 / 71 (11.27%)	7 / 72 (9.72%)
occurrences (all)	4	12	7
Upper respiratory tract infection bacterial			
subjects affected / exposed	2 / 71 (2.82%)	4 / 71 (5.63%)	1 / 72 (1.39%)
occurrences (all)	3	4	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 February 2022	• Clarified, in inclusion criterion 8, that women of childbearing potential were to have negative serum pregnancy test at Screening and a negative urine pregnancy test at randomization and must refrain from egg retrieval and donation while receiving IP. • Clarified, in inclusion criterion 8, that if a change in birth control methods occurred during the trial the participant must employ a barrier method in addition to the highly effective method of contraception for at least 2 months, unless the participant was changing the method to complete abstinence. • Updated the definition of women of childbearing potential throughout the protocol. • Clarified, in exclusion criterion 2, that the Sponsor and Central Review Committee may also review a participant's screening data and find reason not to allow participation in the trial. • Updated exclusion criterion 5 to standardize the amount of time that breastfeeding or pregnant women would be followed after receiving the last dose of IP. • Updated exclusion criterion 10 to add the mg/mmol exclusionary value as it is generally used at ex-United States sites. • Updated exclusion criterion 13 to clarify actions for indeterminate IFN-gamma release assay (IGRA) test results. • Removed the example of fever from exclusion criterion 18 as it can be a manifestation of lupus and thus possibly confusing. • Updated exclusion criterion 19 to clarify the definition of clinically significant cardiac disease. • Updated exclusion criterion 23 to include conventional anti-rheumatic doses for treatment of SLE. • Removed direct Coombs testing, as the specimen has limited stability that often does not allow testing to be performed by the central laboratory within the stability period due to courier transit time and is not needed on a routine basis.
10 February 2022	• Clarified that the Week 48 Visit was also considered an Early Termination Visit and that the Safety Follow-up Period was only for participants who completed the 48-week Treatment Period; specified that participants who permanently discontinued IP should be followed after final IP administration. • Removed PGI of Change on Day 1, as the PG of Change is designed to assess post-treatment change and, therefore, was assessed beginning with the first post-treatment visit. • Updated the 28-Joint Count section to align with the current SLEDAI-2K joint count arthritis definition. • Allowed for additional time at Week 24 for vital sign measurement, laboratory sample collection and ECG recording prior to dosing. • Clarified that tuberculosis (TB) assessments at Screening were to occur only at the central laboratory. • Clarified that if Baseline skin sample(s) were not collected (pre-dose), the subsequent visit samples should not be collected. • Clarified that if the Baseline DNA/epigenetic sample (for consenting participants) was not collected (pre-dose), the subsequent visit samples should still be collected. • Provided guidance on collection times and windows for the optional fecal microbiome sample. • Updated the Sponsor's Quality Assurance contact information for reporting product complaints. • Removed the specific gauge size from the description of IP dose preparation, as specific needles could not be supplied at certain sites. • Clarified how anti-COVID therapeutic antibody treatment was to be handled. • Clarified limitations for the permitted use of as-needed nonsteroidal anti-inflammatory drug (NSAIDs). • Clarified that AESI for viral infection and reactivation only included those that were Grade 3 or higher and all cases of opportunistic infections listed in Appendix 3 of the protocol. • Clarified that AESIs only needed to be immediately reported after randomization and updated the contact information for immediate reporting.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported