Clinical trial results:
A Randomized, Double-blind, Placebo-controlled Study of ALPN-101 in Systemic Lupus Erythematosus

Summary

EudraCT number	2020-004047-86
Trial protocol	FR PL ES HU
Global end of trial date	09 July 2024

Results information

Result version number	v2 (current)
This version publication date	30 August 2025
First version publication date	23 July 2025
Version creation reason	• Correction of full data set Update the outcome measure data.

Trial information

Trial identification

Sponsor protocol code	AIS-A03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04835441
WHO universal trial number (UTN)	-
Other trial identifiers	IND Number: 146045

Notes:

Sponsors

Sponsor organisation name	Alpine Immune Sciences, Inc.a Vertex Company
Sponsor organisation address	188 East Blaine Street, Suite 200, Seattle, WA, United States, 98102
Public contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 617-341-6777, medicalinfo@vrtx.com
Scientific contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 617-341-6777, medicalinfo@vrtx.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 October 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 July 2024
Global end of trial reached?	Yes
Global end of trial date	09 July 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of ALPN-101 compared to placebo in subjects with moderate to severe active SLE

Protection of trial subjects:

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 June 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	Poland: 9
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	United States: 58
Country: Number of subjects enrolled	Taiwan: 4
Worldwide total number of subjects	76
EEA total number of subjects	14

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)	71

From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted in subjects with active systemic lupus erythematosus (SLE) aged 18 years and older.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	ALPN-101 (Acazicolcept)

Arm description:

Subjects received a weight-based dose of 3 milligrams/kilogram (mg/kg) ALPN-101 once every 2 weeks(Q2W) up to 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Acazicolcept
Investigational medicinal product code	ALPN-101
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received ALPN-101 infusion over approximately 30 minutes

Arm title	Placebo

Arm description:

Subjects received placebo matched to ALPN-101 up to 24 weeks.

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

Dosage and administration details:

Subjects received placebo matched to ALPN-101 up to 24 weeks.

Number of subjects in period 1	ALPN-101 (Acazicolcept)	Placebo
Started	38	38
Completed	33	32
Not completed	5	6
Physician decision	4	4
Other	1	1
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	ALPN-101 (Acazicolcept)
Reporting group description:	
Subjects received a weight-based dose of 3 milligrams/kilogram (mg/kg) ALPN-101 once every 2 weeks(Q2W) up to 24 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to ALPN-101 up to 24 weeks.	

Reporting group values	ALPN-101 (Acazicolcept)	Placebo	Total
Number of subjects	38	38	76
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	48.7	47.8	
standard deviation	± 11.20	± 11.08	-
Gender categorical Units: Subjects			
Female	35	35	70
Male	3	3	6
Ethnicity Units: Subjects			
Hispanic or Latino	13	10	23
Not Hispanic or Latino	25	28	53
Unknown or Not Reported	0	0	0
Race Units: Subjects			
White	24	23	47
Black or African American	12	11	23
Other Asian	1	2	3
American Indian or Alaska Native	0	1	1
East Asian	1	0	1
Other	0	1	1

End points

End points reporting groups

Reporting group title	ALPN-101 (Acazicolcept)
Reporting group description:	
Subjects received a weight-based dose of 3 milligrams/kilogram (mg/kg) ALPN-101 once every 2 weeks(Q2W) up to 24 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to ALPN-101 up to 24 weeks.	

Primary: Safety and Tolerability as Assessed by Number of Subjects With Treatment- Emergent Adverse Events (TEAEs) andSerious Adverse Events (SAEs)

End point title	Safety and Tolerability as Assessed by Number of Subjects With Treatment- Emergent Adverse Events (TEAEs) andSerious Adverse Events (SAEs)[1]
End point description:	
Safety set included all subjects who received at least 1 dose of study drug in the treatment period.	
End point type	Primary
End point timeframe:	
Day 1 up to Safety follow-up (up to 28 weeks)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics were planned. No statistical comparisons were planned for the primary safety endpoint.

End point values	ALPN-101 (Acazicolcept)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	38		
Units: Subjects				
Subjects with TEAEs	23	24		
Subjects with SAEs	2	2		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Achieving a Systemic Lupus Erythematosus (SLE) responder index (SRI)-4

End point title	Percentage of Subjects Achieving a Systemic Lupus Erythematosus (SLE) responder index (SRI)-4

End point description:

The SRI-4 is a composite index of SLE disease improvement that consists of scores derived from the SLE Disease Activity Index 2000 (SLEDAI-2K), the British Isles Lupus Assessment Group (BILAG) 2004 Index, and the Physician’s Global Assessment (PGA). Subjects classified as responder if they met all of the following criteria: 1) ≥ 4-point reduction in the SLEDAI-2K total score; 2) no new severe disease activity or more than 1 new moderate organ score (BILAG B) compared with baseline 3) No worsening from baseline in subjects’ lupus disease activity (i.e., increase of ≥0.3 0 on a 3-point scale) in PGA.

Modified intent-to-treat population (mITT), includes all randomized subjects who received any amount of study drug and have completed at least one post-baseline disease assessment. Here "Number of subjects analysed" signifies those subjects who were evaluated for this specific endpoint.

End point type	Primary

End point timeframe:

At Day 169

End point values	ALPN-101 (Acazicolcept)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	37		
Units: percentage of subjects				
number (not applicable)	27	46		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	ALPN-101 (Acazicolcept) v Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.107
Method	Cochran-Mantel-Haenszel

Primary: Percentage of Subjects Achieving a British Isles Lupus Assessment Group-based Composite Lupus Assessment (BICLA) response

End point title	Percentage of Subjects Achieving a British Isles Lupus Assessment Group-based Composite Lupus Assessment (BICLA) response

End point description:

The BICLA is a responder index developed to measure response to therapy, and it includes scores from the BILAG,SLEDAI-2K, and Physician’s Global Assessment (PGA). BICLA response is defined as: 1) at least 1 gradation of improvement in baseline BILAG 2004 scores in all body systems with moderate disease activity at entry (e.g, all B [mild disease] scores falling to C [Stable and mild], or D [no activity]); 2) no new BILAG A or more than 1 new BILAG B scores; 3) no worsening of total SLEDAI-2K score from baseline; 4) ≤ 10% deterioration in PGA score. The PGA is measured on a 0 to 100 mm scale with score 0 to be No Disease Activity and score 100 to be the most Severe Disease Activity. mITT. Here "Number of subjects analysed" signifies those subjects who were evaluated for this specific endpoint

End point type	Primary

End point timeframe:

At Day 169

End point values	ALPN-101 (Acazicolcept)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	37		
Units: percentage of subjects				
number (not applicable)	22	32		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	ALPN-101 (Acazicolcept) v Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.308
Method	Cochran-Mantel-Haenszel

Secondary: Annualized flare rate by British Isles Lupus Assessment Group (BILAG)-2004 flare index

End point title	Annualized flare rate by British Isles Lupus Assessment Group (BILAG)-2004 flare index

End point description:

The BILAG-2004 index covers 86 item assessment across 9 organ systems. Each question is answered as 0-not present, 1-improving, 2-same, 3-worse, to 4-new. The BILAG-2004 index categorizes disease activity in each organ system into five different levels from A to E. Grade A : disease-modifying treatment, Grade B: mild, reversible problems requiring symptomatic therapy, Grade C: mild stable disease, and grade D: no disease activity, but suggests the organ system had previously been affected. Grade E: no current or previous disease activity. Higher scores indicate more severe disease activity. Annualized flare rated is defined as the number of flares observed during the treatment period divided by the flare exposure time in days multiplied by 365.25. mITT. Here "Number of subjects analysed" signifies those subjects who were evaluated for this specific endpoint. Data was planned to be reported as LS Mean and Standard Error.

End point type	Secondary

End point timeframe:

From Baseline to Day 169

End point values	ALPN-101 (Acazicolcept)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	37		
Units: Flares per person-years				
least squares mean (standard error)	3.27 (± 0.426)	2.80 (± 0.426)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v ALPN-101 (Acazicolcept)
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.442
Method	ANOVA

Secondary: Time-to-first Flare by BILAG-2004 Flare Index

End point title	Time-to-first Flare by BILAG-2004 Flare Index

End point description:

Time-to-first SLE flare is defined as the number of days from the administration of first dose to the first occurrence of flare. A flare was defined as having an adjudicated BILAG A or B score in any of the 8 organ systems during treatment. The BILAG disease activity index evaluates SLE activity in 8 organ systems, using a separate alphabetic score (A to E) assigned to each organ system defined as follows. BILAG A: Disease sufficiently active requiring disease-modifying treatment (prednisone greater than 20 mg daily or immunosuppressants); BILAG B: Disease less active than in "A", mild reversible problems requiring only symptomatic therapy such as antimalarials, NSAIDs, or prednisone less than 20mg day; BILAG C: Stable mild disease; BILAG D: System previously affected but now inactive; BILAG E: System never involved. mITT. Here "Number of subjects analysed" signifies those subjects who were evaluated for this specific endpoint.

End point type	Secondary

End point timeframe:

From Baseline to Day 169

End point values	ALPN-101 (Acazicolcept)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	37		
Units: Days				
median (confidence interval 95%)	85.0 (57.0 to 112.0)	113.0 (85.0 to 115.0)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	ALPN-101 (Acazicolcept) v Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.788
Method	Kaplan-Meier methods

Secondary: Percentage of Subjects Achieving Lupus Low Disease Activity State

(LLDAS)	
End point title	Percentage of Subjects Achieving Lupus Low Disease Activity State (LLDAS)

End point description:

The LLDAS is a composite measure designed to identify patients achieving a state of low disease activity. The LLDAS response criteria were: (1) SLEDAI-2K <=4, with no activity in major organ systems (CNS, vascular, renal, cardiorespiratory and constitutional); where "no activity" is defined as all items of SLEDAI-2K within these major organ systems equal to 0. (2) no new features of lupus disease activity compared to previous occurred visit, where the "new feature" is defined as any of the SLEDAI-2K 24 items changed from 0 to greater than 0; (3) PGA (scale 0-3), <=1; (4) current prednisolone (or equivalent) dose <=7.5 mg daily; and allowance for maintenance doses of immunosuppressive drugs and approved biological agents. mITT. Here "Number of subjects analysed" signifies those subjects who were evaluated for this specific endpoint.

End point type	Secondary

End point timeframe:

At Day 169

End point values	ALPN-101 (Acazicolcept)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	37		
Units: Percentage of subjects				
number (not applicable)	14	16		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	ALPN-101 (Acazicolcept) v Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.792
Method	Cochran-Mantel-Haenszel

Secondary: Change From Baseline in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) Total Score

End point title	Change From Baseline in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) Total Score

End point description:

SLEDAI-2K score is used to identify patients with more active disease at study enrollment. Total score is the sum of weighted scores for each organ system. For each system organ with baseline score >0, improvement in SLEDAI-2K improvement is achieved by meeting all the following criteria: • Reduction in system organ scores among subjects with baseline SLEDAI-2K scores >0 •No early discontinuation of study drug • No use of restricted medications beyond the protocol-allowed threshold before assessment SLEDAI-2K uses a weighted checklist to assign a numerical score based on the presence or absence of24 symptoms. Each symptom present is assigned between 1 and 8 points based on its usual clinical importance, yielding a total score that ranges from 0 points (no symptoms) to 105 points (presence of all defined symptoms). Baseline was defined as core study screening visit. mITT. Here "Number of subjects analysed" signifies those subjects who were evaluated for this specific endpoint.

End point type	Secondary
End point timeframe:	
From Baseline to Day 169	

End point values	ALPN-101 (Acazicolcept)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	37		
Units: score on a scale				
least squares mean (confidence interval 95%)	-2.4 (-3.3 to -1.6)	-3.0 (-3.8 to -2.2)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v ALPN-101 (Acazicolcept)
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.302
Method	Mixed models for repeated measures

Secondary: Cumulative prednisone-equivalent dose use through Day 169

End point title	Cumulative prednisone-equivalent dose use through Day 169
End point description:	
mITT. Here "Number of subjects analysed" signifies those subjects who were evaluated for this specific endpoint.	
End point type	Secondary
End point timeframe:	
From Baseline Through Day 169	

End point values	ALPN-101 (Acazicolcept)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	37		
Units: milligram (mg)				
least squares mean (standard error)	1028.28 (± 183.729)	854.59 (± 183.729)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	ALPN-101 (Acazicolcept) v Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.506
Method	ANOVA

Secondary: Percentage of Subjects Achievement of ≥ 50% Reduction In CLASI Activity Score In Subjects With Baseline CLASIActivity Score ≥ 8

End point title	Percentage of Subjects Achievement of ≥ 50% Reduction In CLASI Activity Score In Subjects With Baseline CLASIActivity Score ≥ 8

End point description:

CLASI Activity is scored based on erythema, scale/hyperkeratosis, mucous membrane involvement, acute hair loss and nonscarring alopecia. Evaluation of erythema and scale/hyperkeratosis is based on a table: rows represent anatomical areas and columns represent major clinical symptoms. The extent of involvement for each of the skin symptoms is documented for each anatomic area. The total score ranges from 0-70, with higher scores indicating more severe skin disease. 50% reduction in CLASI activity score compared to baseline was defined by meeting all of the following criteria: • Achieve ≥50% reduction of CLASI activity score at Day 169 compared to baseline. mITT. Here "Number of subjects analysed" signifies those subjects who were evaluated for this specific endpoint.

End point type	Secondary

End point timeframe:

From Baseline to Day 169

End point values	ALPN-101 (Acazicolcept)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: percentage of subjects				
number (not applicable)	30	45		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	ALPN-101 (Acazicolcept) v Placebo
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.659
Method	Fisher exact

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 up to Safety follow-up (up to 28 weeks)	
Adverse event reporting additional description:	
Safety set included all subjects who received at least 1 dose of study drug in the treatment period.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to ALPN-101 up to 24 weeks.	
Reporting group title	ALPN-101 (Acazicolcept)
Reporting group description:	
Subjects received a weight-based dose of 3 mg/kg ALPN-101 Q2W up to 24 weeks.	

Serious adverse events	Placebo	ALPN-101 (Acazicolcept)	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 38 (5.26%)	2 / 38 (5.26%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Hemoglobin Decreased			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Transient Ischemic Attack			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Mental Status Changes			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	ALPN-101 (Acazicolcept)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 38 (42.11%)	18 / 38 (47.37%)	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 38 (13.16%)	2 / 38 (5.26%)	
occurrences (all)	5	2	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 38 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Influenza Like Illness			
subjects affected / exposed	2 / 38 (5.26%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Immune system disorders			
Infusion Related Reaction			
subjects affected / exposed	0 / 38 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Aphthous Ulcer			
subjects affected / exposed	0 / 38 (0.00%)	4 / 38 (10.53%)	
occurrences (all)	0	4	
Abdominal Pain			
subjects affected / exposed	1 / 38 (2.63%)	2 / 38 (5.26%)	
occurrences (all)	1	2	
Diarrhoea			
subjects affected / exposed	0 / 38 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Food Poisoning			

subjects affected / exposed	2 / 38 (5.26%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Nasal Congestion			
subjects affected / exposed	2 / 38 (5.26%)	1 / 38 (2.63%)	
occurrences (all)	2	1	
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 38 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Infections and infestations			
Urinary Tract Infection			
subjects affected / exposed	2 / 38 (5.26%)	4 / 38 (10.53%)	
occurrences (all)	2	5	
Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 38 (5.26%)	1 / 38 (2.63%)	
occurrences (all)	2	1	
COVID-19			
subjects affected / exposed	3 / 38 (7.89%)	0 / 38 (0.00%)	
occurrences (all)	3	0	
Influenza			
subjects affected / exposed	2 / 38 (5.26%)	0 / 38 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 April 2021	Amended to increase the number of study drug doses from 6 to 12, with an associated extension in the treatment duration from 85 days (12 weeks) to 169 days (24 weeks) and in the overall study duration for each subject from 22 to 36 weeks.
29 September 2021	Amended the eligibility criteria (inclusion and exclusion) of subjects.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported